THE EFFECT OF EARLY VERSUS LATE ENTERAL FEEDING ON THE HYPERMETABOLIC RESPONSE OF THE PAEDIATRIC BURNED PATIENT

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02/02/2001

Date
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<thead>
<tr>
<th>Symbol</th>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>Admission</td>
<td></td>
</tr>
<tr>
<td>DC</td>
<td>Discharge</td>
<td></td>
</tr>
<tr>
<td>EEE</td>
<td>Estimated Energy Expenditure</td>
<td></td>
</tr>
<tr>
<td>EEF</td>
<td>Early Enteral Feeding</td>
<td></td>
</tr>
<tr>
<td>FB</td>
<td>Fire Burn</td>
<td></td>
</tr>
<tr>
<td>GH</td>
<td>Growth Hormone</td>
<td></td>
</tr>
<tr>
<td>GIT</td>
<td>Gastrointestinal Tract</td>
<td></td>
</tr>
<tr>
<td>hrs</td>
<td>Hours</td>
<td></td>
</tr>
<tr>
<td>HWB</td>
<td>Hot Water Burn</td>
<td></td>
</tr>
<tr>
<td>IC</td>
<td>Indirect Calorimetry</td>
<td></td>
</tr>
<tr>
<td>IFG 1</td>
<td>Insulin-like Growth Factor-1</td>
<td></td>
</tr>
<tr>
<td>I:G ratios</td>
<td>Insulin:Glucagon ratios</td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
<td></td>
</tr>
<tr>
<td>Kcal/kg/d</td>
<td>Kilocalories per kilogram per day</td>
<td></td>
</tr>
<tr>
<td>LEF</td>
<td>Late Enteral Feeding</td>
<td></td>
</tr>
<tr>
<td>ml</td>
<td>millilitre</td>
<td></td>
</tr>
<tr>
<td>MOF</td>
<td>Multiple Organ Failure</td>
<td></td>
</tr>
<tr>
<td>NGT</td>
<td>Nasogastric Tube</td>
<td></td>
</tr>
<tr>
<td>NJT</td>
<td>Nasojejunal Tube</td>
<td></td>
</tr>
<tr>
<td>REE</td>
<td>Resting Energy Expenditure</td>
<td></td>
</tr>
<tr>
<td>RIA</td>
<td>Radioimmunoassay</td>
<td></td>
</tr>
<tr>
<td>RDA</td>
<td>Recommended Daily Allowances</td>
<td></td>
</tr>
<tr>
<td>RQ</td>
<td>Respiratory Quotient</td>
<td></td>
</tr>
<tr>
<td>RXH</td>
<td>Red Cross Children’s Hospital</td>
<td></td>
</tr>
<tr>
<td>SAT</td>
<td>Sugar Absorption Test</td>
<td></td>
</tr>
<tr>
<td>TBSAB</td>
<td>Total Body Surface Area Burned</td>
<td></td>
</tr>
<tr>
<td>TPN</td>
<td>Total Parenteral Nutrition</td>
<td></td>
</tr>
<tr>
<td>PN</td>
<td>Parenteral Nutrition (supplemental to enteral nutrition)</td>
<td></td>
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Abstract

**Background:** Red Cross Children's Hospital treats an average of 2,000 children per annum with thermal injuries. Five hundred of these are new injuries and 60 patients have a total body surface area burn (TBSAB) that exceeds 20%. There is substantial evidence in adult burn literature that suggests that early enteral feeding (EEF) compared to initial starvation has a profound impact on the hormonal response, metabolic rate and gastrointestinal maintenance post thermal injury. However, research addressing these issues in the burned child (birth to 13 years old), are limited.

**Aim:** To compare EEF, to delayed or late enteral feeding (LEF), and to evaluate whether the practice is beneficial in paediatric burned patients.

**Criteria:** The criteria for the patients were (a) a burn less than 24 hours old and a TBSAB more than or equal to 20%, (b) an age of less than 13 years and (c) admission to the Red Cross Children’s Hospital Burns Unit.

**Objectives:** The objectives were to compare the effect of EEF and LEF on (1) the concentrations of insulin, insulin-like growth factor-1 (IGF1), glucagon, cortisol and growth hormone (GH), (2) the estimated energy expenditure (EEE) and calculated energy expenditure, (3) the respiratory quotient (RQ), (4) the intestinal permeability and (5) the clinical outcome.

**Methods:** The children were assigned to either the EEF or LEF group. Nine patients in each study group completed the study successfully, with similar median ages (4.5 yr.), body weights (14 kg) and TBSAB (30%). The EEF group was enterally fed via a nasojejunal feeding tube within a median time of 10.75 hours post burn, whereas the LEF group fasted for a median of 54 hours, after which enteral feeds were introduced. This study is unique in that enteral feeds were used as part of the resuscitation regime in the EEF group. The EEF group received their full resuscitation volumes from the enteral feed at a median time of 16 hours from initiation. Venous blood samples were taken daily between 7h00 and 8h00, before breakfast, for the hormone measurements. The REE and RQ were measured by indirect calorimetry and compared to the recommended dietary allowances (RDA), Galveston and Solomon's equations, which estimate energy requirements. Small bowel permeability was measured by the sugar-absorption-test (SAT), and expressed as lactulose: rhamnose ratios.
Results: The EEF group’s insulin concentrations were significantly higher (p=0.008) than the LEF group’s. Glucagon concentrations were not significantly different between the two treatment groups. The EEF group however, had significantly higher insulin:glucagon (I:G) ratios up until day 4 (p=0.043), and approaching significance (p=0.081) up until day 12 post burn. Blood glucose concentrations were elevated (EEF:10.3g/l, LEF:8.1g/l) on admission for both study groups, but decreased thereafter to within the normal ranges. The cortisol and IGF1 concentrations did not differ significantly between the two treatment groups and remained within the normal ranges. Growth hormone (GH) concentrations revealed that the LEF group had significantly higher (p=0.03) concentrations up until day 12. The EEE was similar in the two treatments groups. The Galveston burns equation was closer to the EEE than the Solomon’s burns equation, but the RDA compared most favourable for both study groups. There was a steady rise in the RQ of both study groups, but in the EEF group the rise occurred early and was significantly higher (p=0.03) over the first 2 days. Lactulose:rhamnose (L:R) ratios were not significantly different between the EEF and LEF groups, and decreased significantly over time (p=0.02) in both study groups. Three patients in the EEF group had clinically insignificant vomiting episodes. No pulmonary aspiration was found in either study group. Diarrhoea was experienced in 5 patients in the EEF group which settled within 2 to 4 days post burn. In the LEF group 3 children developed diarrhoea which persisted for longer than a week. No stool occult blood was found in either study group. The LEF group lost a median of 7.75% of admission body weight, which is greater than the acceptable range of 5% from admission until discharge, whereas the EEF group only lost a median of 3.01%. The percentage weight change between the two study groups did not differ significantly (p=0.1). Patients in the LEF group required antibiotic treatment for a longer period, but this did not reach significance (p=0.08). Although the LEF group spent a total of 76 days longer in hospital, the median hospital stay per patient was similar (26 days) for both study groups. The difference in hospital stay did not reach significance (p=0.39).

Conclusions: EEF after a burn seems to have an anabolic effect on metabolism as shown by significantly higher insulin concentrations and I:G ratios. The IGF1 concentrations were higher in the EEF group on certain days, but failed to reach significance. Both study groups had insulin, IGF1 and cortisol concentrations within the normal range, which contrast the subnormal concentrations documented for adult burned patients. Glucagon concentrations for both study groups remained elevated throughout the study period. This did not stimulate hyperglycaemia as expected for both study groups, but glucose concentrations were only slightly
elevated on admission and returned to within the normal range for the remainder of the study period. The GH concentrations were significantly higher in the LEF group, which is similar to results found in children exposed to acute and chronic protein and caloric deprivation or fasting. In both treatment groups the GH concentrations did not fall to the subnormal range, which also contrast with the subnormal GH concentrations found in adult burned patients. The RDA compared most favourable to the measured EEE, for both study groups. Although not statistically significant, the EEF vs. LEF group consumed more calories (p=0.7) and protein (p=0.27) over the study period. The EEF group’s weight loss was within the acceptable range, whereas that in the LEF group was not acceptable. The higher weight loss in the LEF group could be explained by either the delayed enteral feeding on admission, or the fewer calories consumed over the study period. EEF did not have any adverse effects on the small bowel permeability. Less antibiotic treatment was required in the EEF group which suggests fewer infections. The LEF group spent more days in hospital, but the median hospital days per patient failed to reach statistical significance when compared to the EEF group. However, the longer hospital stay clearly has cost implications. LEF patients had significantly lower insulin concentrations and I:G ratios, significantly higher GH concentrations, unacceptably high body weight loss, required more antibiotic treatment and had a longer hospital stay. EEF did not compromise the care in any patients. This work has shown that early enteral resuscitation is safe and could therefore be implemented in burned children that are treated in developing countries.
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Chapter 1

Background

Epidemiology and Etiology

It is estimated that approximately 400,000 people are burned annually in South Africa. An average of 2,000 pediatric burned patients per year are treated at the in- and outpatient facilities of Red Cross Children’s Hospital (RXH), Cape Town. Five hundred of these are new patients and approximately 55 to 60 of them have sustained severe burns, affecting more than or equal to (> ) 20% total body surface body area burned (TBSAB). Hot liquid accidents are responsible for 80% burn injuries, followed by 18% fire injuries, 2% chemical injuries and less than 1% electrical injuries.

Classification of burn severity

The severity of the burn injury is assessed by the age of the patient, the depth and size of the wound, the anatomic site and the accompanying nutritional status and disease. The skin does not reach adult thickness until puberty; hence the younger the child, the deeper the burn.  

The depth of the burn is classified as superficial or partial thickness (first degree), deep partial thickness (second degree) and full thickness (third degree). Superficial burns will involve the epidermis of the skin, while deep partial thickness burns will involve the epidermis and dermis of the skin. Full thickness skin burns might have destroyed structures such as sebaceous glands, subcutaneous fat cells, hair follicles, nerves, veins and arteries, lymph vessels and sweat glands. Fourth degree burns extend beyond full thickness skin damage, with muscle and/or bone involvement as well. The extent of the burn injury is expressed as a percentage of the total body surface area burned (TBSAB).

Pathophysiology

The severe burn injury has a devastating effect on all the bodily organ systems, involving both local and systemic responses. The local response at the site of the wound results in edema formation and hemodynamic instability which may lead to systemic changes in the cardiovascular-, respiratory-, renal-, immune-, gastrointestinal and metabolic systems. The size and depth of the thermal injury will determine the magnitude of the local and systemic changes.
Local response

Damage to the human skin by heat results in two types of injury: an immediate direct cellular response and a delayed response due to dermal ischemia. Three zones of injury demonstrate the response of local tissue damage: 1) The zone of coagulation which represents irreversible tissue necrosis, 2) the zone of stasis which indicates vascular injury with vascular dilatation, platelet aggregation and vascular stasis [tissue in this zone might be saved by immediate and adequate perfusion] and 3) the zone of hyperemia contains viable tissue which should heal. Most burns are a combination of superficial and deeper burns.\textsuperscript{1,2}

Oedema formation, Haemodynamic status and Fluid loss

Thermal injury to the zone of stasis and the zone of hyperemia results in increased capillary permeability. Concomitant vasodilation causes an increase in hydrostatic pressure within the capillaries. The increased hydrostatic pressure combined with the increased capillary permeability causes; loss of water, protein, and electrolytes from the circulating volume into the interstitial spaces.\textsuperscript{3}

Oedema develops when the rate at which fluid leaks out of the micro-vascular vessels, exceeds the flow in the lymph vessels draining that tissue mass. The loss of fluid into the interstitial space is rapid and can double within the first hour after the burn injury.\textsuperscript{4} Oedema is not only confined to the burned area, but accumulation of oedema fluid beneath and around the wound can reach extreme proportions until the extravasation of fluid is limited by tissue tension. Without the protection of the skin the fluid loss can be as high as 4.4 millilitre per kilogram per hour (mL/kg/h) in burns involving more than 30% TBSA.\textsuperscript{3,5} A decrease in cellular transmembrane potential is found in skeletal muscle away from the site of injury, and is associated with an increase in intracellular water and sodium. The amount of oedema formation in burned skin depends on the type and extent of injury. Severe burn wound oedema and fluid loss could eventually lead to ineffective circulating fluid volume, hypovolemia and burn shock.\textsuperscript{3}

Systemic responses

Cardiovascular Changes

Decreased plasma and circulating volume leads to a decreased cardiac output and an increased systemic vascular resistance resulting in reduced peripheral blood flow.\textsuperscript{6} The decrease in cardiac output is also attributed to a circulating myocardial depressant factor. Adequate fluid resuscitation should restore the cardiac output to normal levels within 24 to 48 hours post burn. Inadequate or no fluid replacement may have detrimental consequences such as organ dysfunction and ultimate death. Some children are prone to congestive heart failure and pulmonary oedema. In addition,
peripheral circulation in infants is less efficient and more labile, making fluid management difficult.  

Pulmonary Complications

Although the respiratory tree is well protected, respiratory burns (tracheobronchial damage) can result from the inhalation of steam or toxic chemicals produced during combustion and enclosed room fires. These could result in respiratory distress, which is characterized by bronchospasm, necrotising tracheo-bronchitis and inflammation of the lower respiratory tree. Bacterial bronchopneumonia could develop secondary to; airway injury, contamination from intubation, or acquired through haematogenous (septic burn wound) spread of bacteria. Additional fluid may be required for adequate resuscitation. However, the fluid balance should be monitored regularly, since pulmonary oedema could develop from fluid overload as a result of capillary damage and the leakage of fluid into the interstitial spaces of the lung. Pulmonary complications remain the leading cause of death following thermal injury.

Renal System

The renal system is one of the regional circulations compromised during hypovolemia. Loss of fluid from the intravascular compartment causes renal vasoconstriction that in turn leads to reduced renal plasma flow and depressed glomerular filtration rate. Electrical or extensive burns may cause haemolysis with haemoglobinuria, myoglobinuria and renal failure. Blood urea nitrogen and creatinine levels are elevated as a result of tissue breakdown, decreased circulating volume and oliguria. The urine output in the paediatric burn patient should be between 0.5 to 1.0 milliliter per kilogram per hour (ml/kg/h) for adequate glomerular filtration rate.

Susceptibility of infection and wound sepsis

The burnt patient is prone to micro-organism invasion due to impaired local defence mechanisms. The loss of the outer skin barrier, the presence of dead tissue and exudate, occlusion of blood flow that impairs both the humoral and cellular defence mechanisms, as well as decreased phagocyte and lymphocyte function, all contribute to the fact that the burned patient has become a high risk for nosocomial infection. Eighty percent of the total acquired infections are endogenous in origin, with gram positive organisms predominating during the first week. The burn wound harbours 70% gram positive organisms of an exogenous source and 30% of the organisms are from an endogenous source, predominately the GIT. The reduction of infection will be influenced by; the burns unit's wound care and dressing methods, aggressive excision and grafting policy, effective topical antimicrobial treatment and choice of antibiotics.
Hypometabolic Response

Increased metabolic rates in severe burns patients are often encountered, and energy needs may approach 50% to 100% above normal. Gluconeogenesis, severe protein breakdown and muscle wasting, as well as lipolysis are common characteristics post thermal injury. Bodily stores of energy are rapidly depleted unless sufficient replacement is provided and losses are reduced. It could be postulated that the burned child's metabolic rate might react differently to thermal injury to that of the burned adult, especially since children generally have a higher energy expenditure and still need to grow.

Energy requirements can be determined by the measurement of the actual resting energy expenditure (REE) by either indirect calorimetry (IC), or the doubly labeled water technique. Adding an additional activity factor of 20 to 30% to the measured REE, seems to be the most accurate method of predicting the estimated energy expenditure (EEE) in burned children.

Children with burn injuries typically exhibit an elevated body temperature, even in the absence of infection. Heat is lost as a result of the energy-consuming process of evaporation of water from the damaged skin surface. Infants and children are especially vulnerable because of the large surface area relative to metabolically active tissue.

Afferent stimuli from the burn wound i.e. pain and the release of cytokines, tumour necrosis factor and thromboxane, stimulate the hypothalamus to reset the core temperature through catecholamine release from the adrenal medulla and other sympathetic ganglia. In addition, catabolic hormone release i.e. glucagon and cortisol are increased, whereas anabolic hormone release i.e. insulin and insulin-like growth factor-1, are decreased.

However, limited data is available on the paediatric patient's (birth to 13 years) hormonal response post severe trauma. Deshpande et. al. and Sedowofia et. al. agree that the stress hormonal response of the paediatric patient cannot be compared to that of the adult patient. Paediatric patients post surgery demonstrated a stress hormonal response of a greater magnitude than that of the adult, but of a shorter duration. There was a remarkable consistency in its pattern for the 1 to 10 year old age group. Similarities were found in the stress hormonal levels of the paediatric burned patient to that of the surgical patient, but thermal injury seems to have a unique hormonal response concerning the duration of elevation.

A combination of adequate maintenance of the ambient room temperature, occlusive dressings, procedural and ongoing pain management and early enteral
feeding\textsuperscript{30, 31} all seem to play a vital role in the minimizing of the hypermetabolic response post thermal injury.

**Gastrointestinal Tract**

Perfusion of the gastrointestinal tract (GIT) and liver is decreased as a result of alteration in blood flow during hypovolaemia and lack of enteral feeding. The bowel is highly susceptible during this period and the release of stress hormone induced vasoconstriction can lead to decreased gut immune function and gut mucous-integrity. This will predispose the patient to endogenous bacterial and endotoxin translocation into the systemic circulation.\textsuperscript{32} Increasing evidence suggests that damaged intestinal mucosa due to starvation, even for short intervals, could also lead to bacterial translocation.\textsuperscript{33, 36} Enteral feeding can prevent mucosal breakdown and possible bacterial translocation.\textsuperscript{37} The severity of metabolic and gastrointestinal changes that occur after a severe thermal injury, can be ameliorated through early enteral nutritional intervention.\textsuperscript{31}

The adult patient’s small bowel permeability seems to be increased after a burn injury, but returns to normal within 24 hours post burn,\textsuperscript{36} whereas the burned child’s small bowel permeability seems to be increased for a longer period post burn than that of the adult’s.\textsuperscript{37} Furthermore, small bowel permeability only matures at the age of 2 years old. A non-invasive technique of determining small bowel permeability has been devised. It is called the sugar-absorption-test (SAT). The levels of two non-absorbable sugars (lactulose and L-rhamnose) are measured from a 5-hour urine collection after the oral intake of a 100 milliliter (ml) lactulose:rhamnose solution.\textsuperscript{38}

Gastric acid production is initially suppressed for 48 to 72 hours after injury and then surpasses normal levels. Released catecholamines may be a factor in the suppression. The accelerated acid production and release of pepsin significantly increase the risk of erosion and ulceration.\textsuperscript{39} Superficial mucosal erosion, Curling ulcers (stress ulcers) may be present after 72 hours post burn in 67% of burn patients. However, early enteral feeding (within 12 to 24 hours post burn), has shown to restore altered submucosal blood flow and prevent ulcers without the use of antacids.\textsuperscript{40}

Gastric dilation and paralytic ileus often occur following major burn injuries. Digestive gastric and large intestine function virtually ceases, but the small bowel maintains motility and absorptive capacity. Paralytic ileus is often diagnosed by an absence of bowel sounds that represents air moving along the bowel. This air could easily be released by the placement of a nasogastric tube for gastric decompression. Bowel sounds is not an indicator of the absorptive function of the bowel, and therefore should not be used as a diagnostic tool for the initiation or abstinence of enteral nutrition.\textsuperscript{41, 42}
Gastric decompression is necessary to empty the stomach and protect the child from acid aspiration until gastric motility is reestablished. As long as the gastric decompression is maintained, enteral nutrition can safely be supplied to the duodenum or jejunum via a nasoduodenal or nasojejunal feeding tube. The GIT motility is usually restored following adequate fluid resuscitation. Recurrence of the ileus later in the hospital course is suggestive of developing sepsis.

**Management**

**Emergency**

All smouldering or hot clothes must be removed. The smaller burn (less than 25% TBSAB) should be covered with copious amounts of cold tap water (more or less 16 degree Celsius), or clean wet blankets. Larger burns (more than 25% TBSAB) treated in this manner could result in hypothermia. Dry, clean dressings or Bumshield (first aid dressing) are preferred.

**Pain relief**

Acute pain management should be provided as a priority. Standard pain management protocols are in use. Ongoing individual pain assessment is imperative and consists of 3 components namely, acute-, chronic-, and procedural pain management.

**Fluid resuscitation**

Resuscitation should be initiated as soon as possible, in order to correct the haemodynamic instability and fluid losses. The first steps in effective resuscitation are clinical assessment of the extent and depth of the injury, the presence of inhalational injury and accompanying trauma. Crystalloids, in particular (Plasmolyte B), is commonly used as resuscitation fluid. Resuscitation formulae should be seen as a guideline, and assessed regularly according to urine output, serum urea and creatinine values, as well as a clinical assessment.

**Nutritional Intervention**

The nutritional management of the patient influences the metabolic and gastrointestinal changes that occur after severe thermal injury. Before the seventies, it was common to observe burned patients waste away until there was virtually no lean body mass left. Children potentially waste away much faster than adults, as they have limited stores and a low lean body mass in relation to total body surface area (TBSA). High mortality, infections, slow wound healing and failed skin grafts, as well as prolonged hospitalization periods were common.
Workers in the field have suggested that more aggressive nutritional intervention might prevent the wasting and high mortality. Aggressive nutritional intervention would include adequate supply of macro- and micro-nutrients per individual, in order for the patient to maintain a discharge weight within 5% of the admission weight. Additional advantages would include a shorter wound healing period and hospital stay.

Unfortunately severely burned patients usually present with a gastrointestinal ileus as often diagnosed by an absence of bowel sounds. In the past enteral nutrition was excluded until there were clear discernable bowel sounds. Enteral feeding was regarded as unsafe because of the proximal intestinal ileus and the possibility of pulmonary aspiration and pneumonia. In addition it was thought that early enteral nutrition would aggravate the haemodynamic instability, especially during the first 48 hours when these patients have hypotension and decreased cardiac output. Patients were therefore starved for days on end until there were adequate bowel sounds and they were haemodynamically stable.

During the early seventies, total parenteral nutrition (TPN) provided a way to prevent or shorten the periods of starvation. For the first time, adult burned patients lost less than 10% of their admission weight, or even maintained it. However, body composition studies revealed that body mass was maintained by an increase in fat mass with a progressive loss of lean body mass. Even though the mortality figures dropped dramatically as a result of nutritional intervention, it was not the ideal manner of feeding. The central or peripheral lines used to administer parenteral nutrition presented a serious hazard for line sepsis and septicemia. TPN does not maintain the integrity of the small bowel and as a result small bowel villus atrophy occurs. Prolonged starvation and or TPN, leads to increased gut permeability and possible bacterial translocation, which could result in toxemia and multiple organ failure (MOF).

It became apparent that the gastrointestinal ileus affects predominantly the stomach and colon, and that the small bowel may maintain sufficient motility and function to absorb nutrients. In the late seventies and early eighties, the practice of providing enteral feeds within 12 to 24 hours post injury, administered via a transpyloric feeding tube, was initiated. This tube was long enough to pass through the stomach and deposit an enteral feed in the duodenum or jejunum. The tube could either be placed under fluoroscopic guidance, endoscopy, or by a bedside technique. The final position of the tube was confirmed by an abdominal X-ray. Regular (hourly) gastric aspiration was done using a nasogastric tube (NGT) placed through the other nostril, to confirm the ongoing position of the nasojejunal tube (NJT) and to decompress the stomach. Gut motility enhancing drugs were used in patients who had gastric fluid...
aspirates larger than 2 to 3 milliliters per kilogram per hour (mL/kg/h). Early enteral feeding (EEF) gradually became an accepted reality in the management of the adult burned patient.43, 44 Many studies now confirm the safety and efficacy of EEF in comparison to enteral feeds initiated after 24 hours post injury [late enteral feeding (LEF)] in burned animals and human adult patients.40, 50 However, in children the situation is not nearly as clear, and documented clinical data are lacking.

In 1992, the burns team at the Red Cross Children's Hospital (RXH) instituted EEF in children with severe thermal injury. A controlled study comparing EEF to standard feeding practices in children with severe burns was not undertaken, but the clinician felt that the clinical outcome using the new regime was better than with standard practice. It was to gain clarity on the issue that the need for a controlled trial was mooted.

**Reasons for a controlled clinical trial comparing EEF to LEF**

Delayed - or LEF is standard practice on a national level in Africa and South Africa. This is also the case in most other international burn units, with only a selected few that have opted for the practice of EEF. A review of the literature revealed limited information on the hormonal response in burned children (birth to 13 years old) following the initiation of early enteral feeding EEF in comparison to late enteral feeding LEF. Although some authors25, 26 investigated the hormonal stress response of paediatric patients post trauma, they did not specifically compare EEF to LEF. There is substantial evidence in the adult burn literature that suggests that EEF compared to initial starvation seems to have a profound positive impact on the hormonal response, metabolic rate and gastrointestinal integrity post thermal injury.22, 41

The technique of EEF as part of the resuscitation protocol as used at RXH, is unique, not documented in any known literature, and needs to be validated with the evidence of a controlled clinical trial. The lack of sufficient evidence in the literature in favour of EEF in the severely burned paediatric patient, was a strong motivating factor for the initiation for this study.

The ethical committee of the University of Cape Town approved this study on the basis of the lack of sufficient evidence in the literature, concerning EEF and the paediatric burned patient.

All these unanswered probabilities pointed to the need for a controlled clinical trial. In essence, this study was undertaken to investigate whether EEF is more beneficial than the standard practice of delayed – or LEF, in the paediatric burned patient. Furthermore, we needed to determine whether the practice of EEF as part of the...
resuscitation protocol is safe, and whether it is a treatment option for burns in developing countries.

Table 1.1 shows a summary of possible metabolic-related complications after a severe burn injury. It also illustrates the possible advantages of EEF (within 12 to 24 hours post burn) over delayed or LEF (after 24 to 48 hours post burn).³

**Table 1.1: Possible complications post burn injury, and possible advantages of EEF compared to LEF**

<table>
<thead>
<tr>
<th>Early Enteral Feeding (EEF)</th>
<th>Thermal Injury</th>
<th>Delayed or No Enteral Feeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small bowel function and morphological integrity retained</td>
<td>Hypermetabolism</td>
<td>Ischemia and Reperfusion Injury</td>
</tr>
<tr>
<td>Less or no mucosal breakdown</td>
<td>Catabolism</td>
<td>Intestinal Barrier Failure</td>
</tr>
<tr>
<td>Less or no Bacterial Translocation</td>
<td>Increased infection susceptibility</td>
<td>Mucosal Breakdown</td>
</tr>
<tr>
<td>Less Infections and Antibiotic use</td>
<td>Decreased Immune Competence</td>
<td>Increased small bowel permeability</td>
</tr>
<tr>
<td>Enhanced Wound Healing</td>
<td>Organ Failure</td>
<td>Bacterial Translocation</td>
</tr>
<tr>
<td>Shorter Hospital Stay</td>
<td>Multiple Organ Failure</td>
<td>Death</td>
</tr>
</tbody>
</table>
References


Chapter 2

Aims and Objectives

2.1 Aims of the study

The aims of the study were to:

1) determine whether the use of early enteral feeding (EEF) is as effective as late enteral feeding (LEF), in the paediatric burned patient, 2) whether EEF can be used as part of the resuscitation process in the paediatric burned patient so that by 24 hours, all resuscitation fluids are administered enterally, 3) whether EEF modulates the hypermetabolic response as measured by hormonal concentrations, to thermal injury.

2.2 Objectives

A number of objectives were used to assess the effectiveness of EEF vs. LEF on the course and outcome of the management protocols. The objectives of this study were:

2.2.1 to determine whether EEF vs. LEF changes the hypermetabolic response by comparing the hormonal levels of Insulin, Insulin-like growth factor-1 (IGF1), Growth Hormone (GH), Glucagon and Cortisol in burned children following either EEF or LEF regimes,

2.2.2 to estimate energy expenditure \( (\text{EEE} = \text{REE} + 30\% \text{ activity factor}) \) and the respiratory quotient (RQ) as measured by indirect calorimetry (IC) in the EEF and LEF patients. To compare the EEE of both groups to paediatric burns’ equations prescribed energy requirements and the recommended dietary allowances (RDA) for healthy children,

2.2.3 to compare the EEE in both groups (EEF vs. LEF) with the actual caloric intake, and the estimated protein intake (20% of the calculated total calories) to that of the actual protein intake,

2.2.4 to determine whether small bowel permeability as measured by Lactulose:Rhamnose ratios is increased post burn, and to compare the small bowel permeability between the two groups, and

2.2.5 to compare the outcome in terms of gastrointestinal tolerance of enteral feeds, stool patterns, stress ulcers, maintenance of discharge weight within 5% of admission weight, length of time on antibiotic treatment and length of hospital stay.
Chapter 3

Methodology

3.1 Study design

Initially this study was intended to be a randomized clinical controlled trial. However, in the planning stages it became apparent that under the circumstances in which we work, this would not be possible. Hence, the study was changed to a Controlled trial. The change are discussed below.

This study aimed to initiate enteral feeding within 12 hours post burn injury in the EEF group, as this was done as part of the resuscitation protocol. In order to prevent pulmonary aspiration for these patients, the enteral feed could only be started after a nasojejunal feeding tube (NJ) was inserted, and the final position confirmed. The placement of the NJT was mostly performed under fluoroscopic guidance. Unfortunately the Radiology Department had to curtail their services due to financial constraints and staff cuts. They only offered the service for the placement of a NJT between 08h00 a.m. and 23h00 p.m. This would have increased the time for the initiation of enteral feed to beyond 12 hours. The enteral resuscitation would then not have contributed as much of the total resuscitation fluid as was intended.

The decision was therefore taken to place all patients that arrived before 23h00 p.m. in the EEF group, and those that arrived thereafter in the LEF group.

The lack of randomization is a limitation to this study and is discussed in chapter 10.

The Research Ethics Committee of the University of Cape Town formally approved this study. The reference number of this study was: ERC REF NO: 232/97. Informed consent was obtained from the parent or caregiver, after careful explanation of the investigation by the researcher. An example of the consent form is provided in Appendix 1.

3.2 Sample Size

The sample size was calculated with the statistical programme Epistat, on the basis of the measured hormone concentrations. Assuming a 30% change in serum or plasma hormone concentrations between the two study groups, with a 95% confidence level, the estimate was 70 patients. This change was considered to be clinically relevant.

Unfortunately the measurement of the hormonal blood concentrations, which were close to a thousand specimens, was extremely expensive. The funds that were
available for the study were depleted fairly quickly and statistical analyses were initiated in order to monitor progress. It was found that the difference between certain hormonal concentrations between the two study groups had reached statistical significance. These results are discussed in chapter 5. As a result of this analysis, despite its limitations, and an inability to acquire further funding, patient enrollment was stopped.

Since the patients that were studied required intensive monitoring from the author, the nursing staff and the medical staff, the number of patients that could be studied simultaneously, were limited.

Therefore, in the light of the preliminary data analysis, fast dwindling monetary funds and labour intensive patient care during a period of staff shortages, the author decided to discontinue the study before the required sample size of 70 patients was reached. It was decided to rather investigate a smaller cohort of patients thoroughly and with excellent overall care, than a larger number with less detail.

The final sample consisted of 21 patients. The study patients are discussed in detail in chapter 4. The small study sample is a definite limitation to this study, and this is discussed further in chapter 10.

3.3 Study population

Children who met the following criteria were included in the study:

3.3.1 All children had to be admitted within 24 hours post burn, to the Red Cross Children's Hospital (RXH) burn unit or intensive care unit (ICU).

3.3.2 They had to be less than or equal to (<) 13 years of age, with

3.3.3 a total body surface area burn (TBSAB) of greater than or equal to (>) 20%.

Consecutive patients were enrolled in the study from 1st March 1998 to 30th November 1998.

3.4 Initial Management

All patients were admitted to the RXH trauma unit where they received analgesia. All clothes were removed and the child was weighed and then wrapped in a special dressing (Burn Shield). Intravenous (IV) access was obtained and Plasmolyte B was started in order to correct the haemodynamic imbalance and replace fluid losses.
3.5 Burn injury assessment

When the child was satisfactorily sedated, the extent of the injury according to the total body surface area burned (TBSAB), as well as the depth of the wounds was documented. An example of an assessment form is provided in Appendix 2. If the TBSAB was equal to or greater than 20%, the investigator was notified. Only burn injuries sustained from hot water and fire were included in this study.

3.6 Venous blood specimens

3.6.1 Routine Haematology and Chemistry specimens

After admission, blood was sampled weekly for the purpose of the study. Routine blood samples included measurements of full blood count, electrolytes, glucose, albumin, total protein, urea and creatinine, corrected calcium, magnesium and phosphate. Additional haematology and chemistry was measured at the discretion of the medical staff responsible for the day to day care of the patient.

3.6.2 Hormonal Specimens

Venous blood samples were taken on admission and thereafter daily between 7h00 and 8h00 am until day 5, and thereafter on day 12, day 19 and day 26. A total of 9 samples for each hormone per patient were measured. The samples of 3 patients were measured until the time of death.

3.6.3 Procedure

Venous blood [9 milliliters (ml)] was drawn for the estimation of electrolytes, full blood count, insulin, insulin-like growth factor-1 (IGF1), growth hormone (GH), glucagon and cortisol. The blood samples for the electrolyte (1.5ml) and full blood count (1.5ml) was sent to the laboratories at RXH for analysis. The blood samples (6ml) for hormonal analysis were prepared as follows.

Three ml of the remaining blood sample was allowed to clot and 3ml was added to a heparinised tube. Both samples were kept on ice for 30 minutes before they were separated by centrifugation. Serum and plasma were then aliquoted into smaller microfuge tubes which contained Trasylo. All tubes were labeled with the patient's name, the time, the day post burn, the date of sampling and whether they were plasma or serum before being stored at -20°C while awaiting assay in batches.
3.6.4 Assay of hormone concentrations

Serum and plasma samples for hormone assay were stored at -20°C until the analysis was performed. The Medgenix "IGF1-D-RIA-CT" kit was used to assay serum IGF1 levels. Plasma glucagon, serum insulin and serum growth hormone concentrations were measured by radioimmunoassay (RIA). Serum cortisol concentrations were analysed by a heterogeneous competitive magnetic separation assay (MSA). The intra-assay coefficients of variation (CV) for the concentrations of cortisol, glucagon, insulin, IGF1 and GH were 3.1%, 3.9%, 4.9%, 3.9%, and 3.5% respectively.

3.7 Indirect Calorimetry (IC)

Indirect calorimetry (IC) was performed using a Paediatric Calorimeter (Delta Trac), that was serviced and standardized prior to the study by the agents. The equipment was calibrated before use with 100% alcohol and a combination of 95% oxygen and 5% carbon dioxide. The daily barometric pressure was obtained from the meteorological office. The full calibration process was repeated before daily measurements on each patient.

IC was performed on admission, thereafter daily until day 10, and then on day 12, day 19 and day 26 post burn. Each patient was kept nil per mouth (NPM) for 4 hours prior to each measurement. The only exception to this was the resuscitation period (0 to 48 hours post burn) for the EEF group. The enteral feed was provided as part of the resuscitation protocol and via continuous infusion. It could therefore not be stopped for 4 hours.

IC was only possible if a patient could maintain normal haemoglobin saturation in room air for at least 10 minutes, or were fully ventilated. If the patient did receive oxygen, the supervising doctor was asked whether it would be safe to turn the oxygen off for 10 minutes. If he or she felt it was safe, the patient's saturation monitor was used to monitor the saturation levels. The oxygen was then turned off in the presence of the doctor and the child was left to breathe by him- or herself for 5 minutes before the indirect calorimetry was initiated.

IC measures oxygen consumption ($\text{VO}_2$) and carbon dioxide ($\text{VCO}_2$) excretion, to calculate the resting energy expenditure (REE) in kilo-calories per day (kcal/day), using the Weir equation. Five steady measurements were performed while the patient was at rest. If the indirect calorimeter viewed a certain measurement as incorrect or unsteady, the result would be shown in a broken line, also known as an artifact. Measurements that were viewed correctly or steady, were shown in a solid line. No records with artifacts were included. If the patient became distressed while the
measurement was in progress, the measurement was stopped and repeated later during the same day. In order to obtain the daily estimated energy expenditure (EEE) for each patient, an activity factor of 30% was added to the REE. Daily physiotherapy, occupational therapy, change of dressings, possible infections and hyper- or hypothermia, were accounted for by this additional activity factor.

3.7.1 Respiratory Quotient

The respiratory quotient (RQ) was used to determine substrate utilization. RQ is the ratio of carbon dioxide expired to the amount of oxygen inspired: \( RQ = \frac{VCO_2}{VO_2} \). The respiratory quotient (RQ) was recorded along with the REE. McClave et. al. stated, that by excluding protein, the non-protein RQ (npRQ) provided a range of substrate utilization from 0.7 at the bottom (indicating 100% fat utilization and 0% carbohydrate utilization) to 1.0 at the top (indicating the opposite). A npRQ at midpoint would indicate 50% fat and 50% carbohydrate oxidation. This study therefore used a RQ value of less than ( \(<\) ) 0.8 as indicative of lipolysis, and a value of more than or equal to ( \(>\) ) 0.8 as reflective of a combination of carbohydrate and fat metabolism.

3.8 Placement of feeding tube

An anti-spasmodic was given to each patient in both study groups and a 110cm feeding tube was placed nasogastrically by the nursing staff. Thereafter, this feeding tube was placed transpylorically by a radiologist under fluoroscopic guidance. Two of these feeding tubes were placed by bedside technique by a visiting doctor, and the final position was confirmed by X-ray.

A nasogastric feeding tube (NGT) was placed through the other nostril for gastric decompression and hourly nasogastric aspirates in order to monitor the ongoing position of the nasojejunal feeding tube. The NGT was removed, either on day 3 or day 5, in the EEF and LEF groups, respectively.

After the EEF completed their enteral resuscitation, and the LEF group their enteral maintenance, the enteral feed was offered to the patient to drink orally (only where appropriate). If the patient was able to drink the entire maintenance volume from the enteral feed within 24 hours, the NJT was removed. The patient then consumed the enteral feed orally for the remainder of study period. If the patient was unable to drink the enteral feed from either day 3 or day 5, it was offered as soon as the patient was stable enough. Thereafter the NJT was removed.

3.9 Enteral Resuscitation

The investigator calculated and documented the total fluids required for the resuscitation period of 48 hours. An example of the resuscitation form is provided in
Appendix 3. The volume of a standard concentration [1 kilo-calorie per milliliter (kca/l)] polymeric enteral feed (Ensure) was calculated as part of the resuscitation regime and initiated at 1 milliliter per kilogram per hour (ml/kg/h) for the EEF group. The enteral feed was given via continuous infusion and incrementally increased every 3 hours, with a concomitant decrease in intravenous fluids. Hourly nasogastric aspirates were measured to monitor the position of the nasojejunal feeding tube. When the hourly nasogastric aspirate exceeded 2 to 3 ml/kg/h, a gut motility-enhancing drug was initiated. The LEF group received the total fluids required for resuscitation (first 48 hours post burn) from intravenous infusion only, after which the enteral feeds were initiated. A urinary catheter was used to monitor the urinary volume output.

3.10 Enteral feeding: Calorie and Protein Requirements

Day 3 and day 5 completed the resuscitation period in the EEF and LEF groups, respectively. Thereafter, all maintenance fluids were provided from the enteral feed and a gradual increase in calories and protein could be initiated to reach the full estimated requirements as soon as possible. Where possible, the enteral feed was provided orally from either day 3 (EEF group) or day 5 (LEF group). As soon as the full enteral feed volume was taken orally, the NJT was removed.

The energy requirements of the children were estimated using the adapted paediatric Solomon’s formula, the Galveston formula, as well as the Recommended Daily Allowance for healthy children (RDA). It has been shown that the Solomon’s formula overestimates the energy requirements of children with burns more so than the Galveston formula, therefore the Galveston formula was preferred as the guideline for the caloric prescription of each patient. Appendix 4 contains the Solomon’s and Galveston equations, as well as the RDA.

In order to compare results, only one feed was used throughout the study, although the unit’s dietician makes use of other specialized feeds when necessary. The enteral feed that was used throughout the study was a polymeric, nutritionally complete enteral feed (Ensure, Abbott Laboratories). The composition of the feed consisted of 15% protein, 30% fat and 55% carbohydrate of the total energy. Although the ideal enteral feed composition for burned patients would be closer to 20% protein, 3% fat and 77% carbohydrate, there currently is no such enteral feed available in South Africa. The ideal enteral feed composition is discussed in chapter 10.

The final goal was to provide the enteral feed’s composition as 18 to 20% protein, 55 to 60% carbohydrate and 22 to 25% fat. Since the enteral feed that was used contained 15% protein, 30% fat and 55% carbohydrate; the total calories, carbohydrate and protein was increased from day 3 and day 5 post burn in the EEF and LEF groups, respectively. Supplemental carbohydrate and protein were provided
in the form of a glucose-polymer (Polycose, Abbott Laboratories) and whey protein (Promod, Abbott Laboratories). No additional fat supplements were added, as the enteral feed contained 30% fat. The incremental increase of the caloric density was achieved by a concentration increase of 0.1 kilo-calorie per milliliter per day (kcal/ml/d). The standard concentration of Ensure is 1 kcal/ml. The concentration of the prescribed enteral feed never exceeded 1.5 kcal/ml, since that can cause osmotic diarrhoea. 14

3.11 Enteral feeding: Solid food Intake

It is common knowledge amongst nutritionists that patients with severe thermal injuries initially have a poor appetite for solids. This poor appetite can last for days, or even a few weeks; depending on the individual and the severity of the burn. They generally prefer to drink liquids to quench their ever-present thirst. Therefore the liquid enteral feed’s intake is of the utmost importance. In order to ensure that patients meet their nutrient needs, all the nutritional requirements are provided for in the enteral feed, and any solid food consumed are over and above their protein and caloric requirements. In the majority of patients, the initial intake of solid food is negligible.

As the thermal injury recovers and the size of the lost skin decreases with either conservative management or skin grafts, the nutrient requirements are re-calculated according to the corrected percentage burn. When the patient is consuming at least half of the solids offered on a regular basis, the enteral feed is viewed as a supplement and decreased accordingly.

In this study solids were offered to the patients from day 3 (EEF group) or day 5 (LEF group) post burn. The solids were encouraged over and above the calculated enteral feed and consisted of either a standard purity-, toddler- or full ward hospital diet. The patient had the choice of refusal or total consumption. In most cases the patients’ appetites were poor for at least the first two weeks. Those patients who were in the intensive care unit (ICU), receiving almost constant sedation for pain control, or those with a persistent paralytic ileus (prevention of aspiration), only received solids when the sedation could be decreased or bowel sounds were clearly present. A daily list containing all the different food options provided where completed by the nursing staff. An estimated food record was calculated and the additional calories and protein that were provided from the solids were added to the intake provided from the enteral feed (Ensure) from either day 3 or day 5. The total intakes for both study groups were displayed in the graphs in chapter 7.

The EEE (REE x 30% activity factor) 7 for both groups was compared to the calculated values using the Solomon’s, Galveston and RDA equations. The EEE in both groups was also compared to the actual calorie intake.
3.12 Stool Specimens

A stool specimen of each patient was taken once a week, and was examined for the presence of occult blood, by the Hematest. This served to look for bleeding from stress ulcers (Curling).

3.13 Small bowel permeability

The small bowel permeability was measured using a sugar absorption test (SAT) in both groups on day 3 and day 5 post burn. On day 3 post burn, the EEF group had received 2 days of enteral nutrition, whereas the LEF group was enterally starved.

An isotonic solution of lactulose 5g (as Duphalac) and L-Rhamnose 1g was made up to 100ml. Both Lactulose (disaccharide) and L-Rhamnose (monosaccharide) are non-absorbable sugars. Thiomersalate Tincture 0.1% (10mg/100ml) was added to the urine collector to prevent bacterial degradation of the sugars.

The patients were kept NPM for 2 hours before starting the test and for the 5 hours during which all urine was collected. Intravenous fluids were increased accordingly during these 7 hours of starvation. The 100 ml sugar solution was given via the feeding tube.

All patients had been catheterised on admission to monitor urine output. The specimens were stored at -20°C and sugars measured by thin layer chromatography (TLC). A total of 15 patients completed the SAT. Nine patients were in the EEF group, and 6 patients in the LEF group. Fewer patients completed the SAT than the total sample size. If the doctor in charge of a specific trial patient who was on this trial, considered the patient's fluid balance too unstable to be given an additional 100 ml of the SAT solution via the NJT, the test was not performed. The Statistical analysis and comparison of the data could continue, since the two treatment groups were similar with relation to their median ages, TBSAB and admission weights.

3.14 Anthropometry

Weights and recumbent lengths were taken on admission. Wherever possible, a naked weight was obtained within 8 hours post burn, before oedema was present, or as soon as possible post admission. The caregiver was also asked for a pre-burn weight or a “road to health clinic chart”. Thereafter the weights and recumbent lengths were measured weekly until discharge. The weights were taken while the patient was naked, during dressing changes. Oedema and weight loss after a severe excision could influence the patient's weight measurement. The children who could stand were weighed on a digital Seca standing scale and babies were weighed on a digital Seca babyscale. The children that were unable to stand and too heavy for the baby scale
were weighed while the investigator held the child. The investigator’s weight was then subtracted. Unfortunately no bed scales was available at the time of this study.

The recumbent lengths were taken by placing the child on a length measuring board. The child was placed on his/her back, lying straight on the measuring board. The head was held in a straight position, and placed at the top part of the measuring board. The leg least burned was straitened, and the foot flexed in a 90° angle. The moving part of the measuring board was then moved up to the child’s flexed foot. The measurement was then read from the tape measure inserted on the board.

Tricep skinfolds and upper mid-arm circumference measurements were impractical, due to the absence of skin and the presence of oedema. The children’s weight and height/recumbent length measurements were used to score them on the weight-for-height percentiles.

3.15 Statistical Analysis

The Statistica (1998 edition) as well as the Microsoft Excel packages (1997 edition) were used to analyze the data. Ninety-five percent (95%) confidence intervals for continuous variables were determined.

In order to assess whether the EEF and LEF groups were comparable to each other, the outcome variables age, weight and TBSAB were analysed. Descriptive statistics e.g. 95% confidence intervals, median, lower and upper quartiles are provided in Chapter 4. Normality was also assessed for the fixed variables age, weight and TBSAB. It was determined that these were normal and a t-test was performed to determine whether the two groups were comparable with respect to weight, age and TBSAB. They were found to be normal and comparable. Outlying values for TBSAB (patients 10 and 20) were excluded from the data and t-tests performed. This did not yield significant differences between the two groups.

From the 3 patients that died, all results were included up until the time of death. The remainder of the results were then re-analysed according to the remaining amount of patients.

Analysis of repeated measures were performed on the continuous variables measured: cortisol, glucagon, insulin, insulin-like growth factor-1 (IGF1) and the growth hormone (GH) concentrations, estimated energy expenditure (EEE), respiratory quotients (RQ), caloric and protein intakes, caloric balances, and lactulose:rhamnose ratios (small bowel permeability). The parametric method, MANOVA (multivariate analysis of variance) was used for the analysis of the repeated measures variables. Normality was assessed for these variables. In the case of a non-
normal variable, a log transformation was applied to the data and the transformed data was then analyzed. Only GH was analysed in this manner.

A t-test was used to compare quantitative data between the groups. This included; cortisol, glucagon, insulin, IGF1 and GH concentrations, EEE, RQ, total caloric and protein intakes, caloric balances, lactulose:rhamnose ratios (small bowel permeability), admission and discharge weights, percentage change in weight and length of hospitalisation.

Statistical significance was accepted at a 5% probability level. However, due to the small sample size, results that produced p-values of up to 0.08, were also considered as approaching significance.

References

1. Medgenix IGF-1-D-RIA-CT Kit, Catalog Number: 30 158 60, BioSource Europe S.A., Nivelles Belgium

2. Glucagon-RIA Kit, Catalog Number: 07-152101, Separations, ICN Pharmaceuticals Inc. Diagnostic Division, 3300 Hyland Avenue, Costa Mesa, California

3. Coat-A-Count Insulin, Catalog Number: 2 D01-20, Abbott Laboratories (Pty), 149 Samuel Evans Road, Aeroton, Johannesburg S.A.


5. Cortisol (Cort), Technicon Immune 1 Septems Bayer Corporation, Business Group Diagnostics, Tarrytown, NY 1059-5097 USA


Chapter 4

Patient Characteristics

The Study Patients

Twenty-one patients were entered into the study, and 18 patients completed the study successfully. Of these, 11 were assigned to the early enteral fed (EEF) group, and the remaining 10 to the late enteral fed (LEF) group. Nine patients in each group completed the study successfully.

The Red Cross Children’s Hospital (RXH) treats most of the severe (> 20% TBSAB) paediatric burn injuries in the Western Cape Province of South Africa. Although RXH is a state hospital, more than often the burn unit will also accommodate private patients, since thermal injuries require such extensive expertise and treatment. It is therefore very common for the burn unit to treat patients from poor, as well as privileged socioeconomic backgrounds, with quite an even spread between the two ranges.

These study patients came from a variety of demographics and socioeconomic backgrounds, including Khayalitsha (a mostly underprivileged, poor, black suburb), Athlone (a middle – to upper class privileged, coloured suburb), a farm community near Caledon (middle class) and Kraaifontein (a range of privileged to underprivileged white and coloured suburb).

Except for one child who fell on the 10th percentile weight-for-height; all the other children that partook in this study had a normal weight-for-height (ranging from the 25th - 95th percentile weight-for-height). The anthropometrical findings are set out in chapter 9. Overall, the pre-burn nutritional status of the children studied, could be described as healthy, and within the normal ranges.

The patients were studied from admission until day 26-post burn. The patients who were discharged before day 26 were studied on an outpatient basis. Two patients in the EEF group died of organ failure on day 3 and day 19 post burn, and one patient in the LEF group died due to carbon monoxide poisoning on day 5 post burn. None of the 18 patients that completed the study successfully had a positive blood culture, indicating septicemia, throughout the study period. All three these patients sustained severe inhalation injuries, for which they were ventilated until death. All patient data were included until the time of death.

Table 4.1 shows a summary of the clinical characteristics of the study patients. Three patients in each group were ventilated due to an inhalation injury, but the 3 patients...
who survived were only ventilated for a short period (less than 1 week). The patients that died are marked with an asterisk [*].

Table 4.1: Clinical characteristics of the patients in the study

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>TBSAB (%)</th>
<th>Admission weight (kg)</th>
<th>Cause</th>
<th>Inhalation Injury (Ventilated)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>yr= years m= months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEF group (n=11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>8 m</td>
<td>30</td>
<td>8.72</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>2</td>
<td>2 yr</td>
<td>23</td>
<td>12.3</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>3</td>
<td>2 yr, 9 m</td>
<td>30</td>
<td>13</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>4</td>
<td>4 yr, 7 m</td>
<td>31</td>
<td>15.5</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>5</td>
<td>5 yr, 4 m</td>
<td>23</td>
<td>18</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>6</td>
<td>6 yr, 4 m</td>
<td>35</td>
<td>22</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>7</td>
<td>7 yr</td>
<td>20</td>
<td>24.5</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>8</td>
<td>7 yr</td>
<td>33</td>
<td>24.5</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>9</td>
<td>11 yr, 3 m</td>
<td>30</td>
<td>30</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>*10</td>
<td>1 yr, 10 m</td>
<td>75</td>
<td>13.8</td>
<td>FB</td>
<td>(V)</td>
</tr>
<tr>
<td>*11</td>
<td>1 yr, 4 m</td>
<td>30</td>
<td>11</td>
<td>HWB</td>
<td>(V)</td>
</tr>
<tr>
<td>LEF group (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>8 yr, 11 m</td>
<td>20</td>
<td>25</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>13</td>
<td>3 yr, 8 m</td>
<td>25</td>
<td>13.25</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>14</td>
<td>1 yr</td>
<td>25</td>
<td>10.5</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>15</td>
<td>1 yr, 1 m</td>
<td>20</td>
<td>10.95</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>16</td>
<td>9 yr, 1 m</td>
<td>28</td>
<td>15</td>
<td>HWB</td>
<td>X</td>
</tr>
<tr>
<td>17</td>
<td>3 yr, 5 m</td>
<td>32</td>
<td>13</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>18</td>
<td>1 yr, 9 m</td>
<td>29</td>
<td>11</td>
<td>FB</td>
<td>X</td>
</tr>
<tr>
<td>19</td>
<td>4 yr, 6 m</td>
<td>30</td>
<td>19</td>
<td>FB</td>
<td>(V)</td>
</tr>
<tr>
<td>20</td>
<td>1 yr</td>
<td>62</td>
<td>8</td>
<td>FB</td>
<td>(V)</td>
</tr>
<tr>
<td>*21</td>
<td>*5 yr</td>
<td>32</td>
<td>28</td>
<td>FB</td>
<td>(V)</td>
</tr>
</tbody>
</table>
Table 4.2: Descriptive Statistics for Age, Total Body Surface Area Burned (TBSAB) and Weight

<table>
<thead>
<tr>
<th></th>
<th>EEF GROUP</th>
<th></th>
<th>LEF GROUP</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Confidence Interval (-65%)</td>
<td>Confidence Interval (+95%)</td>
<td>Median</td>
<td>Lower Quartile (25%)</td>
</tr>
<tr>
<td>Age</td>
<td>2.39</td>
<td>6.71</td>
<td>4.58</td>
<td>1.83</td>
</tr>
<tr>
<td>TBSA (%)</td>
<td>22.81</td>
<td>42.63</td>
<td>30.0</td>
<td>23.0</td>
</tr>
<tr>
<td>Admission Weight</td>
<td>12.87</td>
<td>22.07</td>
<td>15.5</td>
<td>12.0</td>
</tr>
</tbody>
</table>

The two study groups were similar with respect to their median age, weight and TBSAB. The whole sample was also found to be comparable to those patients who survived. Fifty percent of the patients in this study were younger than 3 years 8 months old. The EEF and LEF groups had a relatively large (but similar) range in admission weights, between 8.72 to 30 kg and 8 to 28 kg respectively. The range of values for TBSAB was quite small, with 50% of the patients having a value lying between 25 to 30%. Note that an outlier in TBSAB was present in each group (EEF = 75%; LEF = 62%).

Even though outliers were present, the statistical comparison showed comparability between the groups, allowing the study to proceed to statistical analysis of the available data.

Table 4.3 is a summary of the required theatre procedures. It shows the day of the first skin graft, the total skin grafts for the 26 day period, cleaning of wounds and dressing changes, and the total amount of theatre procedures.
Table 4.3: The TBSAB and Theatre procedures of the patients in the study

<table>
<thead>
<tr>
<th>Subject</th>
<th>TBSAB (%)</th>
<th>Day of First Skin Graft</th>
<th>Total Skin Grafts</th>
<th>Change of Dressings</th>
<th>Total theatre procedures in 26-day period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>9</td>
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<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
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<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>35</td>
<td>5</td>
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</tr>
<tr>
<td>*10</td>
<td>75</td>
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<td>2</td>
<td>4</td>
<td>6</td>
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<tr>
<td>*11</td>
<td>30</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td>17</td>
<td>24</td>
<td>41</td>
</tr>
</tbody>
</table>

<p>| LEF group (n=10) |
|-----------------|-----------------|-----------------|-------------------|-------------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Subject</th>
<th>TBSAB (%)</th>
<th>Day of First Skin Graft</th>
<th>Total Skin Grafts</th>
<th>Change of Dressings</th>
<th>Total theatre procedures in 26-day period</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>20</td>
<td>N/A</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>25</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>14</td>
<td>25</td>
<td>11</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>20</td>
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<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>16</td>
<td>28</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>17</td>
<td>32</td>
<td>4</td>
<td>2</td>
<td>4</td>
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</tr>
<tr>
<td>18</td>
<td>29</td>
<td>7</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>19</td>
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<td>2</td>
<td>4</td>
<td>6</td>
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<tr>
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<td>62</td>
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<td>2</td>
<td>6</td>
<td>8</td>
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<tr>
<td>*21</td>
<td>32</td>
<td>N/A</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td>13</td>
<td>24</td>
<td>36</td>
</tr>
</tbody>
</table>

Due to the initial difference in nutritional management of the two study groups, it is important to ensure that the number of patients who received their first skin graft within the first 5 days post burn was similar in both groups. No patients in either the EEF group or LEF group received any skin grafts within the first two days post burn. Within the first 5 days post burn 4 children in the EEF group received their first skin graft, versus 3 children in the LEF group. Three patients in the EEF group did not require any surgical intervention, compared to two patients in the LEF group. There were no significant differences between the two treatment groups with respect to the total...
number of skin grafts performed, or the total number of dressing changes done in theatre.
Introduction

Thermal injury results in major changes to the metabolic and physiological systems of children. The control of the metabolic changes post burn injury, shifts from the thyroid axis to that of the sympathetic adrenal axis. Free thyronine ($T_4$) and free 3,5,3'-triiodothyramine ($T_3$) serum levels decrease, while reverse $T_3$ (inactive metabolite) increases. Accelerated releases of mediators cause changes in the hormonal profile. Increased Catecholamines (Norepinephrine and Epinephrine) stimulate $\alpha$-receptors and $\beta$-receptors respectively. The thyroid remains responsive to TSH (Thyroid Stimulating Hormone), even though the levels are diminished. Increased catabolic hormones (cortisol and glucagon), with a decreased anabolic (insulin, insulin-like growth factor-1(IGF1)) response have been documented. These hormonal changes cause an increased rate of tissue catabolism, loss of lean body mass and depletion of energy and protein reserves. Table 6.1 provides a summary of these events. Systemic hypovolemic shock develops due to increased vascular permeability. Fluid moves into the interstitial spaces (oedema) and loss of intravascular fluid leads to dehydration, decreased urinary output and acute renal failure within a few hours post burn. The initial phase of hypotension, decreased cardiac output, hypothermia and decreased oxygen consumption is often referred to as the Ebb phase. Thereafter the Flow phase follows, which is characterized by changes to the metabolic system e.g. hepatic gluconeogenesis. However, the literature does not agree exactly as to when the ebb phase stops, and when the flow phase begins, since the transition is influenced by multiple factors. Examples of such factors could include the timing and effectiveness of the initial resuscitation, different resuscitation protocols, depth and extent of the burn injury and early or delayed enteral feeding.

5.1 The changes in Macro-Nutrient Metabolism

5.1.1 Lipid metabolism

Increased lipolysis occurs as a result of the elevated secretion of cortisol, catecholamines (epinephrine and nor-epinephrine) and glucagon levels. Catecholamines are the predominant stimulator of the hydrolysis of stored triacylglycerols via the enzyme, hormone sensitive lipase. Fatty acids are released at a rate in excess of their rate of oxidation. The non-oxidized fatty acids are "recycled" by being re-esterified to triacylglycerol. If the re-esterification occurs in the liver under
normal circumstances, the newly formed triacylglycerols will be secreted into the blood as very-low-density lipoproteins (VLDL), so that the fat can be transported back to peripheral adipose tissue for storage. Under normal conditions, about half of the fatty acids released by lipolysis are re-esterified. In severely burned patients, the percentage is increased to greater than or equal to (>) 65% because lipolysis is stimulated to a greater extent than is fat oxidation. Consequently, there is a fivefold increase in triacylglycerol-fatty acid recycling in burn injury patients. This indicates that there are far more endogenous fatty acids available as energy substrates, than are required to meet energy demands. The body still prefers to utilize its own triglycerides, even when exogenous fat is provided in the nutritional support. This was shown by the injection of stable isotope tracers. Non-esterified fatty acids (NEFA) are converted into either triglycerides and incorporated into lipoproteins, or get oxidised into Acetyl Co-enzyme-A (ACo-A) in the Krebs' cycle.

5.1.2 Carbohydrate Metabolism

An elevated rate of glucose production is central to the disruption of normal glucoregulation in burn injury. Furthermore, the normal suppressive action of exogenous glucose intake on endogenous production is either diminished or completely lost in burn patients. Consequently, a major component of clinical hyperglycemia is the excess rate of appearance of glucose from endogenous production. High circulating glucagon levels, possible peripheral insulin resistance as well as decreased insulin production and decreased insulin:glucagon ratios (I:G), may result in elevated blood sugar levels and hyperglycemia. Glucagon is the primary stimulator of the excessive glucose production in adult burn patients, with elevated concentrations for weeks, yet maintaining its effectiveness in stimulating glucose production. The persistent effectiveness of glucagon may result from an interaction with other catabolic hormones, such as epinephrine and cortisol, which are usually also elevated at this time.

Wolf et. al. showed that there is no impairment in pyruvate oxidation in severely burned children. Rather, the high rate of lactate production in burn patients derives from the extraordinarily high rate of appearance of pyruvate. The latter is caused in part by the rapid rate of glucose uptake from plasma. The rate of glucose uptake is essentially dictated by the rate of appearance of glucose in the blood, and is therefore not at odds with the notion of peripheral insulin resistance. Once inside the cell, glucose is metabolised similarly in burn and normal patients. Glucose should therefore be a good energy substrate for burned patients, even though normal plasma glucoregulation is altered.
5.1.3 Protein Metabolism

The initial glycolysis post burn injury [formation of lactic acid and pyruvate to ATP (Adenosine tri-phosphate)], is short lived. Together with an increase in catabolic hormones and a concomitant decrease in anabolic hormones, hepatic gluconeogenesis follows shortly thereafter. Severe protein catabolism due to the high alanine and glutamine usage leads to loss of lean body mass. Amino acids and fatty aids, become the preferred source of energy.

However, Wolf et. al. showed that the protein breakdown in the burned patient is evident at the whole-body level as well as at muscle level. It seems that it persists throughout hospitalization as well as after discharge. The elevated stress hormones were always assumed as the mediators, but lowering the glucagon concentration in burn patients had little effect on protein breakdown. The stress hormones returned to baseline in the convalescent phase, but protein breakdown was still accelerated. Thus, the cause of accelerated protein breakdown in catabolic patients was not known. Therefore, the possibility of altered amino acid transmembrane transport kinetics were investigated. Multiple amino acid tracers labeled with stable isotopes were used to quantify the relation between the rates of inward and outward transport of amino acids in muscle, to the rates of muscle protein synthesis and breakdown, as well as to the size of the intracellular free amino acid pool.

There was a reduction in the rate of inward transport of amino acids such as leucine and phenylalanine, and an acceleration in the rate at which a given amount of amino acid was transported out of the muscle into the blood. The intracellular amino acid pool size was also markedly reduced. The change in transport in burn patients favoring a net efflux of amino acids from the intracellular compartment results in reductions in some of the intracellular amino acid concentrations in burn patients at values that are 70% or more below the normal value. Thus, the enhanced net flux of amino acids leads to a drop in intracellular amino acid concentrations, which in turn may be a primary stimulus for breakdown to restore amino acid concentrations to normal values. This probably explains why, in a variety of critically ill patients, nutritional support alone seems to be ineffective in completely inhibiting the net loss of muscle protein.

In an attempt to correct the post burn altered amino acid transmembrane transport kinetics, one would require normal insulin levels as well as adequate dietary protein intake. Insulin treatment has been shown to promote muscle anabolism, stimulate protein synthesis and inhibit protein breakdown. In a recent study done by Ferrando et. al., they treated a group of adult burned patients with a sub-maximal dose of exogenous insulin and then compared them to a non treated group. After the infusion of stable isotopes, they found the net amino acid balance was significantly improved with insulin treatment. The skeletal muscle protein synthesis was also significantly improved.

13, 19
greater in the group that received insulin, and it did not affect the glucose or amino acid uptake or require a greater caloric intake to avoid hypoglycemia.

Diagram 5.1: Summary of the Metabolic and Hormonal response post burn
5.2 The effect of early enteral feeding (EEF) vs. late enteral feeding (LEF) on the hormonal response post thermal injury

Since the seventies, research has shown that the hypermetabolic response could be decreased or even attenuated by the initiation of enteral feeds within 24 hours post burn. Most research was done on burned adults or animals, with a few referring to the paediatric patient (0-13 years).

A number of hormones are involved in the stress response after major injury. Although data on the hormonal response of the paediatric patient to severe stress is limited, most workers in the field believe that the hormonal response of the paediatric patient cannot be compared to that of the adult. In contrast to adult burn patients, paediatric burn patients seem to have a catabolic response that is of a greater magnitude but a shorter duration than that of the adult. There are even marked differences in the catabolic hormonal response post surgery between pre-term neonates, term neonates and children, but a remarkable consistency was found in the stress hormonal pattern of the 1 to 10 year old age group. However, from the pre-term neonate under severe stress to the 10 year old child, each category’s catabolic hormone concentrations responded differently to that of the adult under severe stress. Burned children between the ages of 5 months and 12 years old, demonstrated elevated cortisol levels, which returned to normal within 24 hours post burn.

The anabolic hormones were found to be inappropriately low after thermal injury in the adult patient. Decreased insulin secretion, possible resistance at cellular level and long term (up to 4 weeks) elevated glucagon levels, might explain the hyperglycemia and decreased I:G ratios. However, the child seem to have an enhanced insulin secretion after surgery, which might explain why they often recover faster from surgery than adults. The hormone concentrations that were reviewed by this study include insulin, insulin-like growth factor-1 (IGF1), growth hormone (GH), glucagon and cortisol. The different hormones and their response to feeding or starvation are discussed below.

5.2.1 Catecholamines

During the previous two decades, Wilmore et al. and Alexander et al. found the catecholamines in burned adults and guinea pigs to be elevated post thermal injury. However, Chiarelli et al. found that by feeding these patients within 4.4 hours post burn, the catecholamines stayed within the normal ranges. In contrast to the EEF
group, the other group was fed 55 hours post burn, and had abnormally elevated levels until day 16 post burn. EEF seemed to be able to decrease or attenuate the stress response in the adult burned patient.

Looking at the paediatric burned patient, Cone et. al. found no significant differences in the norepinephrine or epinephrine levels between a group of paediatric patients that developed a hypermetabolic response, and the other group who did not. All 104 of these patients received EEF, but 13 did not develop a hypermetabolic response. These 13 patients had a significantly lower (p<0.05) evaporative heat loss (38.31watts/m² ± 12.0 vs. 49.37watts/m² ± 15.2). This difference was not easily explained, as the burn size, environment and nutritional treatment was virtually identical.

This study did not investigate catecholamine concentrations due to the costly and unavailability of plasma sample analysis.

### 5.2.2 Cortisol

Moss et. al. investigated a group of beagles that underwent intestinal surgery. One group was EEF (within 2 to 36 hours post surgery), and the other was fed late (after 36 hours post surgery). The EEF group's cortisol concentrations returned to basal levels faster, but this failed to reach significance. When pre-burn guinea pigs were compared to those burned and fed with either EEF or parenteral nutrition (PN), the cortisol concentrations were higher in the PN group on day 1 and 4 post burn. The EEF group had similar cortisol concentrations to the pre-burn group. Mochizuki et. al. and Dominioni et. al. also found similar cortisol concentrations in the EEF group when compared to the pre-burn group of guinea pigs. The LEF group had significantly elevated concentrations on day 1 and 14 post burn.

McArdle et. al. compared burned adults that were either EEF (< 48 hours) or LEF (> 96 hours) to healthy volunteers. She found elevated cortisol concentrations up until day 6 post burn in both the EEF and LEF groups. Cortisol concentrations were measured for the first 10 days post burn. However, no significant differences were documented between the EEF and LEF group. Chiarelli et. al. and Jenkins et. al. did not find a significant difference between EEF and LEF burned adult groups. Jeffries et. al. investigated 6 adult burned patients that were fed enterally and parenterally. Their urinary free cortisol concentrations (which is an accurate measure of total cortisol secretion), were elevated for 2 weeks post burn.

In contrast, paediatric burned patients did not demonstrate elevated cortisol concentrations, except during the period of 24 to 36 hours post injury. Thereafter the
concentrations returned to the normal range. Unfortunately the method of feeding was not mentioned.  

5.2.3 Glucagon

Mochizuki et al. found similar glucagon concentrations in the EEF and the pre-burn guinea pig groups. The LEF group only experienced significantly elevated concentrations on day 1 and 14 post burn.

Some authors have reported elevated glucagon concentrations after thermal injury in adult patients, whereas others have not. Jenkins and Gottschlich et al. documented elevated glucagon concentrations for 4 weeks post burn in both their EEF and LEF groups. There was no significant difference between the EEF and LEF groups. However, McArdle et al. compared EEF (<48 hours) burned adults to LEF (>96 hours) burned adults, and found the glucagon concentrations to be surprisingly stable. The concentrations were not above the normal range and no significant differences were documented between the two groups. The only exception was Chiarelli et al., who found significantly lower concentrations of glucagon in the EEF group (adult burns) on day 8, 12 and 20, but not for the entire study period. No specific data was found on the paediatric patient's glucagon response to thermal injury.

5.2.4 Insulin

It was common to observe exceptionally low insulin concentrations in burned patients before early nutritional intervention was instituted. Wilmore et al. had to provide insulin infusions in order to control the elevated blood sugar levels. This particular group of patients only received nutritional support from day 6 post burn. Nutritional support was given either enterally and or parenterally. In contrast, McArdle et al. found no significant differences between the EEF (<48 hours) and LEF (>96 hours) groups, and both groups had insulin concentrations within the normal ranges. The timing of the nutritional intervention seems to be the difference between the Wilmore and McArdle burned patients. Wilmore only initiated nutritional support on day 6 post burn, whereas McArdle started within either < 48 hours or by day 4 post burn. Therefore it seems as if earlier (< 4 days post burn) nutritional intervention results in an more anabolic response.

Chiarelli et al. took EEF one step further, by introducing the enteral feed within 4.4 hours post burn. Significantly higher insulin concentrations in the EEF vs. LEF (>55 hours) group were documented on day 4 and 8 post burn. Therefore, it seemed as if EEF resulted in a degree of anabolism in the burned adult.
No authors were found that investigated the response of insulin to either EEF or LEF in the paediatric burned patient. Deshpande et al. documented enhanced insulin secretion in paediatric patients who underwent surgery, but did not compare the effect of EEF to LEF.

### 5.2.5 Insulin:Glucagon (I:G) Ratios

In contrast to Wilmore et al. who provided nutritional support on day 6 post burn to burned adults, and documented decreased insulin:glucagon (I:G) ratios, Moss et al. found increased I:G ratios in animals who had received EEF within 36 hours post surgery. The EEF animals were compared to LEF (>36 hours) animals. I:G ratios for either EEF or LEF are not well documented in burned adults. No information could be found on burned children.

### 5.2.6 Insulin-like Growth factor-1 (IGF 1)

IGF1 concentrations are often decreased following burn injury. Lang et al. studied the IGF1 concentrations of adult burned patients and compared them to healthy volunteers. They concluded that the burn injury produced dramatic and sustained alterations to the various components of the IGF1 system despite adequate early enteral nutritional support. Abribat et al. and Jeffries et al. also compared adult burn victims to healthy volunteers. They found decreased IGF1 concentrations for up to two weeks post burn, which returned to normal thereafter. The IGF1 concentrations were so low during those first two weeks, that a statistical significant difference was found when the concentrations returned to the higher levels of normal. Both study groups received EEF within 24 hours post burn, and some patients also received parenteral nutrition.

No documentation was found in either adult or paediatric burned patients that compared EEF to LEF and the response of IGF1 concentrations as a result.

### 5.2.7 Growth Hormone (GH)

Similar to IGF1 concentrations, it is quite common to observe subnormal concentrations of growth hormone (GH) after a thermal injury. Jeffries et al. provided adequate enteral and parenteral nutritional support to adult burn patients and compared their GH levels to healthy volunteers. They found the GH concentrations significantly lower than normal and to stay that way, even after 4 weeks post thermal injury. GH is generally very difficult to measure, since the secretion is controlled mostly by the central nervous system and occurs in bursts with more than half of the total daily amount during early sleep. The concentrations are therefore highly fluctuating due to the pulsatile release. However, due to the persistently low GH concentrations in
burned patients, exogenous recombinant human growth hormone treatment was started in the sixties. The positive effects reported after growth hormone treatment included an increased appetite, decreased nitrogen losses, increased retention of nitrogen and potassium, weight gain, more rapid wound healing and increased oxygen utilization. However, it was also shown that GH treatment in burned patients resulted in a decreased respiratory quotient, significant serum elevations of total catecholamines, glucagon and free fatty acids, as well as the induction of insulin resistance by inhibiting glucose transport resulting in hyperglycemia. In a recent study performed on 263 burned children (0 to 18 years old), there were no differences in mortality, septic complications and organ dysfunction between the GH treatment group and the saline placebo group. The GH treatment group required more exogenous insulin due to hyperglycemic episodes, whereas the exogenous albumin requirements and the development of hypocalcemia were reduced. No documentation was found in either adult or paediatric burned patients that compared the effect of EEF to LEF on GH concentrations.
Results

All the venous blood samples for the hormonal analysis were taken on admission, and thereafter between 7am and 8am on days 1 to 5, day 12, day 19 and day 26 post burn.

Cortisol

During the study period there was no significant difference in the serum cortisol concentrations between the EEF and LEF groups as can be seen in figure 5.1. The normal range for the cortisol concentrations is between 5.52 nmol/L and 800 nmol/L. The confidence interval for the EEF group was (424.27; 614.34), and for the LEF group it was (312.29; 509.84).

Figure 5.1: Median serum Cortisol concentrations (nmol/L) over time in the EEF group and in the LEF group

The range of values for patients in the LEF group appeared to be slightly higher than those in the EEF group, but otherwise the median values for the 2 groups were fairly similar throughout the study period. Early on (0 to 24 hours post burn) both groups had cortisol concentrations in the high normal range, which decreased to the lower range...
of normal thereafter. The concentrations remained in this range for the rest of the study period. The majority of the patients in both groups fell within the normal range of values. There were a few extreme values in the LEF group. The Cortisol concentrations decreased linearly over time in both groups.

Glucagon

The EEF group had lower plasma glucagon concentrations than the LEF group on day 3, day 4 and day 26 post burn as can be seen in figure 5.2, but this failed to reach significance. The normal range for the glucagon concentrations is between 25 pg/ml and 250 pg/ml. The confidence interval for the EEF group was (238.98 ; 639.45), and for the LEF group it was (277.28 ; 1015.61).

Figure 5.2: Median plasma Glucagon concentrations (pg/ml) over time in the EEF group and the LEF group

Although the patients in the EEF group experienced lower glucagon concentrations on days 3 ($p=0.09$), 4 ($p=0.6$) and 26 ($p=0.5$) post burn, the results failed to reach significance. There was no significant difference between the EEF and LEF groups for the entire study period. The glucagon concentrations appeared to be increasing over time in both treatment groups ($p=0.01$). The majority of the patients in both groups was
above the normal range for glucagon concentrations, and persisted with it for the entire 26-day study period.

**Insulin**

The EEF group's serum insulin concentrations were significantly higher than the LEF group for the entire study period of 26 days (p=0.008), as shown by figure 5.3. The normal range for the insulin concentrations is between 0 mU/L to 30 mU/L. The confidence interval for the EEF group was (6.88; 28.01), and for the LEF group it was (10.88; 31.56).

**Figure 5.3: Median serum Insulin concentrations (mU/L) over time in the EEF group and the LEF group**

Many of the children in the EEF group had insulin concentrations above the normal range. On days 2, 4 and 5 the median insulin concentrations in the EEF group were above normal (37 mU/L, 48 mU/L and 84 mU/L respectively). On days 12, 19 and 26, the EEF group's insulin concentrations decreased to within the normal range (24
mU/L, 12 mU/L and 16 mU/L respectively). The insulin concentrations in the LEF group remained within the normal range for the whole study period. The LEF group demonstrated insulin concentrations within the lower normal range (4 to 5 mU/L) initially, thereafter the insulin concentrations increased to between 15.5 to 27 mU/L until day 26-post burn.

**Glucose**

There was no significant difference between the median serum glucose concentrations for the EEF and LEF groups, as shown by figure 5.4. The glucose concentrations were measured on admission, and thereafter once a week, for 4 weeks. The normal range for the glucose concentrations is between 3 g/L to 6.5 g/L. The confidence interval for the EEF group was (4.89; 6.46), and for the LEF group it was (3.52; 7.47).

**Figure 5.4: Median serum Glucose concentrations (g/L) over time in the EEF group and the LEF group**

![Box plot of glucose concentrations](image)

Both the EEF and the LEF groups demonstrated elevated glucose concentrations on admission of 10.3 g/l and 8.1 g/l, respectively. However, only glucose concentrations
that persist above 12g/l, or result in documented metabolic acidosis are treated with exogenous insulin. None received exogenous insulin therapy during the study period. During weeks 1 and 2 thereafter, the two treatment groups had glucose concentrations that varied between 6.1 g/l and 7.8 g/l. Both the EEF and LEF groups had glucose concentrations within the normal ranges for weeks 3 and 4.

**Insulin:Glucagon Ratios**

Figure 5.5 shows the I:G ratios were significantly higher in the EEF group up until day 4 (p=0.04), and it approached significance up to day 12 (p=0.08), when compared to the LEF group. Thereafter it phased out. The confidence interval for the EEF group was (0.21 ; 0.06), and for the LEF group it was (0.14 ; 0.76).

**Figure 5.5: Medians for the Insulin: Glucagon Ratios over time in the EEF group and the LEF group**

![Graph showing Insulin:Glucagon Ratios over time](image)

**Insulin-like Growth Factor-1**

The EEF group had higher serum insulin-like growth factor-1 (IGF1) concentrations than the LEF group on day 5, day 19 and day 26 post burn as can be seen in figure 5.6, but this failed to reach significance. The normal range for the IGF1 concentrations...
is between 36 ng/ml - 350 ng/ml. The confidence interval for the EEF group was (93.71 ; 264.68), and for the LEF group it was (87.27 ; 243.55).

**Figure 5.6: Median serum Insulin-like Growth Factor-1 concentrations over time in the EEF group and LEF group**

There was no significant difference in the IGF1 concentrations between the EEF and LEF group during the study period. Most of the IGF1 concentrations and all the median concentrations for both groups fell between the normal ranges.

**Growth Hormone**

Due to the fact that the data was not normally distributed, a log transformation of the serum growth hormone (GH) concentrations was performed as shown in figure 5.7. The normal range for the GH concentrations is between 0.5 mU/l to 150 mU/l, but all the values were changed to log transformation. The geometric mean and standard deviation for both the EEF and LEF groups were 8.9 ±16.6 and 11.64 ±18.33.
respectively. The confidence interval for the EEF group was \((-0.93 \, ; \, 2.77)\), and for the LEF group it was \((-0.11 \, ; \, 2.31)\).

**Figure 5.7:** The log transformation of serum Growth Hormone concentrations (mU/l) over time in the EEF group and the LEF group.

Further examination of the data revealed that there were no particular individuals increasing the variability. The GH data contained a fair amount of missing values, as the serum samples were inadequate on certain days for certain patients. From admission up until day 12 post burn the LEF group had significantly \((p=0.03)\) higher GH concentrations compared to the EEF group. This disappeared thereafter. However, the GH concentrations for both groups stayed within the lower normal range.
for the whole study period. The EEF and LEF groups' standard deviations were quite large, which is not unexpected since the data was not normally distributed.

**Discussion**

There were no significant differences in serum cortisol concentrations between the two treatment groups and both groups only experienced concentrations on the higher range of normal. In the first 24 hours post burn the concentrations were the highest for both groups, but the concentrations dropped immediately thereafter to the lower range of normal. Most serum cortisol concentrations stayed within the normal ranges for the whole study period. Similar results were found in paediatric burned patients, by Sedowofia et al. They only monitored the patients for the first 5 days post burn, but documented an initial rise (0-24 hours post burn) with a decrease thereafter. In contrast, adult burned patients have demonstrated elevated urinary free cortisol concentrations for up to two weeks post burn. This supports the fact that the catabolic response in children is of a shorter duration than that of adults under severe stress. The stress response is controlled by multiple factors, of which pain control plays a vital role. Complications such as an inhalation injury could increase the stress response and pain levels. However, the six children that sustained an inhalation injury, did not have higher concentrations of catabolic hormones compared to those that did not have an inhalation injury. Meticulous pain and temperature control, occlusive dressings and EEF could all play a vitally important role in the management of the stress response. The standard pain control regime for procedural pain as well as background pain were given to all the children that partook in this study. An example of the standard pain management is provided in Appendix 5. All the children received occlusive dressings, were treated at an environmental temperature of 25°C and additional heaters were provided when necessary.

There seem to be similarities in the glucagon concentrations of the patients investigated in this study, and that of adult burned patients treated by Jenkins and Gottschlich et. al. Glucagon concentrations were elevated for 4 weeks in both adult and paediatric burned patients, irrespective of EEF or delayed enteral feeding. Furthermore, our study patients in both the EEF and LEF groups seem to experience an increase in glucagon concentrations over time. Unfortunately, no information was found regarding the glucagon concentrations of the paediatric patient after a thermal injury in order to compare our study results. A controlled clinical trial that investigate glucagon concentrations in paediatric burned patients for longer than 4 weeks post burn, is suggested. Such information might explain this phenomena of ongoing elevation of glucagon values, and at what point post burn the concentrations return to normal.
Chiarelli et al.\textsuperscript{29} was the only author that found significantly lower glucagon concentrations for the EEF vs. LEF adult burned group on days 8, 12 and 20 post burn. The patients in our EEF group also experienced lower glucagon concentrations on days 3, 4 and 26 post burn, but the results failed to reach significance.

Glucagon is documented as the primary stimulator of increased glucose production in the adult burn injury, especially since the concentrations are usually elevated for weeks post burn.\textsuperscript{11} It also seems that its effectiveness in stimulating glucose production is maintained during the largest part of this period.\textsuperscript{12} Both the EEF and LEF (17.9g/l ± 5.3) groups experienced a high incidence of hyperglycemia, requiring exogenous insulin therapy.\textsuperscript{12} The majority of the patients in our two treatment groups had persistent elevated glucagon concentrations for the entire study period of 26 days. However, the median blood glucose concentrations in both the EEF and LEF groups were only slightly elevated on admission (10.3g/l; 8.1g/l, respectively) and thereafter for the first 7 days post burn (6.9g/l; 7.8g/l, respectively). Thereafter, the median glucose concentrations returned within the normal ranges for both treatment groups. Persistent elevated glucagon concentrations in the paediatric burned patient does not seem to stimulate glucose production to the same extent, as it does in the burned adult. The blood glucose concentrations seem to be independent of glucagon concentrations in the paediatric burned patient.

Looking at the anabolic response, the EEF group’s insulin concentrations were significantly higher for the entire 26-day study period when compared to the LEF group. The EEF group initially had insulin concentrations above the normal range, which decreased within the normal range from day 12 post burn and thereafter. In contrast, the adult burned patient commonly has low insulin concentrations post burn.\textsuperscript{24} This might explain why adult burned patients experienced hyperglycemia for long periods,\textsuperscript{12} in comparison to the initial 7 days post burn in paediatric burned patients in our study groups. Although both our study groups experienced initial elevated glucose concentrations (first week post burn), the EEF group had significantly higher insulin concentrations during that period in comparison to the LEF group. Similarly to the glucagon concentrations, the glucose concentrations in both study groups seem to regulate independently of the insulin concentrations. Multiple factors seem to influence the blood glucose concentrations.

In an attempt to normalize and increase the adult burned patient’s insulin concentrations, sub-maximal exogenous insulin treatment resulted in a significantly improved net amino acid balance and skeletal muscle protein synthesis.\textsuperscript{20} It has been shown that the burned adult demonstrates significantly higher insulin concentrations in response to EEF, but only on certain days and not for the entire 28-day study period.\textsuperscript{20} The infant and the child seems to respond to all severe trauma with a more
efficient anabolic response than the adult, as was documented by Deshpande et. al., which may explain why children generally heal much faster than the adult patient. However, the LEF group studied by the investigator had low normal insulin concentrations until day 3 post burn. Enteral feeding was initiated on day 3 post burn, and there was a marked increase in the insulin concentrations (from 5 mU/L to 15 mU/L) that persisted until day 26 post burn. Although it seems as if children have a naturally higher anabolic response to severe trauma, enteral feeding and the timing thereof seems to make a significant contribution.

The difference in insulin:glucagon ratios between the two treatment groups were significantly higher in the EEF group up until day 4, also approaching significance up until day 12 post burn. Together with the significantly higher insulin concentrations in the EEF group, this could suggest that the anabolic processes were faster and more effective in the EEF group compared to the LEF group. Furthermore, when these results were compared to the anabolic response found in burned adults treated with EEF, there seem to be a much more significant anabolic process taking place in the paediatric burned patient also receiving EEF.

As a result of the higher insulin concentrations in the EEF group, one would expect the IGF1 concentrations to behave similarly. However, although the EEF group had higher IGF1 concentrations on days 5, 19 and 26 post burn, this failed to reach significance. There was no significant difference in the IGF1 concentrations between the two treatment groups for the whole study period. What was interesting was the fact that neither of the two groups experienced concentrations below normal for the entire study period. In contrast adult burns had subnormal IGF1 concentrations for 2 weeks post burn. Burned children seem to have a more enhanced anabolic response to EEF than adults.

The LEF group had significantly higher concentrations of growth hormone (GH) up until day 12-post burn when compared to the EEF group. Hypoglycemia was not the stimulus in the LEF group for the significantly higher release of GH, and another mechanism must be involved. GH has demonstrated anabolic as well as catabolic properties. The initial starvation of the LEF group seems to initiate a more active catabolic process, that takes up to 12 days to correct. Increased protein turnover with elevation of both protein synthesis and breakdown, increased free fatty acid levels, increased catecholamine levels, hyperglycemia due to the induction of insulin resistance and inhibition of glucose uptake relative to the availability of insulin and impaired glucose oxidation have been documented with treatment of exogenous GH. On the other hand, improved wound healing, increased insulin and IGF1 concentrations have also been documented. In contrast to adult burned patients, both our treatment groups’ GH concentrations stayed within the normal range.
throughout the study period. Significantly lower than normal GH concentrations were
documented by Jeffries et. al.\textsuperscript{23} in burned adults and these concentrations persisted
as subnormal for more than 4 weeks post burn. GH seems to act in a catabolic
capacity in periods of severe stress, as was demonstrated by the significantly higher
concentrations in the LEF group. There also appeared to be a general decrease in GH
concentrations over time for both groups. The catabolic effect seemed to decrease as
the burned patient recovered over the study period of 26 days.

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6.1 Predictive Equations for the estimation of energy requirements in children with burns

The extent of energy expenditure is influenced by several factors including ambient temperature, severity of the burn, method and care of dressing changes, procedural and total pain control, as well as physiotherapy and occupational therapy. It is unclear how much of the elevation in resting energy expenditure (REE) is due to the presence of the burn injury itself and what proportion each of the above mentioned factors contribute.

It is generally agreed that aggressive nutritional support has improved morbidity and mortality after severe burn injury. However, it is also evident that in severely stressed patients, excessive energy intake cannot completely overcome the protein catabolic response and can have detrimental physiological effects. These effects include peripheral muscle wasting evidenced by spindled extremities balanced by truncal obesity. Such an appearance would support the hypothesis that overfeeding during the hypercatabolic state post burn, results in loss of lean body mass and subsequent central fat deposition. Overfeeding may complicate patient management with delivery of excessive obligatory fluid and increased basal energy expenditure. It is therefore important to estimate requirements as accurately as possible. Often the available equations overestimate energy requirements. Even the original data presented by Curreri argue against the validity of the equation, because those patients receiving significantly less calories than prescribed by the Curreri equation, maintained body weight. The one patient who lost weight received only 20% of the estimated requirements. The adapted paediatric Solomon's formula does not overestimate as much as the Curreri equation, but does more so than the most recent Galveston equations.

The revised Galveston formula is widely accepted as one of the most accurate equations available. Hildreth et al. recently evaluated this equation by stipulating that discharge weight is within 5% of admission weight. The study included 102 children less than 12 years old, with a total body surface area burn (TBSAB) greater than or equal to 30%. Sixty-five children showed a weight loss of 5% from admission to discharge, 34 children gained more than 5% of their dry weight and only 3 children lost more than 5% of their dry weight. The estimate of calories per body surface area (BSA) for each day throughout the hospital stay, was analysed by...
multivariate-regression. Holland et al.\textsuperscript{15} more recently evaluated the Galveston equations, by comparing four different equations to actual energy consumption through the measurement of indirect calorimetry. Twelve subjects between one to twelve years of age with a mean TBSA of 27% were reviewed retrospectively. Analysis of variance was used to compare the patients' energy intake with their estimated energy needs. The Galveston formula was the closest estimate to the actual energy consumption as measured by indirect calorimetry.

Although the recommended daily allowance (RDA)\textsuperscript{16} is designed for healthy children, investigators also suggest that it is a rational method for determining energy needs in burned children. The RDA, in addition to other factors, accounts for physical activity. It has been suggested that reduced activity levels offset increased calorie requirements for hypermetabolism after severe burn injuries.\textsuperscript{17}

6.2 Actual Energy Expenditure measured by Indirect Calorimetry

Energy expenditure as measured by indirect calorimetry (IC) with an additional activity factor of 30%, seems to be the most accurate manner of determining the energy requirements for burned patients. The resting energy expenditure (REE) as measured by indirect calorimetry with an activity factor added, is referred to as estimated energy expenditure (EEE). Maintenance of admission weight is well documented with the use of EEE, and the possibility of overfeeding is far less.\textsuperscript{10, 18, 19}

Although REE as measured by indirect calorimetry has variations even in normal volunteers that is not explained by body size or body composition,\textsuperscript{20} it seems to be the most reliable actual estimate of energy requirements in the burned child.\textsuperscript{6}

Goran et al.\textsuperscript{6, 21} investigated the doubly labeled water technique in order to predict the EEE of burned children. A strong correlation was found when an activity factor of 20% was added to the REE. The REE was measured by indirect calorimetry. The predicted basal energy expenditure (PBEE) was determined by using the Harris-Benedict equation. The indirect calorimetry measurements were done on a daily basis, early in the morning, without the patient going nil by mouth for a few hours, but rather while the continuous feeding was uninterrupted. No attempt was made to standardize conditions e.g. fever, infection, antibiotics, pain medication, nutritional status prior to the injury, excisional surgery and daily activities e.g. dressing changes, physiotherapy and occupational therapy. The rationale for this approach was to examine the determinants of measured REE under the usual clinical conditions. The results indicated that neither time after the burn injury, nor burn size was useful in predicting the magnitude of the elevation in REE. There was also no smooth transition from the hypermetabolic state to the recovery state.
The median ages of the studied groups were similar to the studies by Goran et. al.\textsuperscript{6} and Gore et. al.\textsuperscript{10}, namely 9.9 and 9 years respectively. However, Goran found the predicted EEE to be the most accurate when an activity factor of 20\% was added to the REE (measured by indirect calorimetry), whereas Gore et. al. found that adding an additional 30\% to the REE, maintained admission body weight. Nevertheless, both concluded that predicted EEE, with REE as measured by indirect calorimetry, was the most reliable estimate of energy requirements in the burned child.\textsuperscript{9, 10}

6.3 The Respiratory Quotient (RQ = \text{VCO}_2/\text{VO}_2)

The respiratory quotient (RQ) is measured as part of the indirect calorimetry measurement, and gives an indication of fat- and carbohydrate oxidation.\textsuperscript{22, 23} The literature search found that there were differences between authors in the interpretation of certain values for the RQ in the management of burn patients.\textsuperscript{24, 25, 26} These differences were not significant, but they will be discussed.

The respective authors agreed that the RQ values for fat- and carbohydrate oxidaion were 0.7 and 1.0 respectively. There was also agreement on lipogenesis to have a value of greater than 1. McClave et. al.\textsuperscript{23} stated, that by excluding protein, the non-protein RQ (nPRQ) provided a range of substrate utilization from 0.7 at the bottom (indicating 100\% fat utilization and 0\% carbohydrate utilization) to 1.0 at the top (indicating the opposite). A nPRQ of 0.85 at midpoint in this range would indicate 50\% fat and 50\% carbohydrate oxidation. In other words, a mixed substrate oxidation would yield a RQ of 0.85. Ireton-Jones et. al.,\textsuperscript{24} Hester et. al.\textsuperscript{25} and Matarese et. al.\textsuperscript{22} also suggested that a mixed substrate oxidation was indicated by 0.8, 0.8 to 0.95 and 0.85 respectively. Ireton-Jones et. al.,\textsuperscript{24} and Hildreth et. al.\textsuperscript{27} agreed on a RQ value of greater than or equal to (>) 0.8 as an indication of mixed substrate utilization. Furthermore a RQ value of less than (<) 0.8 was considered indicative of lipolysis. Hildreth et. al.\textsuperscript{27} also suggested that a low RQ (< 0.8) might indicate an inadequate calorie intake, just as a RQ > 0.95 might only suggest a net increase in carbon dioxide (CO\textsubscript{2}) production as a result of the delivery of additional carbohydrate calories.

The investigator therefore reached a conclusion that a RQ between 0.8 and 0.95 was indicative of mixed substrate utilization. A RQ of less than (<) 0.8 was considered indicative of lipolysis or possible inadequate calorie intake. However, if the patient presented with RQ's of < 0.8, but did not lose more than 5\% of his/her admission weight, the patient probably received sufficient calories. The possibility of lipolysis due to the burn injury would then be a more suitable explanation for the low RQ values. Finally, a RQ of more than (>) 0.95 could merely suggest the delivery of additional carbohydrate calories, or lipogenesis as a result of overfeeding. Overfeeding can also be measured when the discharge weight exceeds the admission weight, as normal
growth during the recovery period of a burn injury is highly unlikely.\textsuperscript{28} It was considered far more reliable to view the RQ in combination with anthropometrical measurements of admission and discharge weights.

6.3.1 Enteral Feed composition's relation to the RQ

The enteral feed composition seems to play an integral part in the metabolic adjustments during the recovery of a severely burned patient. A pilot study performed at Red Cross Children's Hospital (1997)\textsuperscript{29} suggested that even though similar paediatric burned patients groups received the same amount of calories, the RQ came closer to the desired range of 0.8 to 0.95 when the enteral feed's fat content was decreased to 20% of total energy. Simultaneously the carbohydrate content was increased to 60% of total energy, while the protein was constant at 20% of the total energy. Wolf et. al.\textsuperscript{30} provided an even lower total fat content (2 to 3% of total energy), higher carbohydrate content (75 to 80% of total energy), and a moderate to high (15 to 20%) protein content, which seemed to yield RQ values between 0.8 to 0.95 from admission in patients with burns covering up to 98% TBSAB. Concerns pertaining such high carbohydrate enteral diets were recently put to rest by Tappy et. al.\textsuperscript{31} They compared a high carbohydrate (75% of total energy), low fat (28% of total energy) enteral diet in the critically ill patient to a high fat and low carbohydrate diet. The results suggested that endogenous glucose production was similarly increased in both groups, with no significant hepatic uptake of glucose in either group. Plasma glucose and insulin concentrations were slightly higher in the high carbohydrate group, but failed to reach significance. Plasma glucagon concentrations tended to be lower in the high carbohydrate group, but similarly failed to reach significance. Plasma cortisol and triglycerides were similar in both groups, but the plasma free fatty acids concentrations were significantly higher in the high fat group.

6.3.2 Respiratory Quotients lower than 0.7

Occasionally, RQ's lower than 0.7 have been observed in some individuals.\textsuperscript{32} It was suggested that if the RQ of ketogenesis should be zero, a measured non-protein RQ less than 0.7 is conceivable when a net synthesis of ketone bodies occurs without further oxidation but subsequent retention and / or excretion. Such a situation was observed when individuals ate a ketogenic diet, or are under starvation. The ketogenic diet generally consists of 90% (plus) fat from the total calories, and the remainder of the calories are provided from a combination of protein and carbohydrates. Whereas starvation sets in motion the process of lipolysis. Both the ketogenic diet and lipolysis produce high levels of ketone bodies. Ketones that accumulate in the blood faster than they can be used by mostly muscle tissue cells for fuel, result in ketosis. In these situations, an accumulation of ketone bodies in the extracellular fluid takes place in the initial phase followed by urinary excretion of ketone bodies.
They also suggested that another metabolic factor that could lower the overall RQ, is the accumulation within the body of newly formed glucose from amino acids (gluconeogenesis). It is suggested that some newly formed glucose accumulates in the muscles. However, it is unclear how much gluconeogenesis contributes to the reduction of the overall RQ. Their theoretical calculations show that low RQ's may be explained either on the ground of increased retention and excretion of products not completely oxidized such as ketone bodies, and/or to a smaller extent by gluconeogenesis from amino acids with subsequent accumulation of glucose.

**Results**

### 6.4 Estimated Energy Expenditure [EEE]

Indirect calorimetry in both the early enteral fed (EEF) and the late enteral fed (LEF) groups were performed on admission, days 1 to 10 post burn, and thereafter on days 12, 19 and 26. An additional activity factor of 30% was added to the actual measured resting energy expenditure (REE).

The number of patients that were included in this analysis was 18. Data was not available for one patient on days 19 and 26, as well as for a second patient from days 7 to 10. The unavailability of the data was due to the death of the first patient and the early discharge of the second patient, who was then followed up on an outpatient basis.
Figure 6.1 shows the median for the estimated energy expenditure (EEE), expressed as kilocalories per kg per day (kcal/kg/d), in the EEF and LEF groups. The confidence interval for the EEF group was (58.89 ; 91.99), and for the LEF group it was (48.61 ; 83.95).

**Figure 6.1: Medians for the Estimated Energy Expenditure (REE x 1.3), in the EEF vs. LEF groups**

Although the median EEE were slightly higher in the EEF group on days 5 to 7, 9, 10, 12 and 26, there was no significant difference when compared to the LEF group during the study period (p=0.2).

### 6.5 Calculated Caloric Requirements

In addition to the indirect calorimetry measurements, the calorie requirements for both the EEF and LEF groups were calculated according the Solomon’s¹² and Galveston¹⁴ paediatric burns equations. In addition to the burns equations, the RDA¹⁶ for each patient was also calculated as a potential predictor of energy requirements. All three of these energy requirement predictors were then compared to the actual indirect calorimetry measurements. Since the calculated median values of the...
mentioned equations are so similar for both the EEF and LEF groups, the medians were used in order to display to values on one graph. Furthermore, the daily median percentage deviation of the Galveston, Solomon's and RDA equations from the EEE was calculated for both treatment groups. This was done to find the most favourable equation compared with the results of indirect calorimetry.

Figure 6.2 and Figure 6.3 show the median values for the calculated Galveston, Solomon's and RDA equations in comparison to the indirect calorimetry measurements (EEE = REE x 1.3), expressed as kilocalories per kg per day (kcal/kg/d), for the EEF and LEF group, respectively.

Unfortunately the box-and-whisker format could not be used for figure 6.2 and figure 6.3. The graph is impossible to read due to the overlapping of the box-and-whiskers from the 4 different comparisons displayed on one graph. The upper (25 %) and lower (75 %) interquartile ranges, and more descriptive statistics are expressed in tables, which could be found in Appendix 6.
Figure 6.2: The medians (kcal/kg/d) for the calculated Galveston, Solomon's and RDA equations, respectively; in comparison to the EEE for the EEF group.

Figure 6.3: The medians (kcal/kg/d) for the calculated Galveston, Solomon's and RDA equations, respectively; in comparison to the EEE for the LEF group.
There is a gradual decrease in the caloric prediction towards the end of the study period in both the Galveston and Solomon's equations. The reason for this being that both equations make use of the total percentage burn, which gradually decrease as the TBSAB is covered with skin grafts. As soon as the surgeon confirms the percentage skin graft that has taken well, the total percentage burn is decreased accordingly. As the burn injury recovered, the EEE in the EEF group were restored closer to that of healthy active children (RDA), whereas the EEE of the LEF group seems to remain lower towards day 26 post burn. The EEE compared favourable to the Galveston equation, which is meant to estimate energy requirements in paediatric burned patients. The Solomon's equation overestimated the caloric requirements. However, the RDA compared most favourable to the EEE in both study groups.

The median values of the deviation percentage (absolute [EEE-equation]-EEE x100) of the Galveston, Solomon's and RDA equations in comparison to the EEE (REE x 1.3) for the EEF and LEF groups, is shown in Figure 6.4 and Figure 6.5, respectively. The median EEE for both the study groups (ideal caloric utilization measurement), is expressed as 0%.

Unfortunately the box-and-whisker format could not be used for figure 6.4 and figure 6.5. The graph is impossible to read due to the overlapping of the box-and-whiskers from the 4 different comparisons displayed on one graph. The upper (25 %) and lower (75 %) interquartile ranges, and more descriptive statistics are expressed in tables, which could be found in Appendix 7.
Figure 6.4: The median deviation percentage of the Galveston, Solomon's and RDA equations, respectively; in comparison to the EEE for the EEF group.

Figure 6.5: The median deviation percentage of the Galveston, Solomon's and RDA equations, respectively; in comparison to the EEE for the LEF group.
The calculated Solomon's equation deviates the most from the EEE in both study groups. The Galveston equation shows less deviation from the EEE than the Solomon's equation, but the RDA demonstrates the least deviation. Therefore, comparing all three energy predictors, the EEE for both study groups compared most favourably with the RDA. There are marked deviations in the different equations when compared to the measured EEE in both study groups on admission, days 2, 8 and 12 post burn. As the burn injury recovered towards the end of the study period, all the calculated equations deviated less from the EEE as measured by indirect calorimetry.

6.6 Respiratory Quotient (RQ)

The RQ values for both treatment groups were measured as part of the indirect calorimetry measurements on admission, days 1 to 10 and thereafter on days 12, 19 and 26.

Figure 6.4 shows the median values for the respiratory quotient in the EEF and LEF groups. The confidence interval for the EEF group was (0.68 ; 0.81), and for the LEF group it was (0.71 ; 0.82).

Figure 6.4: Medians for the Respiratory Quotients in the EEF and LEF groups
The RQ's in the LEF group, compared to the EEF group, was significantly lower (p=0.03) up until day 2 post burn. This occurred while the LEF group was starved, and the EEF fed. Thereafter there was no significant differences between the two groups for the rest of the study period. Interestingly, both study groups experienced several RQ measurements of < 0.7. However, the RQ's for both treatment groups appeared to be increasing over time, as well as exceeding values of > 0.7 within the first week post burn.

**Discussion**

### 6.7 Energy requirements and expenditure

The EEF group had slightly higher EEE on days 5 to 7, 9, 10, 12 and 26, which might be indicative of a more active anabolic process, as indicated by the significantly higher insulin concentrations. However, the difference in the EEE for the EEF group and LEF group did not reach significance (p=0.2). Jenkins et. al. found the opposite in adult burned patients. They found that the LEF group required consistently more energy than the EEF group, as measured by indirect calorimetry. Since the healthy growing child's metabolism is higher than that of the healthy adult, it could be suggested that the paediatric burned child's whole metabolism might react differently to a severe burn, than that of the burned adult.

However, Gottschlich et. al. postulated that the RDA might be a rational method of determining the energy needs in burned children, since it accounts for physical activity. The suggestion was made that reduced activity levels offset the increased calorie requirements for hypermetabolism after burn injuries. Although the RDA is not generally used in clinical practice as a predictor for the energy requirements for burned patients, the results found from this study, is in agreement with the postulation made by Gottschlich et. al. Although the cortisol concentrations for both our study groups remained within the normal ranges, the glucagon concentrations remained elevated for the entire study period. This is suggestive of hypermetabolism in both the study groups. Since the RDA compared most favourably with the measured EEE from both our study groups, it seems as if the reduced activity levels did offset the increased caloric requirements post burn injury. It seems as if the RDA should be considered as a method for determining the energy requirements in paediatric burned patients, and should be investigated further.
Due to the inability of the standard caloric requirement equation to assess for individual needs and treatment procedures, it will always be more accurate to use actual measured energy expenditure. Unfortunately the equipment is not always available, therefore the percentage deviation of the RDA, Galveston and Solomon's equations from the EEE was calculated for both study groups.

The percentage deviations of the calculated RDA, Galveston and Solomon's equations in comparison to the actual EEE for both the EEF and LEF groups, deviated to a larger extent on admission, days 2, 8 and 12 post burn. Although initial shock and a possible increase of catabolic hormonal release, surgical procedures and days spent fasting for other theatre procedures were all investigated, not one common denominator was found throughout days 0, 2, 8 and 12 to explain the larger percentage deviation. The exact reasons why energy expenditure should vary from day to day, individually and between patients with similar burns and required procedures, still requires further investigation. If the entire study period for both study groups is considered as a whole, the Galveston burn equation deviates less from the EEE than the Solomon's burn equation. Similar results were found by Holland et. al. The RDA for both study groups displayed the least deviation when compared to the EEE.

All three equations deviated less from the EEE as the burn injury recovered towards the end of the 26-day study period.

6.8 The respiratory Quotient

In the first 54 hours post burn during which the LEF group fasted, the RQ was significantly lower (p=0.03) in comparison to the EEF group. The highest median RQ for the EEF group over this period was 0.72, whereas the LEF group's highest median RQ only reached 0.63. When a carbohydrate such as glucose (C₆H₁₂O₆), is oxidised, all of the oxygen utilised forms carbon dioxide and therefore the RQ is 1 (RQ = 6 mol CO₂ / 6 mol O₂ = 1.0). However, when fat is utilised some of the atmospheric oxygen forms water, and then the RQ becomes less than 1.0. If a RQ of 0.7 is indicative of 100% fat utilization, any RQ of less than 0.7 is physiologically highly unlikely. Both our study groups demonstrated several measurements of < 0.7 within the first week post burn injury. However, the median RQ's for both study groups increased to measurements between 0.7 to 0.79 thereafter.

Measurements of < 0.7 have previously been documented during the administration of a ketogenic diet or under a state of starvation. Both these situations result in ketosis. It has also been suggested that during gluconeogenesis the newly formed glucose from amino acids accumulates within the body, and contributes to the lowering of the
RQ measurements. It is unclear how much gluconeogenesis contributes to this lowering.

It is commonly documented that the thermal patient experiences lipolysis which is mainly due to the release of catabolic hormones such as catecholamines, cortisol and glucagon. Although the fatty acid levels were not measured by the investigator, both our study groups showed elevated glucagon concentrations for the entire study period. It is therefore quite likely that our treatment groups also experienced lipolysis with elevated levels of fatty acids and ketones. Gluconeogenesis is also well documented in the severely burned patient. A combination of lipolysis and gluconeogenesis might explain the initial RQ's of < 0.7 for both study groups.

Another explanation of these low RQ values could be interpreted as insufficient energy intake. However, when the actual energy intakes (see the following chapter) for the whole study period are compared to the actual measured EEE, the children in both groups ingested more calories than expended. The only exception where the caloric requirements were not met was during the first 54 hours post burn when the LEF group fasted. Therefore, even though the RQ values were below 0.8 throughout the study period, it can be assumed that both treatment groups received sufficient calories.

Another reason for RQ values below 0.8, could be the enteral feed's macro-nutrient composition. Most enteral feeds currently available in South Africa contain between 30 to 45% of the total energy as fat. This is considered too high for the burned victim. High circulating levels of triglycerides post burn and the preference of the body to utilize it's own triglycerides instead of an exogenous fat supply, seems to indicate that minimal exogenous fat is required.

Several other reasons for the initial RQ's of < 0.7 were also investigated.

Further possible options to investigate were a) the adequacy of the calibration of the calorimeter prior to the study and ongoing calibration throughout, b) the use of uncuffed ventilation tubes and possible endotracheal leaks, c) the calorimeter set in ventilator mode vs. the canopy mode, and d) inquiries to results found at different national and international units using similar technology.

The calorimeter was standardized or calibrated by Datex (the supplying company) with the burning of 100% alcohol prior to the commencement of this study. Daily calibration for flow was performed prior to each measurement for each patient, with a combination of 95% oxygen and 5% carbon dioxide. The barometric pressure was obtained from the meteorological office in Cape Town and corrected for each individual's measurement. This process is explained in more detail in chapter 3.
Cuffed tubes are not used for the intubation process in children, and none were used throughout this study. No correction was made for a possible endotracheal leak, which might be one explanation for the RQ's below 0.7 in both study groups. It was also suggested by the servicing company that measurements done on un-cuffed tube-ventilated children, will probably leak equal amounts of O₂ and CO₂, and should therefore not influence the results too much. However, some of the patients in whom indirect calorimetry was performed with the canopy method only, also displayed several RQ's of < 0.7 within the first week post admission.

Nationally there are only 3 other medical units beside the Red Cross Children's Hospital that have calorimeters available. The unit at Tygerberg Hospital that treats thermal injury patients, only acquired their monitor recently and have not used it on thermal patients. A second unit only measures healthy athletes at a sport science institute, and have never encountered RQ's of < 0.7. The remaining unit, the Surgical Intensive Care Unit at Groote Schuur Hospital was approached concerning our results. They have also documented several RQ's of < 0.7. The results of 41 ICU adult patients that had RQ's between 0.5 to 0.69 were examined. These measurements were taken at random between 1994 and June, 2000. A sub-group of eleven of the 41 patients suffered from polytrauma. An initial RQ measurement was taken within the first week of admission. A subsequent RQ measurement was performed at a median of 5 days later. These results are displayed in Appendix 8. Unfortunately, no further follow-on measurements were performed. The 11 patients' initial RQ's were between 0.5 to 0.63, and the subsequent RQ's varied between 0.63 to 0.98. The same trend was observed in both our study groups.

Inquiries at the world renowned Shriner's Burn Institute at Galveston, Texas, confirmed that they have not encountered RQ's of < 0.7. However, since they started indirect calorimetry, they have only used enteral feeds that contain less than 10% fat. Indeed, recently (last 4 years) they have only used enteral feeds that contain between 2 to 3% fat.

One practical method in South African circumstances to lower the enteral feed's fat content, would be to dilute the feed in order to achieve the 2 to 3% fat as suggested by Wolf et. al. 30 and Garrel et. al. 34 Unfortunately, this was not an option as other essential macro- and micro-nutrients would be diluted at the same time. It was therefore decided not to dilute the standard enteral feed (30% fat) currently used in the burns unit. A gradual increase in the feed concentration by additional modular protein and carbohydrate supplementation, was the only other option left to try and decrease the total calories from fat. This gradually decreased the total fat percentage to a minimum of 22%. The feed concentration has to be increased gradually due to simultaneous increase in osmolality, which could cause osmotic diarrhoea if done too
quickly. The maximum feed concentration could only be reached within 4 to 5 days from admission. The patients therefore received 30% fat for the first 48 hours (EEF group) and thereafter the total fat decreased to 22% by day 5-post burn. The LEF group (vs. EEF) took 54 hours longer to achieve the 22% fat, due to the initial fasting period.

In a pilot study performed at Red Cross Children’s Hospital (1997), the group that received a high fat enteral feed (more than or equal to 30%) from admission, seemed to increase their RQ values over time at a slower rate after the feed was changed to a lower fat feed (25%). However, the group that received a lower fat feed (25% fat) from admission, managed to increase their RQ values over time at a faster rate.29 A suggestion to utilize a lower fat enteral feed from admission during the resuscitation phase, in order to promote combined substrate utilization from early on, seems viable.

The initial low RQ’s found in both study groups cannot be explained physiologically. However, these results seem to be real rather than artifact, seen in the light of the results found at Groote Schuur Hospital. The same trend of a RQ increasing above 0.7 (within the week post admission), was also observed by another unit. Further investigation is urgently needed to understand this phenomenon.

In summary, it is suggested that the very low RQ’s found in both treatment groups in our study could be explained by faulty equipment (calorimeter), or a possible endotracheal leak in the ventilated patient measurements. Alternatively, despite our failure to understand it, the high fat content of the enteral feed used, or ongoing lipolysis30 present in the burn patient, may be a factor.

Contributing factors to the increase of the RQ values in both study groups over time could include natural recovery of the burn wounds, decreased lipolysis, or a decrease in the fat content of the enteral feed from 30% to 22% during the study period.

The ideal macronutrient enteral feed composition for the severely burned paediatric patient is discussed in chapter 10.
References


31. Tappy L., Berger M., Schwarz J-M. et. al. Hepatic and peripheral glucose metabolism in intensive care patients receiving continuous high- or low-carbohydrate enteral nutrition. JPEN 1999; 23(5): 260-68


Chapter 7

Energy and Protein Intake

7.1 Factors influencing calorie intake

After the early thirties, when it became clear that aggressive nutritional support improved the mortality and morbidity in the severely burned patient,\(^1\) the ongoing question arose: "How much is actually required?"

As discussed in the previous chapter, the burns equations are mostly flawed due to their inability to account for environmental temperatures and humidity, inhalation injury, dressing changes, skin grafting, pain and anxiety, use of sedatives, and varying activity levels.\(^2\) Equations are now viewed as approximates and guidelines only. Many burn-injury dietetic professionals prefer to compare different equations to determine ranges for estimated calorie needs, rather than absolute values.

The most accurate techniques currently available to determine actual energy consumption, are the doubly-labeled water technique and indirect calorimetry.\(^3\) These unfortunately are not always available, are time consuming and rather expensive.

Whether the caloric requirements are calculated by equations or indirect calorimetry, the patient is not ensured of receiving the calculated amount. Multiple theatre and surgical procedures during the recovery of the burn injury prevent the patient from receiving the required amount of calories. Theatre staff requires the patient to stay nil by mouth for four to six hours prior and post theatre. This is done in prevention of pulmonary aspiration that could lead to pneumonia and/or suffocation. Frequent surgical procedures, clip removals, the stretching of contracted areas and pain controlled dressing changes could result in a total of 8 to 12 hours of daily fasting. This is also often the cause for a great variability in total intakes. The larger the total body surface area burned (TBSAB), the more frequently such procedures are required. Furthermore, the enteral feed could still be provided via the feeding tube, even in the absence of an appetite; but absolutely no force feeding of solids is advised. The absence of an appetite is quite common in severe burn injuries, especially during the first phase of recovery. (Described in chapter 3.) Solid food should initially be considered as supplemental nutrition to the enteral feed, as the amounts of solids consumed are often negligible. Until there is a constant adequate solid intake as well as recognizable recovery of the thermal injury, then the enteral feed becomes a supplement to solid intake. Thereafter, a gradual shift to solid food being the sole source of nutrition, should be made. The timing of this process varies for each individual, and should be assessed on a daily basis.
In an attempt to investigate shortened fasting periods, Pearson et. al.\(^4\) did a retrospective analyses and found that adult burned patients who fasted for 2 hours achieved 28% of their calculated 24-hour caloric goals, compared with 11% in those who fasted for 2 to 8 hours and 6% in those who fasted for more than 8 hours before surgery. The caloric needs were calculated by the McLaurin modification of the Curreri formula.\(^5\) Unfortunately the actual calorie intake was not compared to actual energy expenditure as measured by indirect calorimetry, but to the burns equation mentioned. Burns equations often overestimate the caloric requirements,\(^2\) which might explain why the patients only received 28% of their calculated requirements after as little as 2 hours of fasting. The enteral feeds were provided via nasogastric feeding tubes and hourly nasogastric aspirations were performed. Feeding was withheld if the aspirated volume was greater than two times the hourly feeding rate. No patient had evidence of pulmonary aspiration and they concluded that shortened preoperative fasting periods can safely enhance nutritional support in burned patients.

Jenkins et. al.\(^6\) investigated the safety of perioperative feeding. They provided enteral support to 40 patients throughout 161 surgical procedures, and 40 patients had enteral support withheld during 129 procedures. The ages of the study patients ranged from (0.3 to 26.4) years old. The feeding tubes were placed in the third position of the duodenum under fluoroscopy and secured with staples and sutures. A nasogastric tube was inserted for nasogastric aspirations and gastric decompression. No patient in either group experienced pulmonary aspiration. The unfed group demonstrated a significant caloric deficit \((p=0.006)\) and increased incidence of wound infection \((p=0.02)\). They concluded that enteral nutritional support can be provided safely during the perioperative period and provide the additional benefits of reducing caloric deficits and wound infections.

The combination of early enteral feeding, shortened preoperative fasting periods and/or perioperative enteral feeding, seems to be the most effective nutritional support management for the severely burned patient.

### 7.2 Protein requirements and protein intake

Literature revealed that burns, major trauma and sepsis have a rapid net catabolic effect on the bodily protein stores, and the redistribution of the nitrogen pool. Muscle protein breakdown is accelerated, whereas the acute-phase proteins are produced at an increased rate in the liver. Wound repair and increased immunological activity require accelerated protein synthesis.\(^7\) The maintenance of the lean body mass is not only dependant on the nutritional support, but the provision of dietary protein and/or amino acids are essential for minimizing net protein catabolism.\(^7\) Supplemental amino acids glutamine and arginine are discussed in chapter 9.
The protein component of the enteral feed for burned patients ideally should contain approximately 20 to 25% of the total calories as protein.\textsuperscript{2, 6, 8, 9, 10} Another guideline for children less than 1 year of life, is a maximum of 4 gram per kilogram per day (g/kg/d). This should not be exceeded due to their inability to tolerate a high renal solute load.\textsuperscript{11} However, it is quite a common practice in clinical paediatric dietetics, to rather calculate the protein content as a percentage of the total energy intake. Of the total calories, it is considered quite safe to provide up to 12% protein for the child less than 1 year, even though this might occasionally exceed the 4g/kg/d limit. Weekly serum Urea and Creatinine should be requested to monitor the renal function.\textsuperscript{12}

7.2.1 Nitrogen Balance

Prelack et. al.\textsuperscript{13} compared the estimates of protein balance using the urinary urea nitrogen method. This was done to predict the total urinary nitrogen with isotopically derived estimates of metabolic protein balance as defined by the difference between rates of protein synthesis and breakdown. They concluded that urinary urea nitrogen based estimates of protein balance were imprecise as a predictor of protein balance in burned children.

Mancusi-Ungaro et. al.\textsuperscript{14} compared caloric and nitrogen balances as predictors of nutritional outcome in burned patients. They found the caloric balance to be a more accurate predictor of patient outcome than the nitrogen balance (actual dietary nitrogen intake - urinary urea nitrogen). The inaccuracy of the nitrogen balance as the collection of 24-hour urine and stool samples was mostly impractical. Extra losses during regular surgery and dressing changes, as well as the heavy use of blood products, made nitrogen loss and balance measurements highly unreliable as a guide to therapy. It was concluded that the nitrogen-output and balance, were best predicted by the actual nitrogen and caloric intakes as well as the caloric balance.

Nitrogen balance was not determined in this study, due to the impracticality of 24-hour urine and stool samples. However, the actual protein (nitrogen) intakes were calculated, as well as the caloric balances for both study groups.

7.3 Calorie Intake

The total actual calorie intake in both treatment groups was calculated from admission until day 10 post burn, and thereafter on days 12, 19 and 26. This was then compared to the actual calorie consumption [estimated energy expenditure (EEE)] as measured by indirect calorimetry. Thereafter the actual calorie intakes were compared to the measured EEE for both treatment groups to determine the mean caloric balances and
standard deviations. This was then expressed as kilocalories per kilogram per 24 hours (kcal/kg per day).

Figure 7.1 and Figure 7.2 shows the median actual calorie intake (enteral feed and solids consumed) compared to the measured EEE for the EEF and LEF groups, respectively. These are expressed as kilocalories per kg per day (kcal/kg/d).
Figure 7.1: The Median Actual Calorie Intake compared to the Estimated Energy Expenditure (REE x 1.3), for the EEF group

Figure 7.2: The Median Actual Calorie Intake compared to the Estimated Energy Expenditure (REE x 1.3), for the LEF group
There is a wide range of variability in the median actual calorie intakes for both the EEF and LEF groups over the study period. At the end of day 6 post burn, the calories that were provided from the supplemented enteral feed (without solid food consumed), was similar for both study groups. The solid food consumed was then added to these calories provided. Actual intakes (enteral + solids) varied according to the time spent nil per mouth for theatre procedures, as well as the patient's appetite for the solid food offered. After the initial 54 hours of fasting, the LEF group consumed fewer calories than the EEF group, except on days 6, and 8 to 10. However, excluding the first two days, there was no significant difference in the caloric intake for the two treatment groups for the study period (p=0.7).

After the initial 54 hours of fasting in the LEF group, the actual calorie intake for both treatment groups seem to be higher than the EEE, but this did not reach significance over the study period (p=0.4). The mean caloric balance for both study groups was determined by comparing the actual intakes to the EEE. The mean caloric balances in the EEF and LEF groups for the actual intakes compared to the EEE were +27 ±44 kcal/kg/d and +6 ±50 kcal/kg/d, respectively. There is no desired level for a positive caloric balance in the paediatric burned patient. As long as the patients achieve a positive- and not a negative caloric balance, it is assumed that adequate calories are provided for tissue repair and growth. Excluding the initial two days, the difference between the study groups' mean caloric balances over the study period, failed to reach significance (p=0.3).

7.4 Fasting Episodes

The patients were kept nil by mouth between 4 to 12 hours (mean = 7.14 ± 3.57) each time a theatre procedure was required. Theatre procedures could include debridement and or skin grafts, clip removals, the stretching of contracted areas and pain controlled dressing changes. The hours that a patient fasted on a certain day depended on the time spent in theatre on the required procedure involved, as well as the scheduling of the theatre list for that particular day. This is also often the cause for a great variability in total intakes. Fasting episodes and extensive surgical procedures could decrease the actual total intake and alter the measured EEE markedly. The amount of surgical procedures did not differ significantly for the first 5 days post burn between the EEF and LEF groups. In the EEF group no patients went to theatre between admission and day 2 post burn, whereas 1 patient fasted for theatre in the LEF group. From days 3 to 5 post burn, 7 and 8 fasting episodes were documented in
the EEF and LEF groups, respectively. The total number of episodes that the EEF group fasted over the entire study period was 41, whereas the LEF group had a total of 35 fasting episodes.

### 7.5 Protein Requirements and Protein Intake

The protein component of the enteral feed was calculated as 20% of the total calories provided, and expressed as gram protein per kilogram per day (g/kg/d). The protein from the solids consumed was added to calculate the total protein consumed. Excluding the first two days, the protein intake for the LEF group was a mean of 3.2 ±2.1 (median = 4.2) g/kg/d, whereas the EEF group received a mean of 4.5 ±1.94 g/kg/d (median = 3.1). Although the protein intake for the study period was higher in the EEF group when compared to the LEF group, this failed to reach significance (p=0.27).

### Discussion

#### 7.6 Calorie Intake, Caloric Balance and Fasting episodes

The LEF group was kept NPM during the first 54 hours post burn, during which the EEF group received considerable calories via the enteral feed given as part of resuscitation.

Although the investigator calculated and provided specific calories from the enteral feed, the time spent nil per mouth for theatre procedures determined the amount of calories received. Furthermore, although solids were offered in the form of the hospital ward diet, the patients determined the amount of solids consumed. At the end of day 6 post burn, the calculated calories that were provided from the supplemented enteral feed (without solid food consumed), were similar for both study groups. The gradual increase in supplementation is described in chapter 3 (3.10). Interestingly, it seems as if the EEF vs. LEF group had a healthier appetite, since the total intake (enteral feed + solids) were mostly higher in the EEF group after day 6, except for days 8 to 10. There was no significant difference in the caloric intake for the two treatment groups for the study period (p=0.7).

Theatre procedures such as wound debridements, skin grafts, change of dressings, stretching of skin contractures and clip removals required the patient to fast for a certain amount of hours. The larger the total body surface area burned (TBSAB), the more frequently such procedures are required. The actual time spent fasting per patient per procedure also varied individually, since it depended on the type of procedure performed as well as the order of the patient list in theatre. There was a marked decrease in caloric intake in both study groups on days 4, 7, 8 and 9 post burn.
burn. During these days between 6 to 8 patients fasted between 4 to 12 hours (mean = 10.75 ± 1.26) due to required theatre procedures, whereas the mean fasting period for the rest of the study period was 7.14 ± 3.75.

The latest surgical management of the severe burn wound is early excision and grafting. Muller et al. found this management to be highly effective and is taking severely burned patients to theatre either on admission, or within the first 24 to 48 hours post burn. During the first 24 to 48 hours for both our study groups, only 1 patient (4.7%) was taken to theatre. On day 3 post burn in both our study groups 4 patients were taken to theatre. Recently, Red Cross Children's Hospital also effectively started treating severely burned patients with early excision and grafting were indicated.

Although the surgical management of early excision and grafting is highly effective for wound management, in most burns institutions these procedures will require a total fasting period between 4 to 12 or more hours for surgery. Unfortunately this management would be to the detriment of early enteral feeding and resuscitation.

Furthermore, pain control (especially during the initial acute phase) has also become a top priority in the management of severely burned patients. The patient now goes to theatre daily or bi-daily for dressing changes. Although very effective, it unfortunately only increases the time spent nil by mouth.

Mancusi-Ungaro et al. found the caloric balance to be a significant indicator for clinical outcome, even more so than the weekly nitrogen balance performed. A positive caloric balance (more calories ingested than consumed) had a more favourable patient outcome than a negative calorie balance. There was a marked variability in the mean daily calorie intakes for the study period in both the EEF and LEF groups from our study. As a result the standard deviations for both our study groups were large, and results should be interpreted with caution. The EEF group's caloric balance was +27 ± 44 kcal/kg/d, whereas the LEF group's was +6 ± 50 kcal/kg/d. Although the EEF group's caloric balance was higher, there was no significant difference when compared to the LEF group (p=0.3).

However, since the caloric balance is suggested to be a reliable indicator for clinical outcome, although not significant, the LEF group did consume fewer calories than the EEF group over the study period, which might be indicative of a less favourable patient outcome.
**7.7 Protein / Nitrogen Intakes**

It seems most accurate to calculate the protein component of the enteral feed as a percentage of the total calories required and provided.\(^2\)\(^8\) Although calorie and aggressive protein provision (20 to 25% of the total calories) seem to aid in the maintenance of the lean body mass, it is not the only determining factor of the total nutritional outcome.\(^7\) Nonetheless, provision of dietary protein and/or amino acids are essential for minimizing net protein catabolism.\(^7\)

Mancusi-Ungaro et al.\(^14\) only gave 16% of the total energy as protein, but they found that as long as the caloric needs were met, the nitrogen amount seemed to be adequate. Although the investigator aimed to provide 20% of the enteral feed’s calories from protein, the LEF group consumed less total protein (solids included) than the EEF group. The difference in protein intake between the EEF and LEF group for the study period, did not reach significance (\(p=0.26\)).

None the less, the LEF group lost a median of 7.75% of their admission weight, whereas the EEF group only lost 3.01%. Although this is not statistically different (\(p=0.1\)), the LEF group lost more than the recommended guideline of 5%\(^15\), whereas the EEF group did not.

The reasons that the LEF group lost more weight than the acceptable 5%, could include: the initial fasting period, or the fewer calories and protein consumed over the study period. Although both study groups were offered the same standard solid diet from either day 3 or 5, the EEF group’s patients chose to consume more, themselves. This was especially evident from day 10 until day 26. The children from the EEF group seemed to have a healthier appetite when compared to the LEF group.

Although it seems as if the first two days of fasting did make the difference in the total calories and protein consumed, another explanation could be that the weight that was lost could be due to fewer calories and protein consumed by the LEF group.

However, it is still unclear whether the LEF group lost more weight compared to the EEF group due to delayed enteral feeding on admission, or due to fewer calories and protein consumed for the study period. It seem to be more accurate to compare an EEF vs. LEF paediatric burned group’s weight loss, which consumed similar total calories and protein over the study period. Although this would be difficult in a clinical setting due to different times spent nil per mouth for theatre procedures, it might be possible if all solid food are excluded for a certain period, with only the controlled enteral feed intake.
A solution for the time spent nil by mouth for early excision and grafting, and acute phase pain controlled dressing changes, is to embark on shortened fasting periods pre- and post theatre, and or perioperative feeding. Pearson et. al.\(^4\) investigated shortened fasting periods pre- and post theatre and concluded that no patient had evidence of pulmonary aspiration and that shortened preoperative fasting periods can safely enhance nutritional support in adult burned patients.

Jenkins et. al.\(^6\) investigated the safety of perioperative feeding via a nasojejunal feeding tube, and by feeding 40 patients (0.3 to 26.4 yr.) throughout 161 surgical procedures. No pulmonary aspiration was found. The group that was not fed during surgical procedures demonstrated a significant calorie deficit and increased incidence of wound infection.

Perioperative feeding and or shortened fasting pre-and postoperative periods could be considered strongly as a future option to improve patient outcome.
References:


3. Young-Ming Y., Tompkins R.G., Ryan C.M. et. al. The metabolic basis of the increase in energy expenditure in severely burned patients. JPEN 1999;23(3): 160-68


Small Bowel Integrity

8.1 The intestinal barrier

The maintenance of the intestinal barrier of the small bowel wall is imperative in order to maintain health. When the intestinal barrier is compromised the gastro-intestinal tract (GIT) could play a vital role in the pathogenesis of infection in the critically ill patient. The intestinal mucosal barrier for luminal macromolecules and microorganisms is the result of non-immunological and immunological defense mechanisms as shown in Table 8.1. The stomach and small bowel are essentially sterile in healthy children, while the colon is colonized with hundreds of different bacterial species in various quantities. These enteric bacteria serve a physiological role fermenting nutrients. However, if these organisms pass through the gut wall they can initiate a systemic infection. Compromise of this barrier could lead to increased small bowel permeability and bacterial overgrowth, and have been implicated in the pathogenesis of pneumonia, sepsis, multiple organ failure and mortality. The GIT seems to play a major immunological role in the critically ill patient.

Table 8.1: The components of the Intestinal Mucosal Barrier

<table>
<thead>
<tr>
<th>Non-immunological</th>
<th>Immunological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Acid</td>
<td>Secretory IgA (principle immunoglobulin in the lumen of the GIT)</td>
</tr>
<tr>
<td>Proteolytic activity</td>
<td></td>
</tr>
<tr>
<td>Mucin</td>
<td>Cell-mediated immunity</td>
</tr>
<tr>
<td>Microvillus membrane</td>
<td></td>
</tr>
</tbody>
</table>

Neither the non- nor the immunological defense mechanisms of the GIT are completely mature at birth, but reach maturity at about 2 years of life. The potential etiological role of intestinal barrier failure in the development of systemic infections and the septic state was based on both clinical and experimental evidence. One of the aspects of mucosal barrier function can be estimated by the intestinal permeability for macromolecules. Intestinal integrity or permeability refers to the intestinal mucosa’s capacity to allow molecules to traverse it by unmediated diffusion. Animal studies have shown that the intestine can serve as a portal for entry for bacteria and intraluminal toxins, such as endotoxin. A single dose of endotoxin given to healthy human volunteers, increased their intestinal permeability.
8.1.1 Thermal injury and small intestine permeability

Investigators found that intestinal permeability was increased in septic adult burned patients. The permeability increased as the severity of the infection increased, and it was concluded that the intestine may be a primary source of sepsis, and alternatively, the systemic response to infection may alter the gut barrier. Apparently enteral bacteria traverse the intestinal barriers in a process called bacterial translocation. These bacteria can be cultured from the blood where they might act as potent stimuli for both the immune system and endothelial cells. The severity of the inflammatory sequelae might involve several organ systems up to their failure. The gut has been termed the “motor of multiple organ failure”.

Malnutrition and starvation leads to a decrease in intestinal mucin, and an impaired capacity to maintain mucosal mucin content may be a factor in reducing intestinal resistance to enteric infection and pancreatic proteases. The intestinal mucosal damage that occurs during malnutrition, causes an increased intestinal permeability.

Total parenteral nutrition (TPN) has been shown to cause reduced mucosal weight and thickness of the GIT. It has also been suggested that TPN causes a decreased ability to absorb nutrients, as well as a more permeable gut barrier. Severe bacterial translocation occurs within 2 weeks on TPN. Herndon et al. compared adult burned patients who received either enteral nutrition only, or intravenous supplementation of enteral calories (parenteral nutrition (PN)). The median total body surface area burn (TBSAB) for both study groups covered more than (> ) 50%. The mortality rate was significantly higher in the PN group at 63% as compared with the 26% in the group receiving enteral calories alone. Therefore, neither TPN nor PN, should be considered as an option for the nutritional management of the burned patient, unless there is absolute total gut failure. The possible concurrence of reduced intestinal blood flow and TPN in the critically ill could enhance the role of the “intestinal factor” in the pathogenesis of multiple organ failure and the ultimate mortality in the intensive care unit (ICU).

It seems as if a severe thermal injury could have a profound effect on the GIT. Ischemic necrosis of the intestinal mucosa with gastroduodenal erosions has been recognized at autopsy in patients who died after congestive heart failure, burns, hemorrhage, and sepsis. Endoscopic examination has enabled physicians to observe the occurrence of gastroduodenal erosions within 5 hours of injury in more than 80% of patients with severe burns. Significant prevention of hemorrhagic necrosis of the GIT mucosa and improved survival were obtained in severely burned patients by enteral feeding from the time of admission.
Deitch et al. investigated whether or not the intestinal barrier function is altered within the first 24 hours post burn. He used a lactulose and mannitol solution on adult burned patients who sustained greater than or equal to (\(>\)) 20% TBSAB, as permeability markers. The 6-hour urine collection of the lactulose:mannitol sugar-absorption-test (SAT) was completed between 16 and 30 hours after the burn injury. The patients did not receive oral medication or enteral feeding for the period of urine collection. The lactulose absorption was fourfold higher in the patients than in the healthy volunteers, whereas the lactulose:mannitol ratio was threefold higher. The conclusion was made that patients with moderate to severe burn injuries have increased intestinal permeability in the first 24 hours post burn. No further permeability tests were performed.

Carr et al. found significantly increased permeability in surgical adult patients that were starved for 6 days post gastro-intestinal resection, when compared to those fed within 2 to 3 hours post surgery. The lactulose:mannitol ratio's of both groups were similar pre-operatively. It is speculated whether these patients started off with normal gut permeability, since they had to receive an intestinal resection for chronic GIT disease.

In this study the small bowel permeability was measured by a non-invasive technique called the sugar-absorption-test (SAT). The non-absorbable sugars Lactulose and L-Rhamnose are polar and non-lipid soluble probes which permeate by aqueous pathways and have molecular weights of 342 and 164, respectively. Lactulose is a disaccharide and a relatively large molecule, whereas L-rhamnose is a monosaccharide and a relatively small molecule. Mucosal damage tends to reduce L-rhamnose absorption due to a less absorptive surface area and an increase in lactulose permeation due to impaired barrier function. The use of lactulose and L-rhamnose as probe markers assumes that they are not significantly metabolised and are quantitatively excreted unmodified in urine after absorption. The use of a lactulose:rhamnose (L:R) ratio minimizes extraneous factors such as intestinal motility, renal function, and incomplete urine collection. Thus, the differential absorption of lactulose and L-rhamnose is a sensitive index of mucosal integrity due to a loss of absorption capacity and or breaches of the mucosal barrier.

There have been several suggestions from literature that enteral feeding maintains the small bowel integrity, whereas starvation or TPN does not. No specific data could be found that measured the intestinal barrier function of the paediatric patient post thermal injury and how it would react to either early enteral feeding (EEF) or late enteral feeding (LEF). It still remains to be proven whether EEF could correct the increased gut permeability after a severe thermal injury, or whether the gut integrity will gradually recover by itself as the burn injury recovers. There is also the possibility
that the paediatric (0-13 years old) patient's metabolical changes post burn, might alter the intestinal barrier function differently to the alterations found in the burned adult, as described by the SAT results from Deitch et al.18

Marked differences exist in the paediatric burned child vs. adult responses to thermal injury, as was shown in a previous chapter on the hormonal response to either EEF or LEF. It was also pointed out that the intestinal barrier only matures in the second year of life.2 This part of the study was therefore undertaken to compare the small bowel permeability of the EEF and LEF groups to the normal L:R ratio value, as well as a comparison of the two groups with each other.

The initial (within 24 hours post burn) small bowel integrity was not investigated in this study, since this meant a 7-hour waiting period for the SAT to be completed before the EEF could be initiated. This would have increased the median time of EEF initiation from 10.75 hours to 17.75 hours post burn. The priority of this study was to evaluate the standard practice and start EEF as soon as possible post-admission.

**Results**

Figure 8.1 shows the median values for the lactulose:rhamnose (L:R) ratios in the EEF and LEF groups. The confidence interval for the EEF group on day 3, was (13.12; 43.32), and for the LEF group it was (-2.3; 60.59). On day 5 the confidence interval was (4.41; -5.67), and (36.55; 30.99), for the EEF and LEF group, respectively. The normal range for the L:R ratio's is less than 10.

**Figure 8.1: The median values of the Lactulose:Rhamnose ratios for the EEF and LEF groups on day 3 and day 5 post burn**
From the 21 patients, fifteen patients completed the SAT on day 3 and 5 post burn. Nine patients were in the EEF group, and 6 patients in the LEF group. Fewer patients completed the SAT than the total sample size, as the doctor in charge of these specific patients, considered the patients' fluid balance too unstable to give an additional 100 ml SAT solution via the NJT.

Both the EEF and LEF groups had elevated levels on day 3 post burn, with L:R ratios of 24.29 and 20.95 respectively. The small bowel permeability for both treatment groups decreased from day 3 to day 5 post burn. Although the EEF group's L:R ratio decreased to 13.5 on day 5 post burn, it was still above the normal range. The LEF group's L:R ratio decreased to a level of 4.9, which is within the normal range. The LEF group had two outliers.

Although there was no significant difference found between the two treatment groups, there was a significant decrease in small bowel permeability over time (p=0.02).

**Discussion**

The altered function of the intestinal mucosal barrier, result in an increased small bowel permeability. A compromised gastrointestinal tract could play a vital role in the pathogenesis of bacterial translocation and infection. If enteric bacteria pass through the gut wall they can initiate systemic infection, and have the potential to cause pneumonia, sepsis and multiple organ failure. The maintenance of the small bowel integrity is therefore very relevant for clinical practice.

At completion of the SAT on day 3 post burn, the EEF group had already received 48 hours of enteral feeding whereas the LEF group had been starved. The small bowel permeability in both treatment groups on day 3 post burn, was more than double the normal lactulose:rhamnose (L:R) ratio. Deith et. al. also found elevated lactulose:mannitol (L:M) ratios in the adult burned patient, but only within the first 24 hours post burn, and unfortunately did not repeat the L:M ratio's thereafter. It therefore seems that the gut permeability in the paediatric burned patient increased independent of enteral feeding or starvation.

Possible reasons for the two outliers in the LEF group were investigated such as age and incomplete urine samples. Since no definite reason could be found for these two outliers it was decided to include these two values of this data set.

The LEF group's gut permeability decreased from twice the normal range on day 3, to within the normal ranges by day 5-post burn. The only change in management in this period, was the initiation of the enteral feeds. It therefore seems as if the enteral feed initiation corrected the intestinal barrier function by day 5-post burn. Since the EEF
group received enteral nutrition throughout, it would be expected that the EEF group's L:R ratio's would also have decreased to within the normal range by day 5-post burn. However, the EEF group's L:R ratio was still elevated on day 5-post burn, again indicating that small bowel permeability in the paediatric burned patient is independent of enteral feeding or starvation.

The reason for the decreased L:R ratios in both treatment groups over time seems to either coincide with the recovery of the burn injury over time, or might be due to persistent enteral feeding for the remainder of the study period. However, in the light of the current results, it could only be suggested that the small bowel permeability decreased independently of enteral feeding or starvation. The correction of the intestinal barrier function in the paediatric patient post burn seems to be influenced by multiple factors that needs further investigation.

References:


9.1 Gastrointestinal Intolerances

9.1.1 Pulmonary aspiration and Vomiting

After a severe burn injury, the risk of a stomach and colon ileus, or "paralyzed gut", is common due to the shock. It was always believed that this ileus or paralysis was throughout the whole gastrointestinal tract (GIT). It soon became clear however, that this paralysis affected mainly the stomach and colon, with 80% or more of the short bowel still fully functioning. Bowel sounds were, and often still are used as the indicator of bowel movements, or the absence of paralysis. These bowel sounds are really air moving along the bowel, and after passing a nasogastric tube, this air is often released. This is also known as decompressing of the bowel. For these reasons enteral feeding initially was not considered an option, as the fear of vomiting and possible pulmonary aspiration was too strong. Since the ileus was found to affect mainly the stomach and colon, and the understanding of “bowel sounds” became more clear, it became a possibility to pass a feeding tube past the stomach (pyloric sphincter) and feed directly into the duodenum or jejunum.¹ ²

Nasogastric feeding tubes does not bypass the stomach, and therefore the risk of pulmonary aspiration is much greater. Severe pulmonary aspiration may cause a serious pneumonia that might require intubation and ventilation, or result in death. The placement of a feeding tube that bypasses the stomach and is placed in either the duodenum or jejunum, is far safer in the prevention of pulmonary aspiration than a nasogastric feeding tube. An abdominal X-ray is used to confirm the final feeding tube position.

Sutures or staples, or at least firm plaster should be used to secure the feeding tube in position. A nasogastric tube placed through the other nostril, could be used to monitor the ongoing position of the transpyloric feeding tube by regular (hourly) nasogastric aspirations. If the transpyloric feeding tube should become displaced, then the nasogastric aspiration would confirm this within an hour of the occurrence. In this case, the enteral feed is omitted and the patient receives immediate chest physiotherapy and tracheal secretion suctioning if clinically indicated. Feeding is recommenced when the transpyloric feeding tube is resited. This method of monitoring the ongoing position of the transpyloric feeding tube should prevent any severe pulmonary aspiration.
Every unit that practices early enteral feeding in burns patients or critically ill patients should consider the danger of pulmonary aspiration, and should monitor the position of nasojejunal feeding tubes routinely. No documentation was found on the incidence of pulmonary aspiration with the practice of early enteral feeding (EEF) in any of the world renowned burns units. These units all have a regular (hourly) ongoing transpyloric feeding tube position monitoring systems.\(^3,4,5\)

Only nasojejunal feeding tubes that were secured by staples or firm plaster, were used during the period of this study. The position of the feeding tubes were monitored by hourly nasogastric aspiration using a nasogastric tube that was placed through the other nostril. This method seems to be safe and effective in the prevention of pulmonary aspiration.\(^5,6\)

### 9.1.2 Stool Pattern

Diarrhoea is not a common phenomena associated with EEF, but should it occur, it might complicate patient care by disturbing fluid and electrolyte balance and worsening the nutritional status. Gottschlich et. al.\(^6\) found a significant relationship between the incidence of diarrhoea, dietary lipid content, vitamin A intake and the introduction of enteral feeds after 48 hours in adult burn patients. No relationship was found between diarrhoea and the enteral feed osmolality, the drugs used or hypoalbuminemia. It was concluded that a low fat [less than (<) 20% of total calorie intake] enteral diet, supplemental vitamin A [more than (>) 10 000 IU/day] and enteral feeds introduced within 48 hours post burn, would reduce the incidence of diarrhoea. Other causes that have been related to the incidence of diarrhoea in adult burned patients include a deficiency or use of antacids, potassium or phosphorus supplements, antibiotic use, total body surface area burned (TBSAB) more than 40% and elderly patients.\(^6,7\)

Most burned children will tolerate enteral feeding as early as 3 to 6 hours post burn, if not immediately. However, if diarrhoea should occur in burned children, it is particularly troublesome because of their increased sensitivity to volume deficits.\(^8\)

### 9.2 Curling's Ulcer (stress ulcer)

Multiple factors are implicated as potentially causative of stress ulcers in burned patients. These include: mucosal ischemia, increased acid production, increased acid back diffusion, energy depletion, duodenal-gastric reflux of bile, and direct mucosal injury due to the presence of intra-luminal tubes. The incidence of gastro-duodenal ulcers was previously reported as high as 86%.\(^9\)
Moran et. al.\textsuperscript{10} found that a combination of aggressive fluid resuscitation, antacid therapy, H\textsubscript{2}-receptor antagonist and enteral feeding decreased the overt and occult complications of ulceration to 3\% in 60 adult burned patients. No patient developed a perforation. Unfortunately they only started enteral feeds when bowel sounds were present.

McDonald et. al.\textsuperscript{11} begun enteral feeding within 6 hours post burn, without using any antacids or H\textsubscript{2}-blockers. They found that EEF successfully prevented upper gastrointestinal bleeding and eliminated the need for antacids or H\textsubscript{2}-blockers. EEF has an integral role in the maintenance of the gut structure and the prevention of mucosal atrophy.\textsuperscript{12, 13}

9.3 Anthropometry

9.3.1 Weight

Weight change in a burned patient is usually defined as the difference between weight on admission and discharge. This is usually expressed as a percentage. The acceptable weight loss for a paediatric burned patient should be equal to or less than (\(<\) 5\%) of admission weight.\textsuperscript{14} A weight loss of more than (\(>\) 5\%) could indicate that the patient received inadequate nutritional support.\textsuperscript{14} Certain practical implications have to be taken into account when dealing with the burned patient. Weight changes can be used to assess fluid balance and the response to nutritional therapy, but interpretation could be distorted by oedema or intravenous fluid resuscitation.\textsuperscript{15, 16} This is especially true during the first two weeks post burn. Thereafter the body weight measurement will reflect the “dry weight”, which is more accurate.\textsuperscript{17, 18}

Body composition studies for the severely burned patient >20\% TBSAB, are inaccurate and unreliable. Skinfold measurements and upper mid-arm circumference cannot be measured on an open wound, as the standard tables available were composed with the intact skin. Furthermore, if oedema is present, the measurement is inaccurate.\textsuperscript{16}

9.3.2 Recumbent Lengths or Heights

Sequential weight measurements from birth to the time of admission as recorded on the local “Road to Health Clinic Chart”, were not available in any of the study patients. Only the weight taken on admission to trauma unit was available. The National Center for Health Statistics (NCHS) weight-for-age percentile chart would not reflect the true nutritional status of the child.\textsuperscript{19} A more accurate anthropometrical assessment would be to take the patient’s height or recumbent length into account as well. This would enable the investigator to assess the patient’s weight according to his or her height. The children were therefore scored on the NCHS Weight for Height percentiles.\textsuperscript{19}
9.4 Infection, Sepsis and Antibiotic Treatment

Sepsis, and resulting organ failure, is the most frequent cause of morbidity and mortality in critically ill patients. Although the immediate cause of death may be attributed to the failure of one or more organ systems, the common pathway is generally sepsis. It has been recognized that the gut lumen contains enough bacteria and endotoxin to kill the host a million times over, yet under normal circumstances the intestinal mucosa prevents the bacteria which colonize the gut from invading organs and tissues. Damage to the outside skin barrier by a burn, allows bacteria to colonize the tissue and leads to infection.

Growing evidence indicates that many of the infections seen in our critically ill patients come from bacteria normally found within the gut. This has been termed “bacterial translocation”. Endotoxaemia in the burned patient has two possible main sources: translocation from the gastrointestinal tract and the burn wound. Thermal injury increases intestinal permeability which could lead to translocation, and endotoxin itself increases intestinal permeability. A vicious cycle may well be set up. Secondary infections after severe trauma or operative procedures may also be a result of bacterial translocation.

It became evident that enteral nutrition and specific micro-nutrients alter the ability of the gut to handle bacteria and maintain its immunological function in the stressed patient. Saito et al. found that enteral nutrition protects against mucosal damage and ulcer formation, and maintains mucosal integrity. When no enteral nutrition was provided, the blood supply was shunted away from the mucosa, which caused atrophy and bacterial translocation. On the other hand, when early enteral feeding was provided there was an increase in intestinal blood flow.

Only one documented study was found which compared the outcome of infectious complications and antibiotic therapy in burned patients, who received either EEF or LEF. Jenkins et al. investigated adult burned patients who sustained a burn injury of more than 30% TBSAB. No significant differences were found between the EEF and LEF groups comparing infectious complications documented as sepsis, pulmonary, wound and urinary tract infection. However, when the total infectious complications between the two groups were compared, the EEF group had 7 compared to the 14 found in the LEF group. This approached significance (p=0.07). Furthermore, the EEF group required less antibiotic treatment days per patient (2.8 ± 1.3), than the LEF group (9.4 ± 4.9).
In an attempt to improve the immunological function and decrease possible infectious episodes during severe thermal injury, immune-enhancing supplements have received a lot of attention over the last 5 years. These generally include the amino-acids glutamine and arginine, and omega-3 fatty acids.

Glutamine is the most abundant amino acid in the body, as well as the main intestinal fuel for the enterocytes. The glutamine pool or reservoir decreases very quickly and to very low levels in critical illness. Glutamine is important for the function of lymphocytes and macrophages. Ogle et al. investigated 12 paediatric burned patients with a TBSAB between 32 and 87%. At various times post burn the neutrophils were isolated and their ability to kill Staphylococcus aureus in the presence and absence of glutamine was determined and compared with that in normal subjects. Glutamine caused an improvement in the observed abnormal neutrophil bactericidal function and often restored it to the normal level.

Yu et al. and Lu et al. found little arginine synthesis and an increased rate of arginine degradation as a result of thermal injury in paediatric patients. A high exogenous intake of preformed arginine was needed to maintain homeostasis and promote recovery from catabolism. If 2% of the total energy was derived from arginine, a significantly enhanced T-lymphocyte response was documented. Arginine is an indispensable amino acid for maintaining body protein homeostasis and nutrition in the severely burned paediatric patient.

Saffle et al. investigated burned patients between the ages of 6 to 85 years old. The control group received the standard enteral feed, while the other group received a arginine and omega-3 fatty acid enriched enteral diet. Both groups started their enteral diet within 48 hours post. No difference was found in the incidence of complications or infections between the two treatment groups.

This study only investigated early enteral nutrition as part of the resuscitation regime, and not the different immune supplements that could be added to the enteral feeds in order to enhance the immune response.

### 9.5 Length of Hospital stay

Garrel et al. investigated 25 burned adults, with a TBSAB of >20%, of whom 12 were fed early (within 48 hours post burn), and 13 were fed late (after 72 hours post burn). The conclusion was reached that patients who had received enteral feeding before the third day post burn, spent 38.8 ± 20 days in hospital, compared to 75.8 ± 49 days in the LEF group (p < 0.05). In contrast, Jenkins et al. found no significant difference in length of hospital stay between the EEF and LEF group. The EEF
group's mean hospital stay was 41.8 ± 6.0 days, and the LEF group had a hospital stay of 36.3 ± 6.9 days.

Results

9.6 Gastrointestinal intolerances

9.6.1 Pulmonary Aspiration and Vomiting

Three patients in the EEF group experienced 1 to 2 small vomits during the resuscitation period. Displaced nasojejunal feeding tubes were immediately replaced. The vomiting episodes, had no ill effects. None of the children in the LEF group experienced any vomiting when their enteral feeds were initiated after a median of 54 hours post burn. None of the patients from either group had any episodes of pulmonary aspiration.

9.6.2 Stool Pattern

Diarrhoea was not defined on the basis of stool weight per bodily weight, but rather by stool consistency and frequency. In this study loose or watery stools that took up the shape of the container and could be poured, and occurred more than 3 times per day, was defined as diarrhoea. Five children in the EEF group experienced diarrhoea during the resuscitation period, which settled within 2 to 4 days post burn. Three children experienced diarrhoea in the LEF group after the initiation of enteral feeds, and persisted for longer than a week.

9.7 Faecal Occult Blood (stress ulcer test)

The hema-test was performed weekly on all children's stools, and no occult blood was found in either of the groups throughout the study period.

9.8 Anthropometry of Weights and Heights

Table 9.1 shows the anthropometry results for both study groups, with the admission and discharge weights in kilograms (kg), the heights in centimeters (cm) and the age in years and months. Furthermore, it contains the medians for the percentage weight change from admission to discharge, and the 'weight for height' percentiles on admission and discharge respectively.
Table 9.1: Summary of the Anthropometry results: Heights, Admission and Discharge weights and Weight for Height percentiles for the EEF and LEF groups

<table>
<thead>
<tr>
<th>Subject</th>
<th>AGE</th>
<th>Height (cm)</th>
<th>Admission (Weight in kg)</th>
<th>Discharge (Weight in kg)</th>
<th>Weight for Height (percentile) (A)</th>
<th>(DC)</th>
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<tr>
<td>EEF GROUP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>8m</td>
<td>67</td>
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<td>9.2</td>
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<td>90</td>
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<tr>
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<td>11.5</td>
<td>50</td>
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<td>104</td>
<td>15.5</td>
<td>14.3</td>
<td>25</td>
<td>10 [↓]</td>
</tr>
<tr>
<td>5</td>
<td>5yr. 4m</td>
<td>108</td>
<td>18</td>
<td>18</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
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<td>22</td>
<td>21</td>
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<td>25 [↓]</td>
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<tr>
<td>7</td>
<td>7 yr.</td>
<td>115</td>
<td>24.5</td>
<td>23</td>
<td>95</td>
<td>90 [↓]</td>
</tr>
<tr>
<td>8</td>
<td>7yr.</td>
<td>115</td>
<td>24.5</td>
<td>24</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>9</td>
<td>11yr. 3m</td>
<td>134</td>
<td>30</td>
<td>30</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>10</td>
<td>1yr. 10m</td>
<td>(99)</td>
<td>(13.8)</td>
<td>Died</td>
<td>(10)</td>
<td>N/A</td>
</tr>
<tr>
<td>11</td>
<td>1yr. 4m</td>
<td>(80)</td>
<td>(11)</td>
<td>Died</td>
<td>(50)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Median Percentage weight change (EEF): 3.1%

<table>
<thead>
<tr>
<th>LEF GROUP</th>
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<tr>
<td>12</td>
<td>8yr. 11m</td>
<td>127</td>
<td>25</td>
<td>24.5</td>
<td>50</td>
<td>25 [↓]</td>
</tr>
<tr>
<td>13</td>
<td>3yr. 8m</td>
<td>98</td>
<td>13.25</td>
<td>13.5</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>14</td>
<td>1yr.</td>
<td>77</td>
<td>10.5</td>
<td>9.08</td>
<td>50</td>
<td>5 [↓]</td>
</tr>
<tr>
<td>15</td>
<td>1yr. 1m</td>
<td>75</td>
<td>10.95</td>
<td>9.5</td>
<td>75</td>
<td>50 [↓]</td>
</tr>
<tr>
<td>16</td>
<td>9yr. 1m</td>
<td>130</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>17</td>
<td>3yr. 5m</td>
<td>85</td>
<td>13</td>
<td>11</td>
<td>75</td>
<td>25 [↓]</td>
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<tr>
<td>18</td>
<td>1yr. 9m</td>
<td>79</td>
<td>11</td>
<td>10</td>
<td>50</td>
<td>25 [↓]</td>
</tr>
<tr>
<td>19</td>
<td>4yr. 6m</td>
<td>115</td>
<td>19</td>
<td>19</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>20</td>
<td>1yr.</td>
<td>64</td>
<td>8</td>
<td>7.38</td>
<td>75</td>
<td>50 [↓]</td>
</tr>
<tr>
<td>21</td>
<td>9yr.</td>
<td>(140)</td>
<td>(29.5)</td>
<td>Died</td>
<td>(25)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Median percentage weight change: 7.75%

A = admission; DC = discharge; yr. = years; m = months
Table 9.2: Descriptive Statistics for Admission- and Discharge-Weights, Percentage Change in Weight

<table>
<thead>
<tr>
<th></th>
<th>EEF GROUP</th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Confidence Interval (-65%)</td>
<td>Confidence Interval (+95%)</td>
<td>Median</td>
<td>Lower Quartile (25%)</td>
<td>Upper Quartile (75%)</td>
</tr>
<tr>
<td>Admission</td>
<td>12.67</td>
<td>22.07</td>
<td>15.5</td>
<td>12.0</td>
<td>24.5</td>
</tr>
<tr>
<td>Discharge</td>
<td>13.24</td>
<td>23.53</td>
<td>18.0</td>
<td>14.3</td>
<td>23.0</td>
</tr>
<tr>
<td>% Change</td>
<td>-3.83</td>
<td>5.52</td>
<td>3.1</td>
<td>0.00</td>
<td>4.54</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>LEF GROUP</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Admission</td>
<td>11.09</td>
<td>21.44</td>
<td>13.12</td>
<td>10.95</td>
</tr>
<tr>
<td>Discharge</td>
<td>9.11</td>
<td>19.55</td>
<td>11.00</td>
<td>9.5</td>
<td>19.00</td>
</tr>
<tr>
<td>% Change</td>
<td>0.14</td>
<td>11.76</td>
<td>7.75</td>
<td>0.00</td>
<td>13.24</td>
</tr>
</tbody>
</table>

Table 9.1 and Table 9.2 shows that none of the 18 patients who completed the study successfully were below the 5th percentile weight-for-height on admission. However on discharge, 3 patients from the EEF group decreased their weight-for-height percentiles, compared to 6 patients in the LEF group.

The difference in admission and discharge weight was calculated for each patient, and expressed as a percentage. The median weight loss from admission until discharge for the EEF group was 3.01%, versus 7.75% for the LEF group. There was no statistical difference in the weight loss between the EEF and LEF groups (p=0.1).

9.9 Antibiotic Treatment

Patients were only placed on antibiotic treatment after a positive blood culture, positive histology from a biopsy of a wound, or a positive culture from a wound swab. Septicaemia was confirmed by a positive blood culture. None of the 18 patients that completed the study successfully had a positive blood culture throughout the study period. The two patients that died from organ failure and overwhelming sepsis on day 3 and day 19 post burn, had positive blood cultures 24- and 48 hours, respectively, prior to death. The total number of days spent per patient on antibiotic treatment was recorded, and the median number of treatment days per study group was calculated. The EEF group had a median of 11 days antibiotic treatment per patient, while the LEF group had a median of 14 days per patient. The difference between the two study groups approached significance (p=0.08).
9.10 Length of Hospital Stay

The 9 patients in the EEF group that completed the study successfully, spent a total of 222 days in hospital, whereas the 9 patients in the LEF group spent a total of 298 days in hospital. The LEF group spent a total of 76 days longer in hospital than the EEF group.

However, when the mean days per patient per group was calculated, the EEF group spent a mean time of 20.18 ± 15.54 days per patient in hospital, while the LEF group spent a mean of 29.8 ± 31.3 days per patient in hospital. No statistical difference was reached between the EEF and the LEF group (p=0.39). If the one subject that spent a 114 days in hospital was removed from this calculation, the EEF group spent a mean time of 20.18 ± 15.5 days per patient in hospital, while the LEF group spent a mean of 20.44 ± 9.93 days per patient in hospital. This difference did not reach statistical significance (p=0.96). There was no difference between the median days per patient spent in hospital; in both study groups it was 26 days per patient.

Discussion

9.11 Gastrointestinal Disturbances

9.11.1 Pulmonary Aspiration and Vomiting

The 1 to 2 small vomiting episodes experienced in the 3 patients from the EEF group resulted from the children pulling out their nasojejunal feeding tubes. After the immediate transpyloric reinsertion of the tubes, no further incidents were documented and feeding was resumed without further complications. The vomiting episodes had no lasting ill effects.

No pulmonary aspirations were documented throughout the study period. This was monitored by hourly nasogastric aspiration, as well as, whenever suctioning was done from the tracheal secretions by either the physiotherapists or nursing staff. The doctor and nursing staff of the burns unit also monitored every patient for any clinical signs e.g. fever, cough or dyspnea. None of these signs were ever linked to a possible pulmonary aspiration throughout the study period. Since the initiation of EEF at Red Cross Children's Hospital in 1992, no patient's demise has been linked to pulmonary aspiration. The benefits from properly monitored EEF seem to outweigh the mostly unfounded fear of pulmonary aspiration.

Gastric fluid accumulation in the stomach can be treated effectively with gut motility enhancers. When hourly gastric aspirates become greater than 2 to 3 milliliters per
kilogram per hour (ml/kg/h), gut motility enhancers are advised. Two patients in this study required Cisapride for 1 to 2 days.

9.11.2 Stool Pattern

Gottschlich et al.\(^6\) found a significant relationship in adult burn patients between the incidence of diarrhoea and dietary lipid content (> 20% of total calories from fat), vitamin A intake (< 10 000 IU) and the introduction of enteral feeds after 48 hours post burn. The EEF group in our study started with a fat intake of 30% of total calories, which decreased to 22% in the EEF and LEF groups by days 4 to 5, and 6 to 7, respectively.

There seem to be similarities in the results found in our study, compared to the findings by Gottschlich et al.\(^6\). The diarrhoea in the EEF group settled between 2 to 4 days post burn, whereas the fat content of the enteral feed reached 22% between days 4 to 5 post burn. Furthermore, the diarrhoea in the LEF group seemed to settle by day 7 as 22% fat in the enteral feed was reached.

Both our study groups received 10 000 IU vitamin A per day. No definite conclusion could be reached about the fat composition. It is suggested that initiating a low fat (< 20%) enteral feed, preferably before 24 hours post burn, and providing an additional 10 000 IU of vitamin A per day, is unlikely to lead to severe diarrhoea.

9.12 Faecal Occult Blood (stress ulcer test)

In order to test for a gastrointestinal ulcer that might have developed as a result of stress, occult blood in each patient’s stool was tested weekly. The hema-test was used for this analysis. No occult blood was found in either of the two groups. McDonald et al.\(^{11}\) prevented upper gastrointestinal bleeding in adult burned patients by the introduction of enteral feeds within 6 hours post burn, without the use of any antacids or H\(_2\)-blockers. EEF seems to have an integral role in the maintenance of the gut structure and the prevention of mucosal atrophy.\(^{12}\)

Stress ulcers that were so frequently documented before the mid eighties, were probably due to the delayed introduction of enteral feeds well after 48 hours post burn. More often than not, they waited until bowel sounds were present before any oral intake was allowed.\(^{10}\) This often took over a week. The LEF group in our study did not have any occult blood in their stools. It is feasible that enteral feeds initiated at a median time of 54 hours post burn, is adequate to maintain gut integrity sufficiently to prevent the formation of stress ulcers.
9.13 Anthropometry

Weights and heights were documented on all patients who completed the study successfully. Three patients in the EEF group decreased their weight-for-height percentiles, compared to 6 patients in the LEF group.

Furthermore, the LEF group lost a median of 7.75% of admission weight, which exceeds the acceptable 5% weight loss allowed for a paediatric burned patient. The EEF group only lost a median of 3.01% of admission weight. As a result of the initial 54 hours that the LEF group was kept nil per mount, the EEF group reached their caloric and protein requirements 2 to 3 days earlier than the LEF group. It is feasible that EEF played a vital role in the maintenance of the admission weight of paediatric burned patients.

9.14 Antibiotic Treatment

The median number of days per patient on antibiotic treatment was more in the LEF group than in the EEF group, and approached significance (p=0.08). This could suggest that the EEF group had fewer infections. The only difference in patient management was the initial 54 hours during which the LEF fasted. EEF may prevent susceptibility to subsequent infections.

9.15 Length of Hospital Stay

Although the LEF group stayed a total of 76 days longer in hospital when compared to the EEF group, the median hospital stay per patient was similar. The difference failed to reach statistical significance but clearly has cost implication.

No specific studies that related to the length of hospital stay of paediatric burn (0 to 13 years of age) patients, were found. The general guideline for length of hospital stay is more or less 1 day per percentage burn. Both our study groups spent less than 1 day per percentage burn in hospital. The EEF group that had a median percentage total body surface area burned (TBSAB) of 29.5%, spent 0.88 days per percentage burn in hospital, while the LEF group (median TBSAB of 30.00%) spent 0.87 days per percentage burn respectively. In other words, the EEF group spent 3.5 days fewer in hospital than the general prediction, while the LEF group spent 4 days fewer in hospital.

Due to the similar length of hospital stay in both study groups, no conclusion could be made about the impact of EEF and the length of hospital stay.


19. National Center for Health Statistics, Health Resources Administration, Hattsville, Maryland, Data from the Fels Research Institute, Yellow Springs, Ohio: NCHS Percentiles, Weight for Length – Boys and Girls. 1989


22. Deitch E.A. Intestinal permeability is increased in burn patients shortly after injury. Surgery 1990; 107:411-16


Chapter 10

Limitations

10.1 Sample Size

Unfortunately the final sample only consisted of 21 patients, of which 18 completed the study successfully. Detailed reasons for the small sample size are provided in chapter 3 (3.1). Often time, staff and cost constraints are the most important factors influencing the final sample size, as was the case with this study.

The small sample size is a major limitation to this study, as the results would have to be interpreted carefully for use in clinical practice of paediatric burn patients elsewhere. A small study sample may not be representative, and a few extra cases could swing the outcome either way. A larger study sample would have provided more reliable findings, which could be generalized, for the application to a similar population group.

Future researchers have to consider all these factors carefully before the initiation of a similar study. The costs in terms of finances, manpower, material and time need to be carefully calculated.

10.2 Study design

Although the initial intention was to have a randomized clinical controlled trial, the study design was changed to that of a Controlled trial. A detailed explanation for this change was given in chapter 3 (3.2).

The lack of randomization is a major limitation to this study. Randomization controls unknown confounding variables, and the lack thereof, was therefore a major limitation of this study. It also aims to ensure that patients on different treatments are comparable with respect to baseline characteristics, as well as known and unknown factors. The possibility of confounding variables, which can occur in analytical studies, is thus reduced. It is particularly important in trials with a small sample size, where important confounders are distributed similarly in the treatment and control groups.

10.3 Age Range

Literature on the subject that was investigated in this study is limited, and often studies which included paediatric patients, had age ranges between 2 year olds and adults over 30 years old. Conclusions should therefore be viewed with caution as the validity of the findings might not be applicable for clinical practice. Our study subjects
had a age range between 8 months to 11 years, which in itself is quite a large range. It would have been useful to increase the sample size quite drastically to stratify the subjects into different age categories. This would enhance the validity of our findings significantly, as the researcher could investigate the metabolic response within each age category. This would also be much more relevant for clinical practice.

10.4 Additional Biochemical measurements in the first 7 days

Since there is such limited literature comparing EEF to LEF in the paediatric burned patient, it would have been interesting to document the trend of serum glucose concentrations, as well as electrolytes and albumin on a daily basis during the first week post burn. However, one should consider the clinical relevance of these study objectives, the cost constraints, and most importantly, the total blood volume required for blood analysis. Unfortunately the total volume of blood sample required for the hormonal analysis alone, was already 6 ml/day. Since the patients in this study only had a mean age of 4.5 years old, the total blood volume of such a patient is about 80 ml/kg. Each patient required a venous blood sample of 9 ml on admission. Six ml were required for the hormonal specimens and 3 ml for the standard electrolytes and full blood count. Thereafter, a further 6 millilitres (ml) of venous blood were sampled daily (for 5 days) per patient for the hormonal specimen analysis. This comes to a total of 39 ml within the first 5 days post admission, or 3% of the total blood volume of a 4.5 year old child with a weight of about 16 kg (25th percentile weight-for-age).

Serum albumin is considered to be an inaccurate indicator of nutritional status due to the long half life of 21 days, and the current international controversy surrounding the administration of exogenous intravenous albumin, were reasons for not discussing this topic.

10.5 Inadequate assessment of the hormonal response

According to adult burn literature, catecholamines seem to be a primary stimulator for the release of catabolic stress hormones. Similar measurements for this study group might have added additional insight to the results found from the hormone concentrations measured.

There was a fair amount of inadequate samples for the growth hormone (GH) concentrations on certain days for certain patients, and the available data had a non-normal distribution. A log transformation was applied to the transformed data, which was then analyzed. The data should therefore be interpreted with caution.
10.6 The lack of a ‘control’ Group

The national and international general standard practice for the introduction of enteral nutrition after a severe thermal injury in the paediatric burned patient, is delayed—or late enteral nutrition. It is the selected few who practice EEF, and still need to do controlled clinical trials. Therefore, the investigator used the LEF group (standard practice) in this study as a ‘control’ group, to compare how the severely burned paediatric patient would respond to early enteral nutrition.

However, in the case of indirect calorimetry, it would have been more valid to compare the results (EEE) found in both study groups, to a group of comparable healthy children. Hypermetabolism in our subjects could then have been reflected not only by the hormonal response, but also by comparison to the resting energy expenditure of healthy children.

10.7 Respiratory Quotients below 0.7

The low RQ’s found in both study groups over the first week post burn, could not be explained physiologically. Although another unit found similar results, and our results therefore seem feasible, conclusive explanatory data is not currently available. Possible explanations for these low RQ’s were discussed in chapter 11.

10.8 Failure to measure Nitrogen Balance

Although the nitrogen balance as a predictor of nutritional outcome in the paediatric burned patient seems to be inaccurate, it would have provided insight into the period that it took to reach a positive nitrogen balance. Although twenty-four hour urine and stool collections were possible during the resuscitation period (urinary catheter in place), the extra nitrogen losses during surgery, daily occlusive dressing changes, as well as the extensive use of blood products, makes nitrogen loss and balance measurements highly unreliable as a guide to therapy. Therefore the nitrogen balance, even during the early stages of treatment, would not have provided accurate insight on protein catabolism. Shortly after the resuscitation period the urinary catheters were removed to prevent possible urinary tract infections and discomfort during occupational- and physiotherapy, which makes 24-hour urine collections mostly impractical and inaccurate.

10.9 Validity of Anthropometric Measurements

There were no bed-scales available during the study period, which decreased the accuracy of the anthropometric measurements for selected patients’ weight.
10.10 Absence of a classification criteria for the diagnosis of wound infection

The documentation of infectious wound complications could have provided very important insights into the nutritional impact of early enteral feeding vs. LEF in the paediatric burned patient. Only one study documented the outcome of infectious complications in burned patients who received either EEF or LEF, and this was in adult patients. Since there is such a need in the literature on the outcome of infectious wound complications in the paediatric burned patient that was either early- or late enterally fed, this study could have shed some light concerning this matter.

The number of days spent on antibiotic treatment provided some information on possible infections, but do not give a clear picture of the actual infections that the patient might have had.

The diagnosis of clinical sepsis or septicaemia should be established by the presence of a positive blood culture. None of the 18 patients that completed the study successfully had a positive blood culture during the study period.

10.11 Statistical Analysis

A precision level of 5% for the estimation of sample estimates is viewed as an acceptable level of precision. However, due to the small sample size a precision of 8% was also considered to approach significance. Statistical significance is dependant on sample size and is derived from the standard error, which is directly related to the variability of the observation. The exclusive use of the 95% confidence level (p < 0.05) to assess significance has obvious drawbacks which may result in potentially clinically important observations being discarded (type II error).
Chapter 11

Conclusions

11.1 Hormonal Response

11.1.1 Insulin

When early enteral feeding (EEF) was compared to late enteral feeding (LEF) in the paediatric burned patient, EEF had a significant impact on various outcome variables. An anabolic process seemed to be taking place in the EEF group, since the insulin levels were significantly higher (p=0.008) for the entire study period, when compared to the LEF group. Furthermore, the insulin:glucagon ratios in the EEF group were also significantly higher up until day 4 post burn (p=0.04) and approached significance up until day 12 post burn (p=0.08). In contrast to adult burned patients having subnormal insulin concentrations, the insulin concentrations for both study groups in this study, mostly remained within the normal range. However, the LEF had low normal insulin concentrations until day 3 post burn. Enteral feeding was initiated on day 3 post burn, and there was a marked increase in the insulin concentrations (from 5mU/L to 15mU/L) that persisted until day 26 post burn. The infant and the child seem to respond to different severe traumas with a more efficient anabolic response than the adult, which might explain why children generally heal faster than adults do. Although it seems as if children have a naturally higher anabolic response to severe trauma, enteral feeding and the timing thereof seems to make a significant contribution.

11.1.2 Insulin-like growth-factor-1 (IGF1)

The insulin-like growth factor-1 (IGF1) concentrations were higher in the EEF group on days 5, 19 and 26, but compared to the LEF group, the difference did not reach significance. However, where adult burned patients usually have subnormal levels, both our study groups remained within the lower range of normal. The higher concentrations of IGF found in the EEF group on certain days, seem to correspond well with the anabolic effect suggested by the insulin and insulin:glucagon ratios.

11.1.3 Cortisol

Cortisol concentrations did not differ significantly between the two study groups. Interestingly, neither of the two study groups experienced elevated cortisol concentrations, which contrasts with the elevated cortisol concentrations usually documented in adult burned patients. During the first 24 hours post burn both study groups experienced concentrations in the high normal range, which decreased to within the lower normal range thereafter. Therefore, with the cortisol concentrations...
staying within the normal range throughout the study period for both study groups, this would suggest that neither study group experienced a hypermetabolic response. However, considering the elevated glucagon concentrations for both study groups, it suggests that the absence or presence of hypermetabolism, should not only be measured by the results of a single stress hormone.

11.1.4 Glucagon

Glucagon concentrations were elevated in both study groups for the entire study period, which is similar to those documented in adult burned patients. Unfortunately no literature could be found regarding the glucagon concentrations of paediatric burned patients. Both study groups experienced an increase in glucagon concentrations over time. It would be interesting to investigate the glucagon concentrations of paediatric burned patients for an extended period (beyond 26 days), to monitor at what point the concentrations return to normal.

Glucagon is documented as the primary stimulator for increased glucose production in the adult burn injury. However, the median blood glucose concentrations in this study for both the EEF and LEF groups were only slightly elevated on admission, and thereafter returned to within the normal range. Therefore, persistent elevated glucagon concentrations in the paediatric burned patient do not seem to stimulate glucose production to the same extent, as it does in the burned adult. Another explanation for the normal glucose concentrations might be the initial elevated insulin concentrations, which returned within the normal range after day 12. The adult burn patient, mostly experience subnormal insulin concentrations, together with elevated glucagon and glucose concentrations. Hyperglycaemia has far-reaching side effects for the ICU patient, and the prevention thereof would prevent complications such as anorexia, nausea, vomiting and even coma. Early enteral feeding resulted in significantly higher insulin concentrations when compared to LEF, which might be used as a prerequisite for the prevention of hyperglycaemia.

11.1.5 Growth Hormone

Significantly higher GH concentrations were documented in the LEF group up until day 12 post burn. GH has demonstrated anabolic as well as catabolic properties in times of severe stress. Elevated GH concentrations in children undergoing emotional stress, acute or chronic calorie and protein deprivation and fasting periods, have been documented. In this study, the GH concentrations gradually decreased to within the normal ranges after refeeding was initiated. Therefore, the initial fasting period (calorie and protein deprivation) of 54 hours in the LEF group in this study, could be the initiator of the significantly higher GH concentrations. Although feeding was initiated after 54 hours, the LEF group took 12 days to decrease their GH concentrations to
similar levels found in the EEF group. As the burn injury recovered, there also appeared to be a general decrease in GH concentrations over time for both study groups. However, irrespective of whether EEF or LEF was administered, the GH concentrations did not fall to a subnormal range. This contrasts with the subnormal concentrations found in adult burned patients.

11.2 Indirect Calorimetry (EEE) compared to Estimated Caloric Requirements

Due to the inability of the standard caloric requirement equation to assess individual needs and treatment procedures, it will be more accurate to use actual measured energy expenditure. Unfortunately the equipment is not always available, and therefore the EEE for both study groups was compared to the Galveston- and Solomon’s burns equations. It revealed that the Galveston equation was closest to the measured EEE, but overall, the RDA compared most favourable to the EEE.

It may be that reduced activity levels offset the increased calorie requirements for hypermetabolism after burn injuries, and therefore the RDA might be a rational method of determining the energy needs in burned children. Although the RDA is not generally used in clinical practice as a predictor for the energy requirements for burned patients, these study results suggest that further investigation is needed to compare measured EEE to the RDA. Currently it seems as if the RDA should be considered as a method for determining the energy requirements in paediatric burned patients.

11.3 Percentage deviation from the EEE

The percentage deviation of the calculated RDA, Galveston and Solomon’s equations in comparison to the actual EEE for both the EEF and LEF groups, were greater on admission, and days 2, 8 and 12 post burn. Although initial shock and a possible increase of catabolic hormonal release, surgical procedures and days spent fasting for other theatre procedures were all investigated, not one common denominator was found throughout days 0, 2, 8 and 12 to explain the larger percentage deviation. The exact reasons why energy expenditure should vary from day to day, individually and between patients with similar burns and required procedures, still requires further investigation. If the entire study period for both study groups is considered as a whole, the Galveston burn equation deviates less from the EEE than the Solomon’s burn equation. The RDA for both study groups displayed the least deviation when compared to the EEE, and deviated even less from the EEE as the burn injury recovered towards the end of the 26-day study period.
11.4 Respiratory Quotients

The LEF group had significantly (p=0.03) lower RQ's over the first 54 hours of fasting, when compared to the EEF group that was enterally fed. However, the great concern that both study groups displayed RQ's of < 0.7 during the first week post burn, was thoroughly investigated. If an RQ of 0.7 is indicative of 100% fat utilization, then RQ's < 0.7 is highly unlikely. It is interesting to note that the values became greater than 0.7 after the initial week post burn. Although the indirect calorimeter was standardised prior to the study, faulty equipment could only have been identified if measurements were compared to that of a group of healthy volunteers. This has been discussed under ‘validity of measurements’ earlier on. Another local tertiary hospital confirmed similar findings, with initial RQ's below 0.7, and thereafter a trend of RQ's increasing above 0.7 after the first week post trauma. It seems as if RQ's of < 0.7 is possible in the severely stressed patient, but needs in-depth further investigation.

A combination of lipolysis and gluconeogenesis in the thermal patient due to elevated catabolic hormones such as glucagon, might also explain the initial low RQ's. The ketones produced from elevated fatty acid levels and the accumulation of newly formed glucose from amino acids, have the potential to lower RQ's below 0.7. Unfortunately, the glucagon concentrations remained elevated throughout the study period for both study groups, but the RQ's were elevated above 0.7 after the first week post burn. Lipolysis and gluconeogenesis might only have produced enough ketones and accumulated newly formed glucose from amino acids during the first week post burn, which was detected by the low RQ's. Unfortunately the investigator did not measure the ketone levels or neo-formed glucose to confirm the suggestion made.

Another reason for this phenomena might be the macro-nutrient composition of the enteral feeds currently available in South Africa. The fat content is generally between 30 to 45% fat. It was suggested that high circulating levels of triglycerides post burn injury, and the body's preference to use these for fuel rather than exogenous fat, points to the need of a low-fat high-carbohydrate enteral feed as the preferred choice of nutrition. A world renowned burn unit that makes use of enteral feeds below 10% fat of the total energy, generally see RQ's of > 0.85 from admission. (Personal communication – Hildreth) It seems viable that the macro-nutrient composition of enteral feeds for the severely burned patient should contain < 10% fat of the total energy. The ideal enteral feed composition for these particular patients, are discussed in chapter 12.
11.5 Calorie and Protein Intake

Although not statistically different, the EEF group consumed more calories and protein over the study period than the LEF group. When the EEE and the total caloric intake was compared, both groups displayed a positive caloric balance. The EEF group’s caloric balance was more than the LEF group’s, but the difference also failed to reach significance (p=0.3). The literature suggests that the caloric balance seems to be a relatively accurate measure of patient outcome, which might suggest that the LEF group had a less favourable patient outcome due to the fewer calories consumed.

Although the acceptable limit for weight loss for a paediatric burn, from admission until discharge can be up to 5%, the EEF group only lost a median of 3.01% of body weight, whereas the LEF group lost 7.75%. The difference did not reach significance, but did exceed the acceptable limit in the LEF group.

If a severely thermal patient fasts for a certain period post burn, that patient will take longer to reach a similar total intake when compared to a patient that is fed early. The enteral feed supplementation and intake were similar between the two groups by day 6 post burn, but the EEF group voluntarily consumed more solids, hence the higher calorie and protein intake. It could be suggested that EEF group vs. the LEF group had a better appetite due to EEF. However, it would be more accurate to compare EEF to LEF, if both study groups consumed a similar amount of calories and protein. The most accurate method to control the calorie and protein intake, would be to provide an enteral feed exclusively, excluding all solid intake. It would be difficult to explain to the children that they are not allowed any solids, which might be ethically unacceptable.

Another option for investigating EEF vs. LEF would be to provide more calories to the LEF group over the entire study period. Although this would present practical difficulties after 2 days of fasting, it would provide insight whether EEF or rather the total calories consumed, is the determining factor for a better clinical outcome. The researcher would have to curb the EEF group’s total intake that it still provides the necessary requirements for optimal healing, and weigh up the total amount of calories that the LEF group would be able to tolerate. These results would provide insight whether the initial 24 – to 48 hours nutritional intervention is really of such importance, or if it is actually only the total amount of calories consumed over a certain period.

In summary, although not statistically different, there is potential bias in favour of the EEF group because they consumed more calories and protein over the study period. It is therefore still unclear whether the EEF group lost less weight, compared to the LEF group, either due to early enteral resuscitation, or the total calories and protein consumed over the study period.
11.6 Anthropometric Measurements

The Red Cross Children's Hospital's burn unit treats children from a variety of socioeconomic backgrounds. Interestingly, one would expect that most of these children would be malnourished and wasted, on the contrary, the children are mostly in an acceptable nutritional status ( > 25th percentile weight-for-height). However, if a patient that is undemourished sustain a severe thermal injury, the chances of survival decrease tremendously. The lean body mass present needs to be able to maintain skin graft recovery and wound healing. If the patient is unable to achieve wound healing and constantly has skin graft loss, then the mortality rate increases drastically. Without any bodily stores, hypermetabolism due to catabolic hormonal release, constant surgery, and a possible inability to retain provided calories and protein, it is almost impossible for skin grafts to take 100%. This usually revolves into a cycle of skin graft failure and infectious episodes.

11.7 Small Bowel Permeability

The altered function of the intestinal mucosal barrier, will result in an increased small bowel permeability. A compromised gastrointestinal tract could play a vital role in the pathogenesis of bacterial translocation and infection.

The small bowel permeability in both treatment groups on day 3 post burn, was more than double the normal (< 10) lactulose:rhamnose (L:R) ratio. These results could only be compared to adult burned patients' literature, which only demonstrated elevated L:R ratios within the first 24 hours post burn. The permeability of the small bowel of paediatric burned patients, seems to be affected much more severely, and for a longer period, when compared to the adult burned patient. Both our study groups experienced a drastic decrease in small bowel permeability by day 5 post burn. However, the LEF group's L:R ratios decreased to within the normal range, whereas the EEF group's L:R ratios were still slightly elevated. This therefore suggests that small bowel permeability was not adversely affected by EEF, but demonstrated elevated lactulose:rhamnose ratios irrespective of EEF or early starvation. The significant (p=0.02) decrease in L:R ratios experienced by both study groups over time, is possibly related to the recovery from the burn injury, or persistent enteral feeding during this time period.

11.8 Clinical Outcome

Although those that developed diarrhoea in the LEF group seemed to take longer before the stools settled, 2 more patients developed diarrhoea in the EEF group. The vomiting in the 3 patients in the EEF group did not have any ill effects, and did not reoccur after the replacement of the nasojejunal feeding tubes. No occult blood was
found in the stools of the EEF or LEF groups, and no pulmonary aspiration occurred in either study group.

Although not statistically significant, antibiotic treatment was needed for longer in the LEF group, which might suggest that patients who received EEF had fewer infections when compared to the LEF group.

Although, the median hospital stay was similar for both study groups, the LEF group spent a total of 76 days longer in hospital. The difference in hospital stay failed to reach statistical significance but clearly has cost implications.

11.9 Summary

It is concluded that the benefits of EEF in paediatric burned patients outweigh detrimental affects. EEF does not adversely affect any other known area of treatment, and is safe and highly effective. EEF as part of the resuscitation protocol, continues to be a part of the treatment for the severely burned paediatric patient at the Red Cross Children's Hospital.
Chapter 12

Recommendations

12.1 Further Research Required

Limited data is available on the hypermetabolic response of the paediatric burned patient (birth to 13 years). Therefore more controlled clinical investigations are needed in this field. It is always preferable to change current treatment of patients only after several trials documented similar positive results.

12.2 Caloric Requirements

The Galveston burns equation for the estimation of caloric requirements is the formula of choice if indirect calorimetry or the doubly-labeled water technique is not available. This formula seems to predict caloric requirements more accurately than other burns formulas available (e.g. Solomon's), which mostly overestimate the caloric requirements.

12.3 The Ideal Enteral Feed

The ideal enteral feed specifically catering for the needs of the severely burned paediatric patient must still be formulated. With the current research available, it seems as if the macro-nutrient composition of such a feed should comprise 20% protein, 2 to 3% fat and 77% carbohydrate as total calories. Paediatric burn units should have the capacity to make up modular feeds, specifically catering for the needs of individual patients. The study findings would have been greatly enhanced if a second early enteral feeding group using such an enteral feed, was added to the study findings.

12.4 Immune - enriched Nutritional Supplements

Additional glutamine, arginine and omega-3 long-chain fatty acids may be required in the ideal enteral feed. In view of inconclusive evidence further research is warranted in terms of the effect of immune-enriched nutrition on the morbidity and mortality of paediatric burned patient.

12.5 Shortened Fasting Periods and / or Perioperative Feeding

Where possible, changes need to be made to try and decrease the amount of time the child is starved for procedures in theatre. Shortened starvation periods, and or perioperative feeding have been shown to be safe and effective. Feeding should only be administered via transpyloric feeding tubes and ongoing position needs to be
confirmed prior to theatre procedures. The enteral feed should only be administered
via constant pump infusions, to prevent accidental large bolus deliveries. Hourly
nasogastric aspirates could be taken pre-, post- and during perioperative procedures,
in order to monitor the nasojejunal feeding tube's position and to maintain gastric
decompression. A controlled and ethically approved clinical trial is advised. A
combined effort from the burns surgeons, radiologists, anesthetists, dietician and
nursing staff could make shortened pre- and post operative starvation periods, as well
as perioperative feeding, a safe and effective reality at the Red Cross Children’s
Hospital.

12.6 An option for Developing Countries

This study has shown that enteral resuscitation via a transpyloric feeding tube is safe
and does not have any adverse effects. EEF as part of resuscitation is now part of the
standard protocol at the Red Cross Children’s Hospital. This practice should be
considered in other developing countries where basic equipment for resuscitation,
and the required intravenous fluids are expensive or in short supply. Where
nasojejunal feeding tubes cannot be placed under fluoroscopic guidance, the bedside
placement technique should be implemented, and final positioning could be confirmed
with an abdominal X-ray. However, all burns units should be able to provide a surgical
service for wound debridement and skin grafting (auto- and allografts), blood
transfusions and anesthesia. When facilities for the surgical treatment of burns do not
exist, enteral resuscitation could be initiated, and the child then transferred to the
nearest unit that could provide the necessary surgery and rehabilitation. This would
still save the lives of many, since the time period for the initiation of resuscitation fluids
for a severe thermal injury patient is of crucial importance.

This work has shown that early enteral resuscitation is safe and could therefore be
implemented in burned children that are treated in developing countries.
To Parents/Guardians

Unfortunately there is no perfect way in which to feed children who have suffered severe burns. To improve our feeding schedules of these children we are investigating various alternatives.

I am an experienced senior dietician working in the burns Unit at the Red Cross War Memorial Children's Hospital. We will be comparing two types of feeding procedures on the child's progress in the ward.

1. Feeding your child via a tube placed through the nose, via the gullet and stomach into the bowel. The feeding using a type of milk formula is started shortly after your child is admitted to the ward.

2. Giving fluids and glucose your child needs in an intravenous drip for the first 2 days. Full feeds will be started afterwards.

Both these regimes are in use in Burns Units throughout the world, but which is better has not been established, and your child will receive one of them.

If you allow your child to participate in this investigation please fill out the form below.

Your co-operation is greatly appreciated.

Thanking you

MARCHA VENTER

( Red Cross Children's Hospital - Dept. of Dietetics & Nutrition )

Consent Form

I __________________________, allow my child __________________________ to participate in the investigation being conducted by Marcha Venter at the Red Cross Children's Hospital. I understand the purpose of the investigation and I have the right to withdraw my child from the investigation at any time that I see fit.

Parent/Guardian signature: __________________________ Date: __________

Witness 1. __________________________ Witness 2. __________________________
Appendix 2

**Cause / Classification of burn injuries**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Classification</th>
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<tbody>
<tr>
<td>Warm liquids</td>
<td>Water, oil, tea, coffee</td>
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<tr>
<td>Hot Food</td>
<td>Food in a pot or pan, mixed with either water or oil</td>
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<tr>
<td>Fire</td>
<td>Smoke inhalation could cause respiratory stress or monoxide poisoning</td>
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<tr>
<td>Electrical</td>
<td>Open electric wires or High voltage containers</td>
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<tr>
<td>Chemical</td>
<td>Surface burns or ingestion/esophageal</td>
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</table>

* This study only investigated patients that sustained warm liquids and fire injuries.

**Degree of burn injury**

<table>
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<tr>
<th>Degree</th>
<th>Classification</th>
<th>Damaged Area/Layer</th>
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<tbody>
<tr>
<td>First</td>
<td>Superficial</td>
<td>epidermis</td>
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<td>Second</td>
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<td>Third</td>
<td>full thickness</td>
<td>epidermis, dermis, up to fatty layer</td>
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<tr>
<td>Fourth</td>
<td>deep structures</td>
<td>muscle, tendon, bone</td>
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</table>

Degree of burn classification

**Percentage of Total Body Surface Area Burned (%TBSAB)**

This study investigated TBSAB of more than or equal to (≥) 20%.

## Resuscitation Regime for Burns more or equal to (≥) 20% TBSAB

### Day 1

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<td>Start of Feeds:</td>
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<td>Type of feed:</td>
<td>Burn:</td>
<td>% TBSAB</td>
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### IV Fluid Rate of feed Enteral

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<th>Enteral feed ml/hr</th>
<th>Hours</th>
<th>Total volume</th>
<th>Pulse rate</th>
<th>BP</th>
<th>Urine ml/hr</th>
<th>Total Urine</th>
<th>Asp Vom</th>
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<td>1 ml/kg/hr</td>
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### Formula:

\[
\frac{\text{Maintenance} + \text{Replacement of ongoing losses}}{24} = \text{Total ml/hr required}
\]

\[
\left(\frac{\text{Maintenance} + \text{Replacement of ongoing losses}}{24}\right) = \text{ml/hour}
\]

- **Maintenance (ml/kg/day):** 0–1 year (120); 1-2 yrs (100); 2-5 yrs (80); 5-10 yrs (60); >10 yrs (50)
- **Replacement of ongoing losses:** \(\%\text{TBSA burn} \times \text{weight(kg)} \times 3.5 = \text{ml/24 hours}\)
- **Resuscitation for hypovolaemia:** 10-20 ml/kg SHS or PlasmaLyte B as a bolus
  - \(X\) = The enteral volume is increased every 3 hours by 1 ml/kg/h, until calculated hourly volume is reached.
**Day 2**

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<th>Date</th>
<th>Time</th>
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**Time of Burn:**

**Admission:**

**Start of Feeds:**

**Type of feed:**

**Burn:** % TBSA

**Weight:** kg

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<th>IV Fluid Rate of feed Enteral Hours Total volume Pulse BP Urine Total Asp</th>
<th>Ml/hr</th>
<th>X ml/kg/hour</th>
<th>Total volume</th>
<th>Pulse rate</th>
<th>BP</th>
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</table>

**Formula:** \[
\frac{\text{Maintenance} + \text{Replacement of ongoing losses}}{24} = \text{Total ml/hr required}\\ \]
\[
\frac{\text{Total ml/hr required}}{24} = \text{ml/hour}
\]

**Maintenance (ml/kg/day):** 0-1 year (120); 1-2yrs (100); 2-5yrs (80); 5-10yrs (60); >10 yrs (50)

**Replacement of ongoing losses:** %TBSA burn x weight(kg) x 1.5 = ml/24 hours

**Resuscitation for hypovolaemia:** 10-20ml/kg SHS or Plasmalyte B as a bolus

\[X = \text{The enteral volume is maintained at X ml/kg/h, in order to provide total calculated hourly volume.}\]
Appendix 4

Solomon's, Galveston and RDA Equations

Adapted paediatric Solomon's Formula (1981) for burns

<table>
<thead>
<tr>
<th>Age</th>
<th>Calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants: 0 - 9 kg</td>
<td>RDA + (15 x TBSAB)</td>
</tr>
<tr>
<td>Toddlers: 1 - 3 yrs or 10 - 13 kg</td>
<td>RDA + (20 x TBSAB)</td>
</tr>
<tr>
<td>Children: 3+ yrs or &gt;13 kg</td>
<td>RDA + (30 x TBSAB)</td>
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Adapted paediatric Solomon's Formula (1981) for burns

Galveston formulas

Galveston Infant (0-12 months) 2

2100 kcal/m² + 1000 kcal/m² burn

Revised (1-11 years) 3

1800 kcal/m² + 1300 kcal/m² burn

Adolescent (12 years +) 4

1500 kcal + 1500 kcal/m² burn

Recommended Daily Allowances (1989)

<table>
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<th>AGE</th>
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<td>11-14 years (Boys)</td>
<td>52 - 55</td>
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<tr>
<td>11-14 years (Girls)</td>
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Recommended Daily Allowances (1989)


Appendix 5

Standard Analgesia Medicine Chart for Procedural Pain (RXH)

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<td>2. Infapain (Panado-Codien)</td>
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<td>3. Ibuprofen (Brufen)</td>
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<td>4. Mefenamic Acid (Ponstan)</td>
<td>6.5 mg/kg</td>
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<td>5. Tildine (Valoron)</td>
<td>1 drop per year of age</td>
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<td>6. Hydroxyzine (Aterax)</td>
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<td>7. Morphine</td>
<td>(TBSAB dependent)</td>
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The standard "cocktail" (no. 1, 2 and 3) was given to all the children, ± 30 minutes before the planned dressing change. This usually provided adequate pain control for this procedure. However, if it was found inadequate during the procedure, the procedure was stopped and Tildine was given immediately. Tildine is a quick acting sedative. The "cocktail" was then adjusted accordingly for the next dressing change. Ibuprofen occasionally caused epi-gastric discomfort, and was then replaced with Mefenamic Acid. All severe burns that were admitted to the intensive care unit (ICU), were given constant morphine infusions for at least 3 days post burn. The Morphine infusion was then tapered down gradually and changed to the standard "cocktail".

If any child showed intolerance to Domicum due to overexposure, it was changed to Hydroxyzine. Hydroxyzine was also prescribed for itching during the wound healing process. It was taken into account that all these drugs could have side effects. The children were therefore monitored very carefully. The drugs that were used were all quick acting and had a short duration, which were found to be safe. This regime has been tested over the last few years, with no negative effects reported up until now.

Throughout the stay of each burned patient the "background pain" (if experienced) was treated with extra Infapain and Tildine. A psychiatrist was called in for cases of depression, and Egnolyl was prescribed when necessary.

References


Appendix 6

Descriptive Statistics for the Galveston and Solomons Equations, the RDA, and the Expected Energy Expenditure for the EEF and LEF group, respectively

### Galveston Equation

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Appendix 7

Descriptive Statistics for the Deviations from the Expected Energy Expenditure: Galveston and - Solomons Equations, and the RDA, for the EEF and LEF group, respectively.

Galveston Deviation

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<td>32.3</td>
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<td>37.8</td>
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<td>16.6</td>
<td>40.0</td>
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<tr>
<td>26</td>
<td>29.8</td>
<td>32.4</td>
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</table>
Appendix 8

Respiratory Quotient (RQ) results from Adult Polytrauma Patients

The initial Indirect Calorimetry measurement was taken within the first week of admission and the subsequent measurement, within a median of 5 days thereafter.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Initial RQ</th>
<th>Subsequent RQ</th>
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<tr>
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</tr>
<tr>
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<td>0.79</td>
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<td>0.73</td>
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<tr>
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<td>0.69</td>
</tr>
<tr>
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<td>0.5</td>
<td>0.76</td>
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<tr>
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<td>0.82</td>
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<tr>
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<td>0.94</td>
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<tr>
<td>11</td>
<td>0.59</td>
<td>0.98</td>
</tr>
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</table>

Permission was obtained from the Grootte Schuur Hospital Respiratory Unit, to use these results. These results were measured by Indirect Calorimetry on the individuals between 1994 and 2000, as were requested by the head of the Respiratory Unit. Only cuffed tubes were used on the ventilated patients.