The metabolic response to severe head injury

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Caloric expenditure and nitrogen balance were measured in 14 steroid-treated comatose head-injured patients acutely and up to 28 days after injury. During this period patients were fed with a continuous enteral infusion of a formula containing 2 Kcal/cc and 10 gm nitrogen/liter. Indirect calorimetry was carried out for 102 patient-days. The mean resting metabolic expenditure (RME) for nonsedated nonparalyzed patients was 138% ± 37% of that expected for an uninjured resting person of equivalent age, sex, and body surface area. Nitrogen excretion was measured for 135 patient-days. The mean excretion was 20.2 ± 6.4 gm/day. The mean protein caloric contribution was 23.9% ± 6.7% and was greater than 25% for six patients, compared to normal values of 10% to 15%. Despite hyperalimentation, positive nitrogen balance for any 3-day period was achieved in only seven patients, and required replacement of 161% to 240% of RME with enterally administered formula. Head-injured patients had a metabolic response similar to that reported for patients with burns of 20% to 40% of the body surface.

Key Words: head injury • metabolism • nitrogen balance • alimentation • tube feeding • nutrition

Since Cuthbertson’s observation in 19317 of increased nitrogen excretion in patients with long-bone fractures, the metabolic response to injury has been extensively investigated. Surgery, trauma, burns, and sepsis have been found to produce increased caloric expenditure, which generally varies with the severity of the injury.9,11,14,21 Protein metabolism is also altered after injury, and there is an increase in nitrogen excretion due to increased catabolism of protein. If this response is not treated by appropriate nutritional management, loss of body mass results. The consequences of weight loss from malnutrition were investigated by Studley,17 who found a 10-fold increase in mortality from gastric surgery in patients who had undergone a preoperative weight loss of 20% or greater. Other sources have reported that suppression of immune responses and poor wound healing result from malnutrition.8,12 On the basis of these and other studies, alimentation in the first weeks after injury to meet the increased caloric and nitrogen requirements of patients with burns, sepsis, and multiple trauma has become a principle of their care.

There have been few studies of the metabolic response to severe head injury, a situation due in part to the technical difficulties of measuring caloric consumption in comatose patients who require intensive medical and nursing care. However, observation of comatose head-injured patients suggests that their nutritional requirements are increased in comparison to their normal resting state. Rapid weight loss is seen in such patients, and periods of autonomic hyperactivity expressed as tachycardia, diaphoresis, and hypertension occur frequently. A hyperadrenergic state in head-injured patients has been documented and correlated with tachycardia and hypertension.6 For these reasons, we sought to determine the answers to two questions which are of importance to the management of head-injured patients: 1) To what extent are increased resting metabolic expenditure (RME) and increased protein catabolism present in steroid-treated patients with acute severe head injury? 2) To what extent does usual enteral alimentation begun early after injury meet caloric and nitrogen needs?

Clinical Material and Methods

Study Design

In designing such a study it is necessary to select a level of feeding as one of the variables, since feeding has been shown to have a specific dynamic action of increasing RME, but probably by not more than 10%.10 Protein intake also increases nitrogen excretion.5 Selection of no feeding (starvation) was ethically unacceptable and, in any event, represents an artificial situation.
not met in clinical practice. Another choice of feeding would have been administration of 5% dextrose in 1500 to 2000 cc of fluid (D5W) per day. This would provide approximately 500 Kcal/day, and represents the level of nutrition which many comatose head-injured patients have received in the acute phase of their treatment. Preliminary data in patients fed at this level have shown that both RME and nitrogen excretion were markedly elevated in some patients.

Therefore, we believed that the most clinically valuable initial study that we could perform was a study of the metabolic response to head injury of patients receiving steroid treatment with provision of the best nutrition achievable by enteral methods. Enteral feeding was chosen in preference to intravenous hyperalimentation because of the ability to deliver large quantities of calories and protein without fluid overload and to avoid infectious complications. The primary limitation of an enteral feeding program in studying nutrition is the inability to deliver a constant amount of calories and nitrogen throughout the patient’s course because of the necessity of slowly increasing feedings at first, and the necessity for periods of no enteral intake during surgical procedures. Dexamethasone is another treatment variable which could potentially influence RME and nitrogen excretion. Since corticosteroids are widely used in the treatment of head-injured patients they were administered to this study group. Intubation, tracheostomy, and invasive catheters may have affected RME, but these variables were present in all patients and a uniform effect would be expected. The circumstances of practice dictated these management techniques. Our goal as a first investigation was to study a group of patients managed by a regimen typical for head-injured patients.

**Patient Population**

The patients studied came from a group of 115 patients with severe penetrating and nonpenetrating injuries (Glasgow Coma Scale (GCS) score < 8) who were admitted to the Neurosurgery Service of Ben Taub General Hospital between June 1, 1981, and June 1, 1982. The criteria for entry to the study were the absence of major systemic injuries, survival for the first 48 hours, and coma lasting over 24 hours. Fourteen patients were randomly selected for nutritional studies. One patient had sustained facial injuries, one patient a fracture of the humerus, and another a fracture of the tibia and fibula. There were no other systemic injuries. Table 1 gives the patients’ demographic characteristics, primary diagnosis, GCS scores, and outcome at 3 months after injury. No patient entered into the study had died within the first 3 months after injury; however, two patients who had remained in a persistent vegetative state died within 6 months of injury.

**Patient Management**

The mean time from injury to admission was 2 hours. Patients were intubated upon admission to the Emergency Department and treated with volume ventilation and supplemental oxygen. Patients underwent computerized tomographic (CT) scanning within 45 minutes of admission. Patients with intracranial hematomas underwent craniotomy and removal of the hematoma. Those with gunshot wounds had surgical debridement. Mannitol, 1 gm/kg, dexamethasone, 20 mg intrave-

<table>
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<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Diagnosis</th>
<th>GCS Score</th>
<th>3-Month Outcome</th>
<th>Average RME (% of expected)</th>
<th>Average Nitrogen Intake (gm)</th>
<th>Average Nitrogen Loss (gm)</th>
<th>Protein Caloric Contribution (%)</th>
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</table>

* Nutritional data expressed as a mean ± standard deviation of all data obtained for each patient during the first 9 days. Data from periods of paralysis or sedation are excluded except for Case 2, where all data were obtained during barbiturate coma. RME = resting metabolic expenditure; EDH = epidural hematoma; SDH = subdural hematoma; ICH = intracerebral hematoma; DBI = diffuse brain injury; GSW = gunshot wound; GCS = Glasgow Coma Scale; GR = good recovery; MD = moderate disability; SD = severe disability; PVS = persistent vegetative state.

$Outcome assessed by the Glasgow Outcome Scale.

†This patient received barbiturates.

§Subsequently died within 6 months.
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nously, and a loading dose of phenytoin, 18 mg/kg intravenously, were given in the Emergency Department. During the 1st week after injury, PaO$_2$ was maintained at 100 mm Hg or greater by supplemental oxygen and volume ventilation, and PaCO$_2$ was maintained between 27 and 30 mm Hg. Morphine and pancuronium bromide were used when necessary to control ventilation. All patients had Swan-Ganz catheters, radial or femoral arterial catheters, and intracranial pressure (ICP) monitors (either a ventriculostomy or subarachnoid bolt) placed within a few hours of admission. Patients were managed with the following medications: phenytoin, 100 mg; dexamethasone, 4 mg; and cimetidine, 300 mg, each given intravenously every 6 hours. Dexamethasone was continued for the first 14 days after injury in study patients. Nafcillin 4 gm/day, was given prophylactically during the period of ICP monitoring. Intracranial pressure was elevated in two patients. In one patient, after the failure of hyperventilation, paralysis, sedation, and mannitol to control ICP, pentobarbital (2 mg/kg/hr) was used for ICP control.

Patients were fed through a nasogastric tube by continuous infusion. Tube feedings were begun as soon as bowel sounds were heard, that is, within 24 hours of injury for all but two patients, who were first fed on the 7th day after injury. The formula used for feeding came from a single lot, which had a nitrogen content of 10.023 gm/liter (70 gm protein/liter) measured by the micro-Kjeldahl technique, and contained 14% of its calories as protein.* Tube feedings were begun by continuous infusion of 25 to 50 cc/hr of full-strength solution and increased by 25 cc/hr every 12 hours to a maximum rate of 100 cc/hr. Tube feedings were not decreased unless gastric residual volume exceeded 300 cc. Tube feedings were stopped 12 hours prior to and for 24 hours after surgical procedures, such as tracheostomy. Tracheostomy was performed for all patients remaining in coma on the 7th to 10th day after injury, resulting in a 36-hour period of no oral intake. Patients also received intravenous fluids consisting of D$_2$W 1/2 normal saline in amounts ranging from 1300 to 3000 cc/day (mean 2150 ± 937 cc/day) providing 430 ± 187 Kcal/24 hrs. Diarrhea occurred in two patients and responded to a decrease in the enteral infusion rate.

Metabolic Methods

Metabolic measurements were carried out only if the patients were in coma, and were carried out to the 9th day if patients remained comatose. In addition, in four patients with persistent coma, studies were extended to the 28th day after injury. The patient's metabolic status was evaluated by daily measurement of RME with the technique of indirect calorimetry, by measurement of nitrogen intake and urinary nitrogen excretion, and by measurement of weight at weekly intervals.

Caloric consumption was measured by indirect calorimetry. This technique calculates caloric requirements from oxygen consumption (VO$_2$) using the following factors: volume of gas inspired and expired and fraction of oxygen inspired and expired. Expired volume is directly measured by use of a Tissot cell, a water displacement device. Since inspired volume comes from a ventilator and cannot readily be measured directly, it is calculated by the ratio of the concentration of nitrogen expired with respect to nitrogen inspired. Nitrogen is a non-diffusible gas and its amount remains constant, although volume of gas inspired may be different from that expired, depending upon the degree of oxygen utilization and CO$_2$ excretion. Standard references discuss the technique of indirect calorimetry and conversion of VO$_2$ to RME.\textsuperscript{19} Resting metabolic expenditure is derived from the known caloric yield of a given volume of oxygen, utilizing the measured respiratory quotient (RQ). Excretion of CO$_2$ (VCO$_2$) is used to calculate the respiratory quotient (RQ = VCO$_2$/VO$_2$) and to convert VO$_2$ to RME.

To measure gas concentrations, duplicate samples of inspired and expired air were collected in 50-cc syringes from the inhalation port of the ventilator and from the Tissot cell. These were analyzed for CO$_2$, O$_2$, and N$_2$ content by a gas chromatograph accurate to within 10 ppm (parts per million). Duplicate samples that differed by more than 5% were discarded, as this indicated a mixing of the sample with room air. The period of time required to fill the Tissot cell was 4 to 9 minutes, depending upon the ventilatory rate. To extend the sampling period, three sequential collections were made, twice daily, and the values averaged and extrapolated to a 24-hour period. The maximum difference in VO$_2$ between sequential samples was 15%.

A major potential source of error in measurement of RME is lack of steady-state conditions. Movement, hyperventilation, or hyperventilation during collection can change the amounts of CO$_2$ and O$_2$ exhaled and may give inaccurate VO$_2$ and RQ unless very long sampling times are used. To ensure steady-state conditions, patients were not suctioned, turned, or stimulated for 15 minutes prior to sampling or during sampling. Patients were studied only when respiration was controlled with a volume ventilator. Patients were not studied when there had been any recent change in respiratory status or during spontaneous posturing. Heart rate, rectal temperature, and blood pressure were recorded at the time of sampling.

Urine for nitrogen determination was collected from the Foley catheter in an acidified jar and 60-ml aliquots were frozen. Urinary nitrogen was measured by the micro-Kjeldahl technique. To estimate total nitrogen loss, 2 gm was added to the value for urinary nitrogen excretion, to compensate for fecal and transcutaneous nitrogen loss.\textsuperscript{3} Fecal nitrogen loss was measured during enteral alimentation for 5-day balance periods in two head-injured patients subsequent to those reported here; the mean value was 2 gm of nitrogen per 24-hour
the accuracy of 24-hour urine collections.

Weight was measured on admission, on the 7th day after injury if the patient was still under study, and on the last day of study for 12 of 14 patients. Two patients were weighed only on admission and 2 weeks later because of reapplication of a lower leg cast in one patient and a cast of the arm in another.

Results

General Characteristics

The nutritional data of a patient who is representative of those studied are shown in Fig. 1. This 30-year-old man (Case 12), who sustained an intracerebral hemorrhage as a result of a fall, maintained a GCS score of 7 throughout the period of study, and recovered with moderate disability. His RME remained relatively constant during the first 9 days, with a mean value of 123% ± 13% of expected levels. Enteral feedings were rapidly increased and he received 4000 Kcal during his first 24-hour period post-injury. On the 4th day, his ICP monitor was replaced in the operating room. This resulted in 48 hours of caloric intake of under 2000 Kcal/day. His nitrogen excretion remained relatively constant during the first 9 days, averaging 22.4 ± 3.1 gm/day.

The period of low caloric and nitrogen intake did not result in a significant decrease in nitrogen excretion or RME. The patient never came into positive nitrogen balance and had a cumulative negative nitrogen balance for the first 9 days after injury of 93.2 gm. His weight declined slowly throughout the first 2 weeks.

Table 1 gives for each patient the percent of RME expected for a patient of that age, sex, and body surface area without injury, the mean and standard deviation of daily nitrogen loss, and the protein caloric contribution (PCC) during the first 9 days after injury. This table summarizes 72 patient-days of indirect calorimetric data and 104 patient-days of nitrogen balance studies. The values given are average daily values. Expected RME was taken from standard tables. The PCC is the percent of consumed calories derived from protein. Its derivation is discussed below. Increased RME and nitrogen excretion were found in all patients, but to varying degrees; no obvious correlation with sex, age, primary diagnosis, or outcome was observed in this small group of patients.

The nutritional data for Days 1–3, 4–6, and 7–9 were averaged for each patient to determine if there were significant trends. The data analyzed in this manner are shown in Fig. 2 and Table 2, expressed as a mean with standard deviation. Patients were no longer studied after they began to follow commands, so that the nutritional data shown for 3-day balance periods are only for patients in coma, and consequently the number of patients studied in successive 3-day periods declined. Mean values of RME ranged from 2125 ± 374 Kcal on Days 1–3 to 2504 ± 582 Kcal on Days 7–9. The change in RME over the first 9 days was not statistically significant by the Student t-test. Dietary intake was highest on Days 4–6, with an average intake of 3118 ± 1396 Kcal. In the first 3 days, tube feedings were being slowly increased. The fall in average intake on Days 7–9 to 2538 ± 1260 Kcal was due to a period of no oral intake for tracheostomy in some patients. Nitrogen intake paralleled these changes as did nitrogen balance. With an average dietary intake of 3118 Kcal and 13.5 gm of nitrogen per day on Days 4–6, net positive nitrogen balance for that 3-day period was infrequently achieved. Changes in average nitrogen loss in successive 3-day periods were not statistically significant when compared by the Student t-test. It can be seen that while caloric needs were often met by caloric intake, nitrogen needs were infrequently met.

The mean RQ's for Days 1–9 are shown in Table 2. With a normal diet, RQ is about 0.8. An RQ of 1.0 indicates dietary carbohydrate loading, and an RQ greater than 1.0 indicates fat synthesis due to excess carbohydrate calories. If RQ's are less than 0.7 or greater than 1.2, it generally indicates inaccuracies in indirect calorimetry. The mean values for RQ ranged from 0.92 ± 0.17 on Days 1–3 to 1.0 ± 0.12 on Days 7–9, reflecting large dietary carbohydrate intake, as the enteral formula was composed largely of carbohydrate.
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Calculation of RME by Indirect Calorimetry and from the Fick Equation

To examine the relationship of RME measured by indirect calorimetry and that measured by the more widely available technique of arteriovenous oxygen differences, the arterial-central venous oxygen differences and cardiac output were measured 34 times in 14 patients using the thermodilution technique with the Swan-Ganz catheter during indirect calorimetry. The Fick equation was used to solve for VO$_2$ and the value extrapolated to 24 hours. There was a significant correlation between VO$_2$ determined by the Fick equation and that determined by indirect calorimetry when data were pooled and compared by regression analysis (n = 34, r = 0.56, p < 0.01). However, the differences in values for the two techniques were frequently too great to rely on arterial-central venous oxygen measurements as a technique for guiding nutritional therapy. The reason for this appears to be the shorter sampling time used for deriving VO$_2$ from cardiac output and arteriovenous $O_2$ difference, when compared to the longer sampling time used in the technique of indirect calorimetry.

Sources of Variation in RME Measured by Indirect Calorimetry

Body surface area, age, sex, temperature, specific dynamic action, gross motor activity, and probably muscular tone all influence the expected metabolic rate for normal individuals. Standard tables give expected values at rest based on body surface area, age, and sex.$^4$ All patients were studied in the absence of gross motor activity. However, the possibility of subclinical muscular tension affecting the results must be considered. In an attempt to study this, RME was compared in patients at rest and without sedation or paralysis and those sedated, paralyzed, or in barbiturate coma. The RME was elevated 138% ± 37% of the expected values for nonsedated patients at rest for all days of measurement. Ten samples from three patients either paralyzed, heavily sedated, or in barbiturate coma were excluded from this average. In these patients, the mean RME was 89% ± 03% of normal. Figure 3 shows the distribution of RME for 102 patient-days of indirect calorimetry in rested patients. Patients who were sedated and paralyzed generally had lower RME’s than those at rest and not sedated. There was a wide variation in daily RME’s among nonsedated patients varying from 99% of normal to 250% of normal, possibly related to muscle tension, since there was no gross motor activity during RME measurement. Values of caloric consumption of 5000 to 12,000 Kcal (calculated out to a 24-hour period) were measured when patients spontaneously postured. If patients became more spontaneously active during the 1st week, their measured RME increased.

There was a suggestion that lower GCS scores were

| TABLE 2
| Average metabolic data in 14 head-injured patients* |
|-----------------|-----------------|-----------------|
| Metabolic Data  | Days 1–3         | Days 4–6         | Days 7–9         |
| RME (Kcal)      | 2125 ± 374       | 2354 ± 579       | 2504 ± 382       |
| caloric intake (Kcal) | 2089 ± 1144    | 3118 ± 1396      | 2538 ± 1260      |
| nitrogen intake (gm) | 8.0 ± 6.1       | 13.5 ± 7.3       | 11.2 ± 6.9       |
| nitrogen loss (gm) | 18.6 ± 6.4      | 20.3 ± 6.5       | 22.1 ± 6.0       |
| nitrogen balance (gm) | −10.0 ± 9.9     | −8.2 ± 11.1      | −9.4 ± 11.6      |
| respiratory quotient | 0.92 ± 0.17     | 0.99 ± 0.12      | 1.0 ± 0.12       |

*Values expressed as means ± standard deviations. RME = resting metabolic expenditure.

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associated with higher RME's (Table 1), but regression analysis of all RME's versus the corresponding GCS scores did not yield a significant correlation. Heart rate and mean arterial pressure also failed to correlate with the ratio of measured to predicted RME when tested with regression analysis by the method of least squares when all data were pooled. Elevated temperature was associated with elevation of RME (n = 104, r = 0.44, p < 0.01). Temperature was elevated greater than 37.5°C in 50% of samples, but was never higher than 39°C. An increase in temperature of 1°C results in a 10% increase in RME, so that even at 39°C, metabolic rate would be increased only 15%. Therefore, the RME's measured were far in excess of those that could be expected from elevation of temperature in this group of patients.

Administration of carbohydrate and of protein in normal man has a specific dynamic action which produces an increase in RME. For predominantly carbohydrate diets, this will result in a maximum increase in RME of 10% of ingested calories, and for high protein diets, 17% of ingested calories. Hence, it is unlikely that specific dynamic action would be the sole cause of the high RME's measured.

The course of RME over time changed little over the first 9 days unless the patient became febrile or more spontaneously active and more responsive to pain. In four patients who had a posturing motor response to pain and remained in coma, studies were continued beyond the first 9 days for 13 to 28 days after injury. A total of 30 days of RME were collected, and mean RME was 2477 ± 803 Kcal. Thus, RME remained increased throughout the period of coma for up to 28 days in four patients.

Nitrogen Excretion

The mean nitrogen excretion was 20.2 ± 6.4 gm/day, which is equivalent to that found in burned and severely traumatized patients, and considerably greater than the nitrogen excretion of 12 gm/day in a normal fasted man. Very high levels of nitrogen excretion of 30 to 35 gm/day were found periodically after injury in four patients. Increased nitrogen excretion persisted after the first 9 days in four comatose patients. The mean value of nitrogen loss for 31 days of measurement from 10 to 28 days after injury was 21.5 ± 6.9 gm/24 hrs. Cumulative nitrogen balance for 12 of 14 patients who had been weighed on admission and on Days 5–7 was compared by regression analysis to the percent change from admission weight. There was no significant correlation. This probably related to changes in fluid status in the phase of acute management. The mean percentage of weight change for the time from admission to Days 5–7 after injury was −2% ± 7.9%.

The amount of nitrogen excreted can be influenced by the level of caloric and nitrogen intake. Catabolism of protein with excretion of administered nitrogen has occurred with caloric intakes of less than 50% of RME. With the enteral formula used, a high caloric density made it likely that sufficient calories had been provided for nitrogen utilization so that catabolism of administered nitrogen due to caloric deficiency was unlikely. The possibility also exists that feeding of large amounts of calories and nitrogen can stimulate metabolism and nitrogen turnover. Very high levels of nitrogen excretion were found in patients who were fed large amounts of protein, as well as those who were fed small amounts of protein at the time of measurement.

![Figure 3](image-url)
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Protein Caloric Contribution

The PCC is the percent of calories consumed derived from protein and can be calculated by the following formula where N = nitrogen:

\[
PCC = \frac{\text{gm} \ N \times 6.25/\text{gm protein}}{\text{gm} \ N \times 4.0 \ Kcal/gm protein} \times 100.
\]

In ambulatory, uninjured man, the PCC is 10% to 15%. Duke, et al.,\(^9\) found the maximum PCC in moderate systemic injuries to be 20%. In major systemic injury treated with steroids, PCC's of up to 30% have been found.\(^14\) This elevated PCC reflects the increased catabolism of protein for calories occurring as a result of trauma. In the present series of patients, using data obtained when the patients were not sedated or paralyzed, the mean PCC was 23.9% + 6.7%. Values of PCC greater than 20% often occurred in patients with minimal RME in whom nitrogen excretion remained high (Table 1). A mean PCC of greater than 25% for the first 9 days was found in six of 14 patients. Calculation of PCC is dependent upon grams of nitrogen excretion and RME. Since protein intake may influence nitrogen excretion, the level of feeding could influence PCC. In the series of Duke, et al.,\(^9\) daily nitrogen intake was 10 gm. Nitrogen intake varied among patients in this series, but high PCC's were found in those who received low nitrogen intake, such as Cases 6 and 7, and in those who received larger intake, such as Cases 8 and 14. In only one patient was average nitrogen intake greater than 14 gm/24 hrs (Table 1). Hence, the high PCC's found were not related exclusively to dietary nitrogen loading.

There were wide variations in PCC that were due to varying degrees of elevation in RME and nitrogen excretion seen in individual patients. Two patients (Cases 1 and 7) had a high average RME of 170% ± 32% and 190% ± 48% of the expected levels, respectively; yet in Case 1 urinary nitrogen loss was only 13.19 ± 2.5 gm, while in Case 7 nitrogen loss was much higher (20.7 ± 6.0 gm). Two other patients (Cases 12 and 13) with relatively low RME's of 123% ± 13% and 117% ± 6.5% of expected levels, respectively, had elevated urinary nitrogen losses of 22.4 ± 3.1 gm (Case 12) and 25.1 ± 4.6 gm (Case 13). Other patients ranged between these extremes. This variation resulted in mean PCC's for the first 9 days ranging from 15.4% to 30.8%. The PCC's found in this group of head-injured patients are higher than those reported in other forms of trauma, with similar increases in RME, indicating a high obligatory usage of protein.

Relationship Between Caloric Intake and Nitrogen Balance

A question to be answered from this study was whether an enteral formula alone administered as early as possible could provide sufficient caloric and protein intake to achieve positive nitrogen balance early in the course of recovery. Table 3 presents the data for the best nitrogen balance attained for any consecutive 3-day period for each patient. Net nitrogen retention was achieved in only four patients for any 3-day period and usually when calories were grossly over-replaced at 200% of RME and at levels of nitrogen intake of 0.3 gm/kg/24 hrs. In normal man, a protein intake of 8.5 gm/day with adequate calories has resulted in nitrogen equilibrium.\(^5\) The caloric content of the protein of the enteral formula used was 14%. Due to provision of calories from supplemental D.W., 12% of calories used were derived from protein at maximal infusion rates. The losses of nitrogen averaging 20 gm/24 hrs were

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Days Post-Injury</th>
<th>RME (Kcal)</th>
<th>Enteral Intake (Kcal/kg/24 hrs)</th>
<th>% RME Replaced Daily</th>
<th>Nitrogen Intake (gm/kg/24 hrs)</th>
<th>Nitrogen Loss (gm/24 hrs)</th>
<th>Nitrogen Balance (gm)</th>
<th>Cumulative Administered Calories from Protein (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-6</td>
<td>2432 ± 503</td>
<td>67.6 ± 11.0</td>
<td>161 ± 55.8</td>
<td>0.2990 ± 0.05</td>
<td>12.4 ± 0.9</td>
<td>+4.5 ± 3.5</td>
<td>+13.6</td>
</tr>
<tr>
<td>2</td>
<td>2-4</td>
<td>1149 ± 238</td>
<td>49.5 ± 7.5</td>
<td>257 ± 31.0</td>
<td>0.1873 ± 0.04</td>
<td>15.2 ± 2.9</td>
<td>-1.3 ± 3.0</td>
<td>-11.9</td>
</tr>
<tr>
<td>3</td>
<td>3-5</td>
<td>1762 ± 652</td>
<td>36.9 ± 7.3</td>
<td>169 ± 89.7</td>
<td>0.1602 ± 0.10</td>
<td>17.6 ± 2.7</td>
<td>-5.8 ± 9.8</td>
<td>-17.4</td>
</tr>
<tr>
<td>4</td>
<td>3-5</td>
<td>2316</td>
<td>69.3 ± 7.2</td>
<td>199 ± 10.9</td>
<td>0.2951 ± 0.03</td>
<td>17.8 ± 5.8</td>
<td>-44.0 ± 2.0</td>
<td>+12.1</td>
</tr>
<tr>
<td>5</td>
<td>10-12</td>
<td>2027 ± 72</td>
<td>66.4 ± 3.9</td>
<td>105 ± 14.0</td>
<td>0.308 ± 0.03</td>
<td>16.5 ± 4.4</td>
<td>+3.0 ± 1.7</td>
<td>+9.0</td>
</tr>
<tr>
<td>6</td>
<td>7-9</td>
<td>1744</td>
<td>35.1 ± 16.2</td>
<td>157 ± 58.5</td>
<td>0.1443 ± 0.08</td>
<td>18.4 ± 1.1</td>
<td>-10.4 ± 8.6</td>
<td>-31.3</td>
</tr>
<tr>
<td>7</td>
<td>19-21</td>
<td>4948</td>
<td>32.5 ± 3.5</td>
<td>157 ± 17.1</td>
<td>0.1457 ± 0.02</td>
<td>14.8 ± 0.9</td>
<td>-0.5 ± 2.5</td>
<td>1.6</td>
</tr>
<tr>
<td>8</td>
<td>3-5</td>
<td>2090 ± 202</td>
<td>73.5 ± 14.3</td>
<td>231 ± 32.8</td>
<td>0.2881 ± 0.03</td>
<td>23.8 ± 12.0</td>
<td>-11.1 ± 17.1</td>
<td>-33.2</td>
</tr>
<tr>
<td>9</td>
<td>3-5</td>
<td>1868 ± 122</td>
<td>59.3 ± 9.0</td>
<td>196 ± 44</td>
<td>0.2846 ± 0.07</td>
<td>21.3 ± 2.5</td>
<td>-6.4 ± 5.4</td>
<td>-19.2</td>
</tr>
<tr>
<td>10</td>
<td>5-7</td>
<td>3113</td>
<td>42.6 ± 6.6</td>
<td>121 ± 18.8</td>
<td>0.1814 ± 0.04</td>
<td>17.8 ± 3.0</td>
<td>-2.1 ± 5.4</td>
<td>-6.3</td>
</tr>
<tr>
<td>11</td>
<td>3-5</td>
<td>1797 ± 21</td>
<td>60.8 ± 5.7</td>
<td>240 ± 20.5</td>
<td>0.2838 ± 0.04</td>
<td>12.1 ± 2.3</td>
<td>+8.1 ± 2.8</td>
<td>+24.2</td>
</tr>
<tr>
<td>12</td>
<td>5-7</td>
<td>2128 ± 116</td>
<td>29.0 ± 6.7</td>
<td>129 ± 10.2</td>
<td>0.1335 ± 0.04</td>
<td>23.5 ± 4.0</td>
<td>-11.9 ± 2.1</td>
<td>-39.6</td>
</tr>
<tr>
<td>13</td>
<td>24-26</td>
<td>2302 ± 500</td>
<td>54.9 ± 17</td>
<td>204 ± 81.9</td>
<td>0.2914 ± 0.05</td>
<td>26.4 ± 4.5</td>
<td>-5.4 ± 1.9</td>
<td>-7.7</td>
</tr>
<tr>
<td>14</td>
<td>1-3</td>
<td>2240 ± 78</td>
<td>54.6 ± 8.4</td>
<td>191 ± 32.9</td>
<td>0.2457 ± 0.04</td>
<td>23.8 ± 6.0</td>
<td>-4.3 ± 7.9</td>
<td>-12.9</td>
</tr>
</tbody>
</table>

*Values are expressed as the mean ± standard deviation. Resting metabolic expenditure (RME) was recorded only once in the 3-day period for four patients.

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rarely replaced by enteral feeding, which provided an average of 10 gm/24 hrs. For this reason, nitrogen equilibrium was rarely achieved.

The difficulties encountered in achieving positive nitrogen balance were, in part at least, related to an inability to maintain the high enteral infusion rates necessary to deliver more than 20 gm of nitrogen per 24-hour period without producing diarrhea and gastric distention in some patients. Therefore, feedings were begun with 25 to 50 ml/hr of full-strength formula and advanced by 25 cc/hr every 12 hours, using continuous infusion. Ventriculostomies were changed on Day 5, if still needed, and tracheostomies replaced on Days 7–10, and these patients had no enteral feeding immediately prior to or after the procedures. These two factors, the slow progression to full feedings and periods of no enteral intake for surgical procedures, resulted for the first 9 days in enteral infusion rates below 75 ml/hr for 42% of 109 patient-days and below 100 ml/hr for 80% of patient-days.

Additional Metabolic Consequences of Hyperalimentation

Serum glucose levels greater than 100 mg% occurred in all patients, and levels greater than 150 mg% were recorded in 50% of patients. The degree of hyperglycemia did not correlate with the rate of enteral infusion. When infusion rates reached 100 ml/hr, insulin was required to regulate blood glucose of greater than 250 mg% in five patients.

In three patients in the acute phase of head injury in whom tube feedings were increased to 100 cc/hr, PaCO₂ rose over 10 mm Hg within 24 hours on the same ventilator setting using intermittent mandatory ventilation (IMV). In one of these patients, ICP increased and responded to an increase in the IMV rate. Smaller increases in PaCO₂ were seen in other patients as tube feedings were increased. Hyperuricemia did not occur in any patient. With supplemental water provided intravenously, electrolyte abnormalities were not seen. Liver enzymes were not measured after the 1st week.

Discussion

The metabolic response to head injury in these steroid-treated patients was characterized by an increase in caloric consumption which is similar to that observed in patients with burns over 20% to 40% of their body surface. In most patients the PCC exceeded 20% so that considerably more calories were derived from protein catabolism than in many other trauma patients. The elevation of RME could be a catecholamine-mediated response to neural injury. Arterial epinephrine and norepinephrine have been shown to be increased in severe head injury, and oxygen consumption as measured by the Fick equation has been found to be increased in proportion to catecholamine elevation. Other factors that could elevate RME in head-injured patients are temperature, specific dynamic action, and increased muscular tone. Specific dynamic action has been documented in normal man, but not in injured patients or patients with sepsis. Since paralysis and sedation decreased RME in some patients, muscular tone probably influences RME. The cause of elevation of RME in head-injured patients is likely to be multifactorial and determined by the hormonal response to head injury, to management variables such as feeding, and to secondary effects of head injury, such as muscular tone and motor response.

Nitrogen excretion in normal man is closely linked to RME, but this may not be the case in head injury. The large nitrogen excretions found in some patients with low RME, particularly those who had been paralyzed and sedated, suggests that RME and nitrogen excretion may be influenced by different factors. Nitrogen excretion may be influenced by nitrogen intake, body muscle mass, lack of muscular activity (as in paralysis and barbiturate coma), and possibly steroid usage, as well as by the factors which could potentially influence RME. Progressive escalation of nitrogen feeding has been found in burned patients to increase nitrogen excretion, and this phenomenon may make the achievement of nitrogen equilibrium difficult. Whether the use of exogenous steroids in clinical practice contributes to hypercatabolism is probably dependent upon the dose used. Dexamethasone, 24 mg/24 hrs, has been associated with a 15% increase in nitrogen excretion in six head-injured patients with multiple trauma as compared to a group of multiply-injured patients without head injury or steroid treatment. Administration of exogenous cortisone in doses of 30 to 200 mg/24 hrs has failed to alter urinary nitrogen excretion in fasted adults. In animal studies, daily doses equivalent to five to 10 times that administered to this group of patients have been required to cause loss of muscle mass and increased nitrogen excretion. The doses of steroids used in these patients (24 mg/24 hrs) probably did not substantially alter nitrogen excretion.

Appropriate nutritional management hinges on knowing the causes of increased RME and increased nitrogen excretion, so that the response may either be modified to decrease protein and caloric needs or these needs met by hyperalimentation. Possible modes of decreasing RME are beta adrenergic blocking agents, barbiturates, paralysis, and antipyretics. Possible ways of decreasing nitrogen excretion are discontinuing steroid usage and muscular stimulation. The lack of knowledge about the cause and consequences of the metabolic response makes it impossible to judge at present the optimal extent of nutritional replacement. Management of the metabolic response to head injury by hyperalimentation with a goal of meeting or exceeding caloric expenditure and achieving positive nitrogen balance is of unproven benefit and may be associated with complications such as hyperglycemia, hypercarbia, and fluid overload. Positive nitrogen balance may not be achievable without very high levels of feeding, due to an escalating urinary nitrogen excretion in response to RME.
The metabolic response to severe head injury
to nitrogen feeding. Approximately 20% of patients will
not tolerate early enteral feeding, and it requires par-
enteral alimentation with its attendant risks to provide a
high level of nutrition. Data are lacking that show the
benefit of early hyperalimentation in other injured,
hypermetabolic patients, so that little insight is gained as
to the appropriate level of replacement from existing
knowledge in other diseases with a similar response.
Yet to fail to treat the hypermetabolic response in head
injury is probably undesirable, since head-injury deaths
are often due to infection, which could be related to
malnutrition. The causes of increased RME and nitro-
gen excretion, and the effect on outcome of modifying
the metabolic response and of hyperalimentation are
subjects for future investigation.

Several practical problems make it difficult to achieve
positive nitrogen balance and to meet caloric needs in
management of severe head injury if this proves to be
the most appropriate therapeutic modality. The heter-
genoty of the nutritional response makes it unlikely
that a standard nutritional protocol for all comatose
head-injured patients will be satisfactory. To optimally
meet nitrogen excretion and caloric expenditure with-
out overflow feeding, measurement of urinary nitrogen and
RME are needed. At present, these techniques are ex-
pensive, and are not performed routinely. The attain-
ment of positive nitrogen balance in head-injured pa-
tients is made difficult by the limitations of volume
which can be enterally administered. Patients seldom
tolerated more than 2.5 liters of enteral feedings per
day, and feedings were increased over 3 days to achieve
gastrointestinal tolerance. Whether early nitrogen equi-
librium will be attainable by enteral means alone using
any presently marketed formula is doubtful.

As discussed above, further study of the causes of the
metabolic response to head injury and the response to
treatment is indicated. However, on the basis of the present
data and experience with injured patients in general,
tentative recommendations for the nutritional
management of head-injured patients can be given. Our
current recommendations for nutritional management
in head injury are to begin feeding enterally within 48
hours of injury by continuous infusion, with the goal
of providing at least 0.24 gm nitrogen/kg body weight/
day. Supplemental water is required, either intrave-
nously or enterally. Use of the enteral formulas with
the highest protein content available will most nearly
fit the needs of this group of patients. If enteral feedings
are not tolerated within the first 48 to 72 hours, intra-
venous hyperalimentation should be begun, as the pa-
tient who does not tolerate enteral feedings early after
injury is not likely to do so for many days. It should be
noted that the protein-sparing effect of intravenously
administered D,W is minimal even with large volumes.
Dextran (5%) in fluid contains only 200 Kcal/liter of
solution so that use of conventional intravenous fluids
for nutrition can be expected to neither appreciably
spare protein nor supply more than a small percentage
of calories utilized in head injury. Because of the ex-
treme elevation of caloric consumption produced by
posturing, paralysis or sedation is helpful in reducing
caloric requirements. Blood glucose and PaCO2 should
be monitored carefully when high rates of caloric intake
are reached. Use of insulin and adjustment of ventilator
settings are necessary to avoid metabolic derangements.
Anthropometric data have not been useful in guiding
acute management, as accurately measurable somatic
changes occur too slowly to be useful in the 1st week
after injury. Urinary nitrogen loss measured by 24-hour
urine collections for urea or nitrogen provides the most
useful index of the protein needs of the patient.

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