ANNALS OF SURGERY
Vol. 223, No. 4, 395–405


# Sequential Changes in the Metabolic Response in Critically Injured Patients During the First 25 Days After Blunt Trauma

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## Background

Understanding the changes in energy expenditure and body composition is essential for the optimal management of the critically injured, yet these changes have not been quantified within the current context of trauma care.

## Methods

Ten critically injured patients (median Injury Severity Score = 35) had measurements of energy expenditure and body composition as soon as they were hemodynamically stable and then every 5 days for 21 days.

## Results

Resting energy expenditure rose to 55% above predicted and remained elevated throughout the study period. Total energy expenditure was 1.32 × resting energy expenditure. Body fat was oxidized when energy intake was insufficient ($r = -0.830$, $p < 0.02$). Body water changes closely paralleled body weight changes and were largely accounted for by changes in extracellular water. Over the 21-day study period, there was a loss of 1.62 kg (16%) of total body protein ($p < 0.0002$), of which 1.09 kg (67%) came from skeletal muscle. Intracellular potassium was low (133 ± 3 mmol/L, $p < 0.02$) but did not deteriorate further after hemodynamic stability had been reached.

## Conclusions

These results show that the period of hypermetabolism lasts longer and the protein loss is greater in critically injured patients than previously thought. Most, but not all, the protein is lost from muscle. Fat loss can be prevented and cell composition preserved once hemodynamic stability is achieved.

In his classical studies carried out more than 50 years ago, Cuthbertson described in considerable detail many aspects of posttrauma metabolism.[1] These studies were complemented by isotopic dilution studies carried out by Moore and his colleagues,[2] who confirmed many of Cuthbertson's findings besides making fundamental new advances. Together, these workers showed that the injured patient early after trauma shows a characteristic picture in which hypermetabolism occurs, protein and fat are consumed, and body water and salt are conserved. These fundamental discoveries lie at the heart of the present day management of the critically injured patient, yet many of the changes described have not been quantified and the original experiments were carried out before modern systems of trauma care had been established.

The availability of body composition methodology, which has been adapted for use in critically ill patients in intensive care,[3] has enabled us to quantify the sequential changes in energy expenditure and body composition that occurred in a group of critically injured patients after blunt trauma. These patients were all treated in a modern trauma center according to specific protocols and with state-of-the-art technologies.

## METHODS

### Patients and Clinical Methods

Between January 29, 1993, and August 15, 1994, 235 patients suffering from major blunt trauma (an Injury Severity Score of 16 or greater)[4,5] were admitted to the Department of Critical Care Medicine (DCCM) at Auckland Hospital, Auckland, New Zealand. Thirty-four of these patients were recruited for the present study. Trauma care in Auckland takes place in a coordinated system of prehospital and in-hospital care that includes medical control of prehospital care, radio–telephone communication, and a high-level, in-hospital trauma team response, which includes rapid assessment, resuscitation, and stabilization according to well-established principles.[6]

All patients studied were intubated and ventilated shortly after hospital admission. A team of four full-time intensivists had overall responsibility for clinical management and coordinated in a consensus fashion all other specialties, which provided early definitive treatment of injuries. As soon as clinically indicated, study patients were given early enteral feeding with an elemental formula (4.2 kJ/mL) containing glutamine at 14.2 g/L and arginine at 1.8 g/L (Ross Laboratories, Columbus, OH) administered by the nasogastric or nasojejunal route. The caloric distribution of the formula was 21% protein, 13% fat, and 66% carbohydrate. Nutritional intake was increased up to 1.3 × the measured resting energy expenditure (REEm) according to a standard protocol, and the enteral feeding was continued until oral food could be tolerated.

The study was approved by the North Health Ethics Committee, and informed consent was obtained from each patient's next of kin before entry to the study.

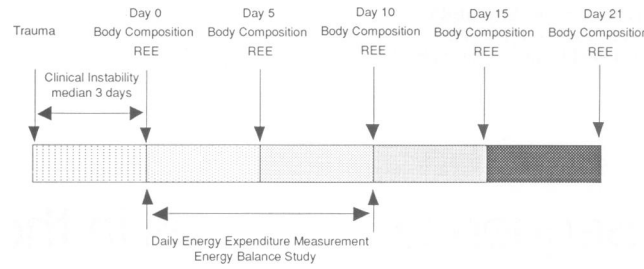


**Figure 1.** Study design.

### Study Design

Patients underwent serial measurements of body composition and energy expenditure over a period of 21 days. The first studies were performed as soon as hemodynamic stability was achieved without either colloid infusion or increasing inotropic support (day 0), and body composition studies were repeated on days 5, 10, 15, and 21 (Fig. 1). The body composition measurements were performed in the department of surgery in a facility especially designed for studying critically ill patients.[7] Patients received all necessary intensive therapy during the 4-hour study periods. The REE was measured twice daily at the bedside, initially in the DCCM, and later in the surgical wards.

### Body Composition

Body weight (BW), total body nitrogen (TBN), total body fat (TBF), total body water (TBW), extracellular water (ECW), and total body potassium (TBK) were measured on days 0, 5, 10, 15, and 21. The BW was recorded to the nearest 0.1 kg using a hoist-weighing system, used to transfer the patient from the bed to the body composition scanners.

Supported by a grant from the Health Research Council of New Zealand. Dr. Franch-Arcas was the recipient of grant CIRIT BE92-139 from the Direcció General d'Universitats of the Generalitat de Catalunya.

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Accepted for publication September 19, 1995.

## Total Body Nitrogen

The TBN was determined using prompt gamma *in vivo* neutron activation analysis, whereby TBN is calculated independently of total body hydrogen using a method previously described.[8] The body was scanned twice with a precision of 2.5% and an accuracy compared to chemical analysis of within 4% (based on anthropomorphic phantoms).[3] Total body protein (TBP) was calculated as 6.25 × TBN.

## Total Body Fat

The TBF was measured by dual-energy x-ray absorptiometry (DEXA) (model DPX+, software version 3.6y, Lunar Radiation Corp., Madison, WI). Using anthropomorphic phantoms of known fat content and with different levels of overhydration, the precision of the technique was 1.3% and the accuracy better than 5%.[3]

## Total Body Water

The TBW was measured by tritiated water dilution according to previously published methods.[9] Each patient received 3.7 MBq tritiated water intravenously in 10 mL sterilized water at the time of each body composition measurement. By analysis of previously reported data,[9] the precision of the method varies from 1.5% when a single sample is taken to 0.9% when three samples (at 4, 5, and 6 hours) are taken. No correction has been made for nonaqueous exchangeable hydrogen.

## Extracellular and Intracellular Water

The ECW was estimated by the dilution of sodium bromide. After an initial blood sample was taken for the basal serum bromide concentration, 50 mL of 5.0% (w/v) sodium bromide was given intravenously from a syringe that was weighed before and after injection. Samples of blood were taken at 4, 5, and 6 hours after injection, at which time equilibration of sodium bromide in the ECW had occurred. For each patient in DCCM, a value of the ECW at the time of injection was calculated from the mean of three values derived from the 4-, 5-, and 6-hour serum samples in a manner exactly analogous to the method used for TBW. Patients convalescing in the wards had only a single serum sample taken at 3 hours. The overall mean precision for the measurement of ECW varied from 6%, when a single sample was taken, to 4%, when three samples were taken. For serum bromide analysis, 250 μL of serum was deproteinized and assayed by high-performance liquid chromatography using a partition technique with acetyl-trimethyl ammonium hydrogen sulfate as the ion-pairing agent, a Waters Novo-pak (Waters, Milford, MA) reversed phase column and ultraviolet detection at 195 nm. The ECW was calculated from the following equation[10]:

The ECW (L) = 0.95 × 0.90 × Br dose (mmol)/[serum Br] (mmol/L), where 0.95 is the Donnan equilibrium factor for univalent anions, 0.90 is a factor correcting for intracellular bromide penetration, and [serum Br] is the bromide concentration of protein-free serum ultrafiltrate after correction for basal bromide concentration. Protein was removed from serum using a 30-kd microfiltration sample tube (Amicon, Beverley, MA) spun at 4800 rpm for 30 minutes.

The intracellular water (ICW) was calculated as the difference between TBW and ECW. The overall mean precision for the measurement of ICW was estimated to vary from 7%, when single serum samples were taken for each of TBW and ECW, to 4%, when three samples were taken.

## Total Body Potassium

The TBK was measured by analysis of the gamma spectrum emitted from naturally occurring $K^{40}$ using a shadow shield counter.[11] The overall precision for a single measurement of TBK is 3% as determined from replicate measurements of anthropomorphic phantoms with different levels of overhydration (L. D. Plank, unpublished observations, 1992).

A value for intracellular potassium concentration ($[K]_i$) for each study day was calculated as:

$$[K]_i \text{ (mmol/L)} = (\text{TBK(mmol)} - [\text{serum K}]\text{(mmol/L)} \times \text{ECW (L)})/\text{ICW (L)},$$

where [serum K] is the serum potassium concentration.

## Skeletal Muscle Mass

Appendicular skeletal muscle mass was derived from regional analysis of the data obtained by DEXA scanning using the method of Heymsfield et al.[12] Briefly, the fat-free mass (FFM) of the limbs less the mass of wet bone of the limbs was assumed to approximate limb skeletal muscle mass. Version 3.6y of the DEXA software allows the legs (below the pelvic triangle) and arms to be analyzed for tissue composition without interference from trunk tissue. Application of the method to critically ill patients requires a correction to the measured FFM to account for the deviation from normal hydration of lean tissue commonly seen in these patients. For each patient, the limb FFM was adjusted to "normal hydration" using the following equation:

Hydration-corrected appendicular FFM = appendicular FFM × (1-hydp)/(1-hydn), where hydn = ratio of

TBW to whole-body FFM in healthy subjects (0.73 for women and 0.71 for men)[13] and hydp = TBW/FFM for the patient. The hydration-corrected appendicular FFM was converted to appendicular muscle mass by subtraction of wet bone mass (1.82 × appendicular bone ash as determined by DEXA). Total skeletal muscle mass was calculated from appendicular muscle mass by multiplying by 1.25, a factor established from computed tomography scanning of normal subjects (S. B. Heymsfield, personal communication, 1994). Protein content of total skeletal muscle was assumed to be 17%.[14] Remaining protein in the body was referred to as nonmuscle protein.

## Energy Measurements

### *Measured Energy Expenditure*

Oxygen consumption ($VO_2$) and carbon dioxide production ($VCO_2$) were measured twice daily (Deltatrac metabolic monitor MBM-100, Datex/Instrumentarium, Helsinki, Finland) between 8:00 A.M. and 10:00 A.M. and 4:00 P.M. and 6:00 P.M., beginning as soon as possible after DCCM admission and continuing at least through day 10 and again on days 15 and 21. The average REEm[15] was calculated from these two measurements using the Weir equation:

$$\text{REEm(kcal/day)} = 5.5 \times VO_2\text{(mL/min)} + 1.76 \times VCO_2\text{(mL/min)}.$$

Nitrogen excretion was neglected.[16]

To minimize error in the measurement of $VO_2$ and $VCO_2$, a number of steps were taken. Nursing procedures were not performed on the patient during the 30 minutes before the measurement. If necessary, patients (including those being ventilated) received supplemental oxygen from a blender (Bird Corporation, Palm Springs, CA), which mixed air and oxygen regulated to a constant pressure of 55 psi by two high-precision valves (Bellofram, Burlington, MA), thus eliminating fluctuations in $FIO_2$.[17] Inspiratory sampling in patients receiving humidified gases was always taken immediately after the humidifier to allow complete gas mixing. Cooperative patients were asked to remain at rest in the recumbent position for at least 20 minutes before the measurement.

### *Predicted Energy Expenditure*

For each patient, a value of predicted resting energy expenditure (REEp) was derived on the day of each body composition study from measured TBK according to the following equation derived from 40 nonstressed hospitalized patients in our department[18]:

$$\text{REEp(kcal/day)} = 0.34 \times \text{TBK(mmol)} + 494 \quad (r^2 = 0.494, \text{SEE} = 262 \text{ kcal/day}, \text{CV} = 17.4\%).$$

### *Energy Balance*

The construction of energy balance is described in detail elsewhere.[19] An energy balance for the time between each pair of body composition measurements was calculated from changes (Δ) in measured components of body composition (TBF, TBP, and total body glycogen [TBGly]) according to the following equation:

$$\text{EB(kcal)} = (\Delta\text{TBF} \times 9.44) + (\Delta\text{TBP} \times 4.704) + (\Delta\text{TBGly} \times 4.18)$$

where 9.44, 4.704, and 4.18 represent the energy equivalent of the oxidation per gram of fat, protein, and carbohydrate, respectively.[20] The TBGly was obtained as described elsewhere[19] from BW by subtracting TBF, TBW, TBP, and total minerals, where the latter is the sum of bone mineral content given by DEXA and nonbone mineral estimated from TBP.

### *Total and Activity Energy Expenditure*

Total energy intake was calculated from recordings of all nutritional intake including oral, nasogastric, and nasojejunal intake, intravenous dextrose, and human serum albumin. Total energy expenditure (TEE) was calculated from the difference between this and the energy balance:

$$\text{TEE(kcal/day)} = (\text{Total Energy Intake(kcal)} - \text{EB})/\text{days in study},$$

and activity energy expenditure (AEE) was derived as follows:

$$\text{AEE(kcal/day)} = \text{TEE} - \text{REEm}.$$

## Radiation Dosimetry

The *in vivo* neutron activation analysis and DEXA scanning involve a radiation dose to the patient of approximately 0.3 mSv on each day of measurement. The estimated radiation dose from each dosage of tritiated water in intensive care patients is approximately 0.1 mSv.

## Statistical Analysis

Repeated-measures analysis of variance with asphericity correction was used to detect significant changes over time (SAS Institute, Cary, NC). Student's t test was used when two samples of paired data were compared. Bivariate correlations were assessed using Pearson's correlation coefficient. In all cases, the 5% level was chosen

for statistical significance. All numerical values are expressed as mean ± SEM.

## RESULTS

### Patients

Ten of the 34 patients who were recruited into the study completed the protocol, and their clinical details are listed in Table 1. Of the 24 patients who did not complete the protocol, 3 died, 10 were transferred to another hospital, and the remaining 11 were too restless to remain within the scanners for the required length of time. All 10 patients who completed the protocol were well before trauma, and Table 1 lists that all but 2 of the patients were men, all suffered major multiple blunt injuries (median Injury Severity Score = 35), and all were initially treated in our critical care unit (median time in critical care, 9 days). All survived and left hospital in a median time of 34 days.

### Measurements

Table 2 lists the mean (± SEM) data for the measurements of body weight, TBF, TBW, ECW, TBN, skeletal muscle mass, and TBK on days 0, 5, 10, 15, and 21.

### Energy Metabolism

#### *Hypermetabolism Over the Study Period*

Seven of the 10 patients had complete indirect calorimetry measurements of daily REE from 3 days after trauma through 15 days with subsequent measurements 18 and 24 days after trauma. Figure 2 shows the mean (± SEM) daily results and the mean (± SEM) predicted REE (calculated from TBK) on study days 0, 5, 10, 15, and 21. It can be seen that there was a significant elevation in REE on each study day, rising to a maximum on day 10 after trauma where it averaged 55% above predicted. There was still a significant degree of hypermetabolism (35% above the predicted REE) on day 24. Shown also is the mean REE calculated from the Harris–Benedict equation.[21] It can be seen that REE predicted in this way gives values greater than those calculated from TBK. This shows the error of using measured body weight in this prediction equation in critically ill patients with fluid overload.

#### *Total Energy Expenditure and Activity Energy Expenditure in the Early Posttrauma Period*

Accurate energy intake was recorded for 8 of the 10 patients between days 0 and 10. Table 3 lists the results of energy balance studies on these patients performed between study days 0 and 10. It can be seen that the average TEE was 9173 ± 1042 kJ/day. From measurements of REE, it can be calculated that energy expended as physical activity during this period was 2873 ± 567 kJ/day, comprising 24% of the TEE. The average TEE was 1.32 × the average REEm.

#### *Fat Metabolism*

Eight patients were involved in energy balance studies. Figure 3 shows the relationship between the 10-day changes in total body fat and the energy deficit calculated by subtracting the energy intake from the TEE. A close correlation ($r = -0.830$, $p = 0.011$) is seen showing that fat oxidation occurred in those patients whose energy intake was insufficient to achieve energy balance. There is, however, no relationship between the quantity of enteral protein administered and the amount of total body protein that was hydrolyzed ($r = 0.244$, $p = 0.6$).

### Body Weight in the Posttrauma Period

Figure 4 shows the changes in body weight that occurred in the group of 10 patients over the 21-day study period. Over the period of clinical instability before study day 0, during which time the patients received crystalloids and colloids for resuscitation, there was a positive fluid balance of 4.73 ± 1.55 L. After day 0, when hemodynamic stability had been reached and the patients were receiving enteral nutrition and maintenance fluids only, the mean weight fell steadily (approximately 0.6 kg/day), pretrauma weight being reached around day 10.

### Water Metabolism in the Posttrauma Period

Figure 4 shows the changes in TBW and ECW that occurred over the 21-day study period. Once hemodynamic stability had been reached (day 0), TBW began to return to normal. By day 10, despite having lost an average of 4.53 ± 2.17 L of water and the mean value of TBW returning to pretrauma levels, relative overhydration of the FFM was still present (TBW/FFM = 0.74 ± 0.01, which should be compared with normal values of 0.71 and 0.73 for men and women, respectively).[13] In Figure 4, it can be seen that most of the TBW changes can be accounted for by changes in ECW.

### Protein Metabolism in the Posttrauma Period

#### *Total Body Protein*

Figure 5 shows the changes in TBP that occurred over the 21-day study period. It can be seen that the losses

**Table 1. CLINICAL DATA OF 10 PATIENTS WHO UNDERWENT SEQUENTIAL METABOLIC STUDIES OVER A 21-DAY PERIOD AFTER MAJOR TRAUMA**

| Patient | Sex | Age (yrs) | ISS | Diagnosis | Surgical Procedures* | Complications | Prescan† (Days) | Ventilated (Days) | Inotropic‡ Support | Days in DCCM | Days in Hospital |
|---|---|---|---|---|---|---|---|---|---|---|---|
| A | M | 31 | 34 | Compound skull fracture, frontal lobe laceration, fractured facial bones with facial contusions. | Tracheostomy (0)<br>Craniotomy (0 and 8) | — | 5 | 10 | 1 | 16 | 32 |
| B | M | 50 | 35 | Subdural haematoma, L) tibial plateau fracture. | Tracheostomy (3)<br>Internal fixation (4) | — | 2 | 5 + 2§ | — | 11 | 27 |
| C | M | 54 | 34 | Pneumothorax, splenic rupture, minor liver laceration, L) Colle's fracture, L) greater trochanter fracture. | Splenectomy (0)<br>Tracheostomy (5)<br>Dehiscence repair (8)<br>Computed tomography drain subphrenic abscess (11)<br>External fixation (15) | Laparotomy dehiscence, Staph. aureus empyema, subphrenic abscess | 4 | 20 | 1,2 | 24 | 49 |
| D | M | 16 | 35 | Extradural haematoma, fractured L) wrist, fractured L) tibia. | Craniotomy (0)<br>Internal fixation (0)<br>Tracheostomy (6) | — | 3 | 7 | 1 | 9 | 35 |
| E | M | 70 | 50 | Compound skull fracture, facial contusion, fractured ribs, pneumothorax, fractured forearm. | Eyeball enucleation (3)<br>Tracheostomy (6) | ARDS, atrial fibrillation | 5 | 20 | 1, 2, 3, 4, 5 | 23 | 45 |
| F | M | 21 | 38 | Intracerebral bleeding, fractured elbow, fractured forearm, fractured R) tibial plateau. | Debride R) knee (2)<br>Tracheostomy (3)<br>ORIF R) knee (4) | — | 5 | 6 | 1, 2, 4 | 9 | 41 |
| G | F | 19 | 29 | Splenic rupture, pancreatic contusion. | Splenectomy and Distal pancreatectomy (0) | — | 1 | 1 | 2 | 3 | 26 |
| H | M | 64 | 29 | Subdural haematoma, contusions of left forearm and left knee. | Craniotomy (0)<br>Tracheostomy (3) | — | 3 | 2 | 1 | 5 | 58 |
| I | M | 36 | 43 | Compound skull fracture, L) fronto-temporal subdural, facial fracture, pneumothorax, fractured femur. | Craniotomy (0)<br>Tracheostomy (4)<br>Internal fixation (5) | Aspiration pneumonitis | 2 | 7 | 1 | 9 | 25 |
| J | F | 18 | 29 | Intracerebral bleeding, facial contusion, lung aspiration. | Tracheostomy (1) | — | 2 | 4 | 1 | 7 | 30 |

ISS = Injury Severity Score; DCCM = Department of Critical Care Medicine; ORIF = open reduction and internal fixation.
* Parenthetical figures are days from trauma.
† Prescan refers to the interval between injury and time of first body compositional analysis (day 0).
‡ 1 = noradrenaline; 2 = dopamine; 3 = dobutamine; 4 = adrenaline; 5 = phenylephrine.
§ Patient readmitted to the DCCM with pneumonia and reventilated.

**Table 2. RESULTS OF BODY COMPOSITION MEASUREMENTS OVER A 21-DAY PERIOD AFTER MAJOR TRAUMA IN 10 PATIENTS**

| | Day 0 | Day 5 | Day 10 | Day 15 | Day 21 | p* |
|---|---|---|---|---|---|---|
| BW (kg) | 79.93 ± 5.19 | 77.25 ± 6.15 | 73.39 ± 5.82§ | 70.79 ± 5.29‡ | 69.13 ± 5.29† | <0.0001 |
| TBF (kg) | 17.32 ± 2.84 | 16.91 ± 2.77 | 16.63 ± 2.65 | 16.84 ± 2.78 | 16.67 ± 2.78 | 0.31 |
| TBW (L) | 46.63 ± 2.93 | 45.84 ± 3.47 | 42.10 ± 3.00§ | 39.82 ± 2.57‡ | 39.01 ± 2.74 | 0.002 |
| ECW (L) | 23.30 ± 1.29 | 22.72 ± 2.04 | 20.47 ± 1.75† | 19.80 ± 1.42 | 18.97 ± 1.54 | 0.01 |
| TBN (g) | 1675 ± 100 | 1551 ± 92§ | 1469 ± 95‡ | 1413 ± 88† | 1416 ± 88 | <0.0001 |
| SMM (kg) | 27.09 ± 1.84 | 22.84 ± 1.94‡ | 22.69 ± 2.00 | 21.95 ± 1.96 | 20.69 ± 1.34 | 0.0007 |
| TBK (mmol) | 3299 ± 267 | 3069 ± 248 | 2846 ± 217† | 2701 ± 214† | 2564 ±189† | <0.0001 |

BW = body weight; TBF = total body fat; TBW = total body water; ECW = extracellular water; TBN = total body nitrogen; SMM = skeletal muscle mass; TBK = total body potassium.
Values are mean ± standard error of the mean.
* Repeated measures analysis of variance.
† $p < 0.05$.
‡ $p < 0.01$. for paired t test *vs.* preceding measurement.
§ $p < 0.001$

were greatest over the first 10 days of the study, amounting to approximately 1.2% of TBP/day. Further losses beyond day 15 did not occur. Over the 21-day study period, a total of 1.62 kg (15.5%) of TBP was lost.

### *Origin of Protein Lost*

Figure 5 shows that over the first 5 days of the study, there were large losses of protein from skeletal muscle in our patients, although after this time, it appears that the protein loss was shared between the nonmuscle tissues and the skeletal muscle. The 1.09 kg loss of skeletal muscle protein over 21 days equates to 67% of the total protein lost over this period. Thus, most, but not all, of the body protein lost after major trauma comes from the hydrolysis of skeletal muscle protein.

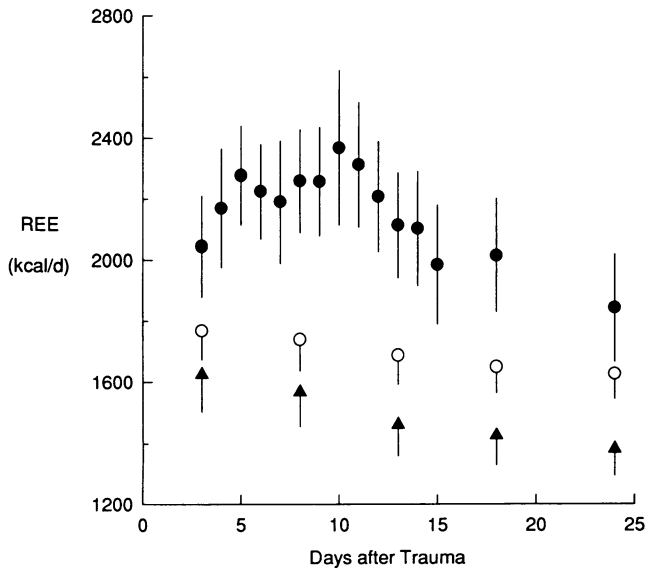


**Figure 2.** Resting energy expenditure (REE) in seven severely injured patients measured over 26 days after trauma (closed circles) with predicted REE from the Harris-Benedict equation (open circles) and total body potassium (triangles) (mean ± SEM).

## Cell Composition

Figure 6 shows the changes in TBK, ICW, and $[K]_i$ that occurred over the study period. Over the 21 days of the study, TBK and ICW fell significantly, but there was no change in $[K]_i$ (mean = 133 ± 3 mmol/L). This value is significantly lower than the normal value for our laboratory (152 ± 9 mmol/L, $p < 0.02$),[22] but it appears that once hemodynamic stability had been reached, no further deterioration in cellular composition occurred.

## DISCUSSION

These results shed new light on the sequential changes in energy, water, fat, and protein metabolism and cell composition that occur in critically injured patients after blunt trauma. The patients in this study each received state-of-the-art prehospital and in-hospital trauma care and, as such, are generally representative of blunt trauma patients treated in modern day tertiary institutions.

Our measurements of metabolic expenditure give values that are of the same order of magnitude as those described by others,[23,24] although the length of the period of hypermetabolism we found in our patients was prolonged when compared with that measured by others.[25] There have been few studies of the AEE in critically injured patients while they are in the critical care unit receiving mechanical ventilation. Indeed, it is sometimes assumed that the energy expended as physical activity in

**Table 3. ENERGY BALANCE IN 8 BLUNT TRAUMA PATIENTS BETWEEN DAYS 0 AND 10 OF STUDY**

| Patient | Intake (kcal) | Eox P (kcal) | Eox F (kcal) | Eox Gly (kcal) | TEE (kcal) | REEm (kcal) |
|---|---|---|---|---|---|---|
| A | 1965 | −452 | 1104 | −1547 | 2858 | 2608 |
| B | 1383 | −423 | −1760 | 452 | 3113 | 2398 |
| C | 1748 | −550 | −2313 | 395 | 4212 | 2670 |
| E | 980 | −466 | −1709 | 547 | 2607 | 2068 |
| G | 1622 | −362 | 686 | −690 | 1985 | 1431 |
| H | 1306 | −866 | 74 | −573 | 2668 | 1960 |
| I | 1605 | −546 | −347 | −531 | 3029 | 2315 |
| J | 1558 | −188 | −245 | −46 | 2037 | 1589 |
| Mean* | 1521 | −482 | −564 | −249 | 2814 | 2130 |
| SEM | 106 | 68 | 437 | 255 | 248 | 160 |

Eox P, Eox F, and Eox Gly = energy of oxidation of protein, fat and glycogen lost in each of the patients; TEE = total energy expenditure; REEm = measured resting energy expenditure by indirect calorimetry; SEM = standard error of the mean.
* Values are the daily mean for each patient during the study period.

such patients is negligible. Our results show, however, that AEE was around 24% of TEE. The practical lesson here is that the measurement of REE, which is done with the patient in the undisturbed state in the DCCM, is not TEE. In clinical practice, total energy requirements are usually calculated by multiplying the REEm by 1.3.[26] This factor of 1.3 is confirmed in the present study, where over a 10-day period, during which an energy balance was conducted, the average TEE was 1.32 × the average REEm.

It has been stated that fat oxidation is a major fuel source in critically ill patients,[27,28] but our data show otherwise. When energy intake fell short of energy requirements, fat was burned; if energy intake was sufficient, total body fat stores were preserved.

The patients had retained nearly 5 L of resuscitative fluids by the time they were hemodynamically stable. Af-

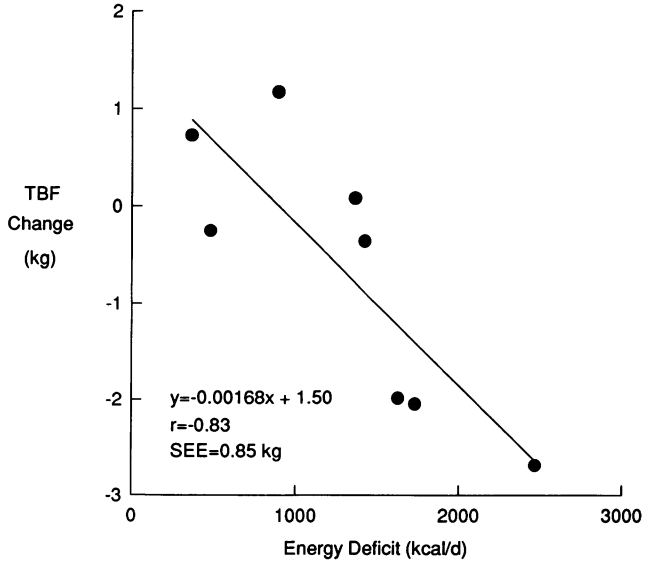


**Figure 3.** Relationship between 10-day changes in total body fat (TBF) and energy deficit in eight trauma patients.

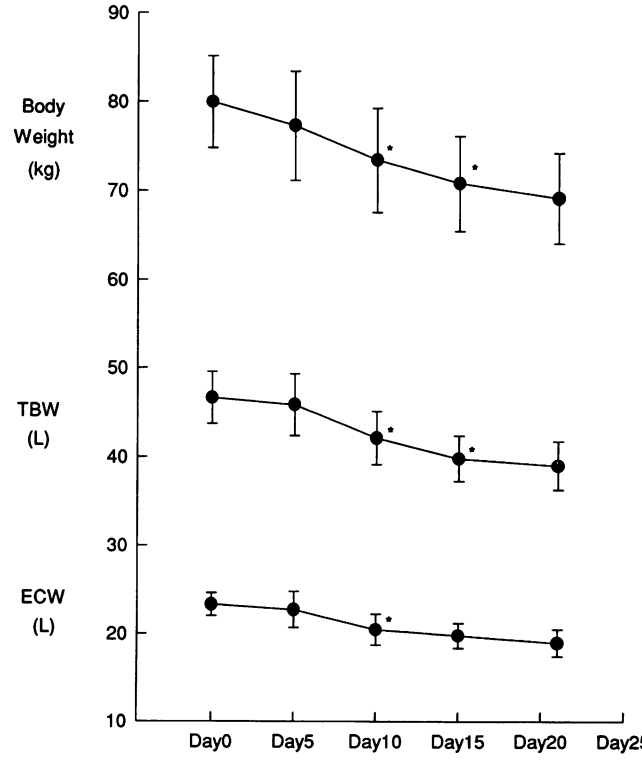


**Figure 4.** Body weight, total body water (TBW), and extracellular water (ECW) in 10 severely injured patients measured over a 21-day period after trauma (mean ± SEM). * = a significant ($p < 0.05$) change from previous measurement.

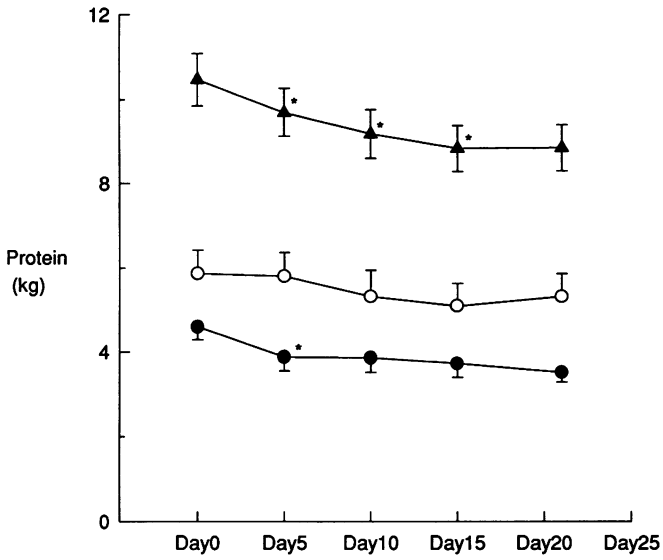


**Figure 5.** Total body protein (triangles), skeletal muscle protein (closed circles), and nonmuscle protein (open circles) in 10 severely injured patients measured over a 21-day period after trauma (mean ± SEM). * = a significant ($p < 0.05$) change from previous measurement.

ter this time, BW began to fall because of the loss of body water, mainly ECW. The ICW fell steadily also but in proportion to the loss of TBK. Cellular composition was abnormal when measured at the time hemodynamic stability had been reached and remained so, but without further deterioration, throughout the study period. Critical illness has been shown to be associated with an alteration in muscle cell composition, as measured by a decrease in skeletal muscle transmembrane potential difference ($E_m$), increased cellular sodium and water levels, and depletion of intracellular potassium,[29,30] so this is not surprising. Perhaps more surprising is the fact that intracellular potassium did not fall further in the face of continuing hypermetabolism and proteolysis.

Our studies of total body protein changes in these critically injured patients and the confirmation that most of this protein is from skeletal muscle are in accord with the original work of Cuthbertson[1] and the observations of Moore.[2] Our results give new insights as well. For instance, Moore and Brennan[31] calculated that the mass of muscle tissue lost over the first 2 weeks after severe injury in which the patient received no nutritional support is approximately 6 kg. However, if the same patient were to receive early intravenous feeding, they calculate that there would be a much reduced muscle loss (approximately 2.3 kg over the first 2 weeks). Our results show, however, that even with modern nutritional therapy, (the enteral feed was enriched with glutamine and arginine), the muscle losses we measured are far in excess of these estimates. We found a muscle protein loss of 1.09 kg, that is, an average loss of skeletal muscle of approximately 6.4 kg over the 21-day study period. This finding serves once again to emphasize the fact that the nitrogen balance technique in patients who are critically ill may underestimate the losses of nitrogen and minerals in patients who are in negative balance.[32] The multitude of day-to-day problems encountered in the care of critically ill patients makes for great difficulty in carrying out a proper metabolic balance study; hence, the use of body composition techniques such as we use in this study is a real advantage in showing the true magnitude of the losses encountered.

Cuthbertson[1] first suggested that the origin of the nitrogen loss in trauma is from skeletal muscle. He found that the excretion of nitrogen, sulfur, phosphorous, zinc, and magnesium in the urine was in proportion to its composition in skeletal muscle and concluded that the origin of the nitrogen loss indeed was from skeletal muscle. Others have pointed this out, also citing as evidence the increased excretion of creatinine and creatine after injury, the visible shrinkage of skeletal muscle bellies, and the lack of any evidence for important contribution of nitrogen from other protein-rich sources, including viscera and connective tissue solids.[31] Our results show that these observations are only partially true. They show that approximately two thirds of the protein loss is from skeletal muscle, but the remainder has come from other

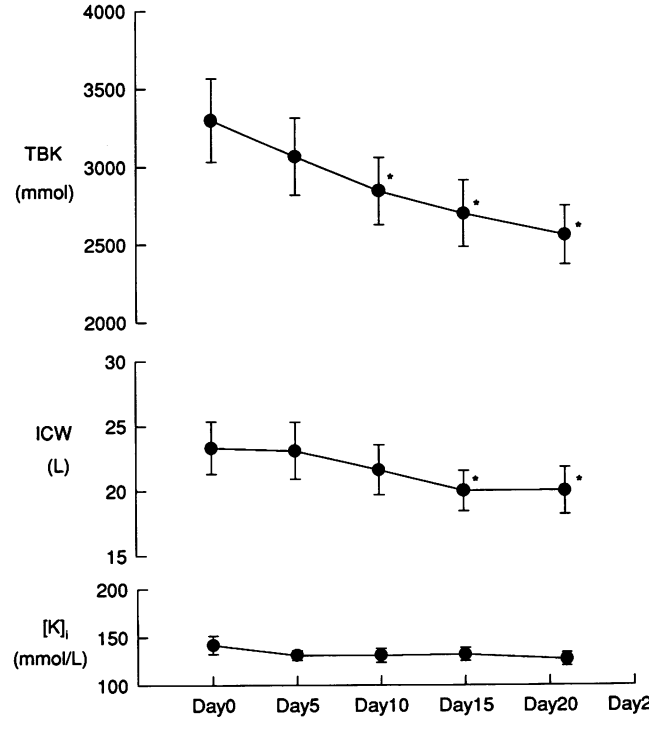


**Figure 6.** Total body potassium (TBK), intracellular water (ICW), and intracellular potassium concentration ($[K]_i$) in 10 severely injured patients measured over a 21-day period after trauma (mean ± SEM). * = a significant ($p < 0.05$) change from the day 0 measurement.

sources. In critically injured patients, resuscitation before hemodynamic stability is reached involves the administration of protein-rich fluids, including albumin, gelatin, red cells, and plasma. The consumption of nonmuscle protein over the first 5 days of the study (Fig. 5), but not thereafter, suggests this additional protein may, to some extent, have been hydrolyzed.

The measurement of skeletal muscle mass by DEXA technology is quite new. Heymsfield's postulate, that appendicular muscle as calculated from the lean tissues using DEXA technology could represent the total skeletal muscle of the body, must be treated with some caution.[12] Heymsfield has compared appendicular muscle with total body skeletal muscle in 35 subjects in whom he has calculated total skeletal muscle content from serial computed tomography scans (S. B. Heymsfield, personal communication, 1994). We have used his factor in our present study but acknowledge that some modification may be required in the future as to the precise quantities of muscle lost.

What are the implications of our findings for modern management of critically injured patients? We confirm that the understanding of the degree of hypermetabolism that occurs in such patients is largely correct, although the surgeons and critical care specialists treating these patients should understand that this period of hypermetabolism will likely last for 3 weeks or longer in the majority of such patients. The finding that REE, as measured by an indirect calorimeter morning and evening, does not translate into TEE shows that the mechanically ventilated patient has a component of metabolic expenditure over and above that measured by the indirect calorimeter due to the considerable, but sometimes underestimated, manipulations that are part of critical care management.

Regarding fluid therapy, it is clear from this study that most of the administered resuscitative fluids are retained within the extracellular space. Once hemodynamic stability is reached, body hydration slowly returns to normal. It seems unlikely that much can be done to preserve cellular composition before hemodynamic stability is achieved, but state-of-the-art intensive care management, which included enrichment of the enteral feed with glutamine and arginine in the present study, appears to have prevented further deterioration.

It has been shown by our work that fat oxidation is a function of energy intake, and if it is important clinically to preserve fat stores, this can be done by ensuring that total energy requirements are met. Protein losses, which occurred predominantly from skeletal muscle, were greater than had been thought in the past. It is likely that this degree of loss profoundly affects muscle function and, hence, weaning from the ventilator and convalescence. We have shown that this loss of protein is not influenced by the amount of protein administered. In the present study, the losses were considerable despite the enriched enteral feed.

In conclusion, our study has shown that Cuthbertson and Moore's teaching that major trauma is associated with hypermetabolism, lipolysis, proteolysis, and ECW gain is true. We have, for the first time, quantified these changes and have shown that they are more prolonged and greater than expected. We also have shown that state-of-the-art management is able to meet energy requirements, prevent lipolysis, and avoid further deterioration in cellular composition. The study further highlights how important it is to focus on research designed to prevent the massive loss of skeletal muscle protein that occurs in association with multiple injury.

## Acknowledgments

The authors thank the dedicated medical and nursing staff of the Department of Critical Care Medicine whose enthusiasm and complete cooperation helped ensure the success of this study. The authors also thank Dr. Gerald Woollard for his expertise in establishing the high-performance liquid chromatography assay for serum halide.

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