The effect of uraemia, acidosis, and dialysis treatment on protein metabolism: a longitudinal leucine kinetic study

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Abstract

**Background.** Uraemia and dialysis are viewed as catabolic processes resulting in malnutrition in chronic renal failure (CRF) patients. To sort out the effects of uraemia, acidosis, and dialysis on protein metabolism, we measured leucine flux in CRF patients before and after initiation of maintenance dialysis.

**Subjects and methods.** Whole-body leucine flux was measured by primed-constant infusion of L[1-¹³C] leucine in nine CRF patients longitudinally; twice before and once after initiation of maintenance dialysis (D). Before dialysis, one leucine flux was measured when the patients were acidotic (A), and the other, when acidosis was corrected with NaHCO₃ (NA). Five normal subjects underwent one single leucine flux measurement to serve as control (N). Both patients and normal subjects consumed a constant diet for 6 days and leucine flux was measured on the 7th day 12 h post-absorption. Diet for the CRF patients was identical during the three periods. Plasma L[1-¹³C] leucine and L[¹³C]KIC were measured by gas chromatography/mass spectrometry and expired ¹³CO₂ by isotope ratio spectrometry. Leucine kinetics were calculated using standard equations.

**Results.** Plasma CO₂ levels were 19, 26 and 31 mmol/l in A, NA and D periods respectively. All kinetic results (µmol/kg/h) are presented as means±SD in the order of A, NA, D, and N, and CRF values that are statistically different from N are identified (*). The amounts of leucine release from endogenous protein breakdown (Ra or Q) were 101±12*, 95±9*, 113±22, and 117±6. Leucine oxidation (C), quantities of leucine irreversibly oxidized to CO₂, were 16.5±5.4, 9.7±3.7*, 12.3±3.0*, and 23.2±3.1. Leucine protein incorporation levels (S) were 85±10, 85±8, 101±19 and 94±6. The S of 101 in CRF patients at period D was statistically higher than those during A and NA periods.

**Conclusions.** These data indicate that when acidosis was corrected, CRF patients adapted to lower protein intake by reducing amino-acid oxidation and protein degradation, and maintained protein synthesis at normal levels. Metabolic acidosis impaired the downregulation of amino-acid oxidation. Maintenance dialysis treatment longitudinally restored protein flux to normal and increased protein synthesis. The general notion that uraemia and dialysis are protein catabolic is not supported by this work.

**Key words:** leucine kinetics; protein turnover; uraemia

Introduction

Protein malnutrition, prevalent in chronic renal failure (CRF) patients [1–6], is generally attributed to the protein catabolic nature of uraemia and dialysis treatment [7]. There is a voluminous literature demonstrating marked protein catabolism in uraemic rat models [8–13]. Dialysis, with its obligatory protein and amino acid loss, is inherently a catabolic stress [14–16]. Furthermore, during haemodialysis, protein degradation may be enhanced by bioincompatible membranes [17]. To sort out the effects of uraemia, acidosis, and maintenance dialysis on protein metabolism, we measured in vivo whole body protein turnover in end-stage renal disease patients shortly before and 8–10 weeks following the initiation of maintenance dialysis treatment. The results from these patients were compared to values obtained from normal control subjects, and the data suggest that chronic uraemia in humans is not a protein catabolic state. Moreover, maintenance dialysis treatment improved protein synthesis.

**Subjects and methods**

**Study subjects**

Nine CRF patients and five normal control subjects were recruited for this study. For the CRF patients, there was one woman and eight men, their mean age was 55.8 years. Three patients had chronic glomerulonephritis, two focal segmental glomerulosclerosis, two obstructive uropathy, and...
one each hypertensive nephropathy and renal amyloidosis. Before initiation of dialysis, mean serum urea nitrogen was 8.9 ± 8.6 mmol/l, and mean serum creatinine, 1087 ± 300 μmol/l. All were clinically stable. Medications included phosphate binders, iron, multivitamins, antihypertensive drugs, calcitriol, and in three patients recombinant human erythropoietin (Epo). None received steroid or immunosuppressive agents; one patient received levotheroxine. Following completion of the first two measurements, seven patients chose haemodialysis (HD) and one patient, chronic ambulatory peritoneal dialysis (CAPD). One subject did not complete the dialysis study because of renal transplantation. The single CAPD patient was using four 2-litre exchanges daily; her weight was 46 kg. The haemodialysis patients were dialysed with reused F80 dialysers, using a 3.5mEq/l of Ca and 40 mmol bicarbonate dialysate, Kt/V was >1.3 in all patients. The five normal control subjects were not taking medication, their mean age was 50.2 years.

Demographic characteristics of the normal and the renal patients are listed in Table 1.

### Table 1. Demography of the study subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>M/F</th>
<th>Age (years)</th>
<th>Ht (cm)</th>
<th>Wt (kg)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control 4/1</td>
<td>50.2 ± 12.0</td>
<td>172.2 ± 8.0</td>
<td>79.8 ± 7.2</td>
<td>27.0 ± 1.8</td>
<td></td>
</tr>
<tr>
<td>CRF 8/1</td>
<td>55.8 ± 10.6</td>
<td>176.2 ± 10.3</td>
<td>86.5 ± 25.0</td>
<td>27.4 ± 5.6</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index = Wt (kg)/Ht (m²). NS, statistically no significant difference was found between control subjects and the CRF patients.

### Leucine turnover kinetics

L-[1-13C]leucine and NaH[13CO3] were infused at 99% and 95% respectively, were purchased from Mass Trace (Woburn, MA 01801). Infusates were prepared aseptically the afternoon before the experiment. Intravenous catheters were inserted into one arm for blood drawing and the contralateral arm for infusion; the hand/arm for blood drawing was wrapped in a heating pad. In haemodialysis patients who had an arteriovenous fistula or graft, catheters were inserted into the arterial and the venous ends of the vascular access, the former for blood sampling, and the latter for infusion.

Leucine kinetics were measured by a primed-constant infusate technique under substrate and isotopic steady state. The priming doses consisted of 4.0 μmol/kg of L-[1-13C]leucine and 0.11 mg/kg of NaH[13CO3] and the sustaining infusion rate of L-[1-13C]leucine was 4.0 μmol/kg/h for 4 h. Moles % enrichment of L-[1-13C]leucine and L-[1-13C]3-keto-isocaproate (KIC) in the plasma and 13CO2 in the expired breath were quantitated by gas chromatography–mass spectrometry and isotope ratio mass spectrometry respectively. Plasma leucine was converted to heptafluorobutyral, n-propylester and the 13C abundance was determined using positive chemical ionization mass spectrometry with selected ion monitoring to mass-to-charge ratio 370 and 371. The trimethyl-1-13C propionic acid derivative of plasma α KIC was prepared and 13C abundance was determined using electron-impact ionization mass spectrometry with selected ion monitoring to mass-to-charge ratio 232 and 233 [18–20].

CO2 production rate and expired gas collection were performed as previously described [16]. The first 2 h of the infusion were used to achieve isotopic equilibrium, and measurements were made every 30 min during the last 2 h. Leucine flux (Q) which denotes movement of leucine into (rate of appearance (Ra)) and out of (rate of disappearance (Rd)) the metabolic pool is calculated as:

$$Q = \frac{E_i}{E_p - 1} \times i$$

where $E_i = L-[1-13C]$ leucine enrichment in the infusate which is 100%, $E_p = L-[1-13C]$ leucine or $L-[1-13C]KIC$ enrichment in the plasma at isotopic plateau, and $i = L-[1-13C]$ leucine infusion rate (μmol/kg/h).

The rate of 13CO2 release from tracer leucine oxidation was calculated as follows:

$$F^{13}CO_2 = \frac{(VCO_2 \times ECO_2/BW) \times (60 \times 41.6/100 \times 0.77)}{VCO_2 \text{ production rate (ml/min), } ECO_2 \text{ is } 13C \text{ enrichment in the expired breath at isotopic steady state, BW is body-weight (kg). The constants 60 (min/h) and 41.6 (μmol/ml at standard temperature and pressure) convert } VCO_2 \text{ from ml/min to μmol/h. The factor 100 changes moles % enrichment from a percent to a fraction. Instead of the conventional factor of 0.81 to account for the fraction of } 13CO_2 \text{ produced by } L-[1-13C] \text{leucine oxidation released from the body bicarbonate pool into the expired gas [21], we used a factor of 0.77. This value was derived from additional experiments in which } 13CO_2 \text{ recovery was determined in six pre-dialysis (not the same patients as those who underwent leucine flux studies), two haemodialysis patients, and six normal control subjects. Recovery studies were done twice with each pre-dialysis subject, once each with and without sodium bicarbonate supplement. After a 12-h overnight fast, a loading dose of 4.71 μmol/kg NaH[13CO3] was given intravenously and followed by a constant infusion of 4.71 μmol/kg/h for 4 h. Breath } 13CO_2 \text{ enrichment and } VCO_2 \text{ were measured at baseline and every 30 min during the 3rd
and 4th hour of infusion. \(^{13}\text{C}\)O\(_2\) recovery = \(F^{13}\text{CO}_2/^{13}\text{C}\) infusion. The mean recovery rate for the acidic and non-acidotic pre-dialysis patients were respectively \(75.4 \pm 8.5\%\) and \(76.1 \pm 7.7\%\), that of the haemodialysis patients and normal subjects were respectively \(85.2 \pm 7.6\%\) and \(72.8 \pm 6.2\%\).

Statistical analysis by one-way ANOVA failed to show any differences in the recovery rates among these four subject groups. Consequently, the equally weighted arithmetic mean, \(77.38 \pm 5.38\%\), was used in the computation of \(F^{13}\text{CO}_2\) for all studies.

The rate of leucine oxidation (C) is then:

\[
C = F^{13}\text{CO}_2 [1/E_p - 1/E_i] \times 100
\]

The quantitation of amino acid metabolism is based on the mass balance relationship stating that \(Q = S + C = B + I\), where \(Q\) is flux or total turnover rate, \(S\) is the rate of amino-acid incorporation into protein, reflecting protein synthesis, \(C\) is the rate of irreversible oxidation of leucine to \(\text{CO}_2\), \(B\) represents the rate of amino-acid release from endogenous protein breakdown, and \(I\) the rate of exogenous intake. In the post-absorptive state, \(I = 0\), and \(B\), therefore, equals \(Q\). In the presentation of our data, although we show leucine appearance rates into the plasma and into the total body leucine pool, we have only used the latter, derived from plasma \([1-^{13}\text{C}]\text{KIC}\) enrichment, to calculate leucine oxidation and synthesis rates. Because deamination of leucine occurs intracellularly, and the appearance of \([1-^{13}\text{C}]\text{KIC}\) in the plasma is more representative of the movement of leucine into the total body leucine pool [22,23].

**Statistical analysis**

The differences in leucine kinetics among the three periods of the CRF patients were assessed by one-way repeated measures analysis of variance, and the differences between any two periods by multiple paired comparisons using Student–Newman–Keuls test. The differences in leucine kinetics between the controls and the three periods of the CRF patients were assessed by Student’s t test and the \(P\) values were corrected using Bonferroni’s method. The analyses were performed using the statistical software package Sigma Stat (Jandel Scientific Software, San Rafael, CA).

**IRB approval**

All protocols were approved by the Institutional Review Board (IRB) of the University of Iowa College of Medicine.

**Results**

Table 2 summarizes arterial blood gases and renal function during the three study periods in the CRF patients. Bicarbonate and dialysis effectively corrected the metabolic acidosis; in fact, a 38 mmol dialysate bicarbonate concentration overcorrected the acidosis as total \(\text{CO}_2\) was 30.5 mmol/L. BUN and serum creatinine were significantly lower in period D.

Table 3 illustrates two points:

(a) Plasma \([^{13}\text{C}]\)leucine and \([^{13}\text{C}]\text{KIC}\) enrichment was reduced and leucine appearance rates (Ra leu) in the plasma leucine pool and body leucine pool were increased following initiation of dialysis.

Leucine appearance in the plasma leucine pool was derived from plasma \([^{13}\text{C}]\text{leucine}\) enrichment, whereas leucine appearance in the total body leucine pool was from plasma \([^{13}\text{C}]\text{KIC}\) enrichment. In the post-absorptive state, leucine appearance is equal to the amount of leucine released from endogenous protein breakdown.

(b) Breath \([^{13}\text{C}]\text{CO}_2\) enrichment and \([^{13}\text{CO}_2\) production rate were highest when patients were acidic and uraemic. Correction of acidosis, but not uraemia, resulted in a reduction in \([^{13}\text{CO}_2\) production. This increase in \([^{13}\text{CO}_2\) production was due to enhanced leucine oxidation as \(\text{VCO}_2\) was not different in the three periods.

The upper half of Table 4 compares leucine kinetics amongst the ESRD patients themselves. Both leucine release from protein breakdown and leucine incorporation into body protein were lower before as compared to those after the initiation of maintenance dialysis. Thus maintenance dialysis increased whole-body protein turnover. Leucine flux rose from 95 to 113 \(\mu\text{mol/kg/h}\), and leucine protein incorporation from 85 to 101 \(\mu\text{mol/kg/h}\). Irreversible oxidation of leucine into \(\text{CO}_2\) was highest when the patients were acidic (CRF-A). \(C/Q\) and \(S/Q\), representing the ratios of leucine oxidation and leucine protein incorporation to total leucine flux, changed reciprocally. During acidosis, when leucine oxidation was enhanced, \(C/Q\) rose and \(S/Q\) decreased. Correction of acidosis reversed the pattern. The lower half of the table lists flux activities of normal controls; these values are most similar to those of the CRF patients following initiation of dialysis, with one exception, i.e. leucine oxidation rate was lower in the dialysis patients. Fraction of leucine released from endogenous protein degradation that went into protein synthesis (\(S/Q\)) was actually higher in ESRD patients.

The nutritional indices and dietary intake of the controls and the CRY patients are found in Tables 1 and 4. Unlike many ESRD patients, the patients selected for this study had no comorbid illnesses, their nutritional indices were normal; their mean body mass index of 27 was not different from control (none of the patients had oedema), and their serum albumins were 40, 39 and 40 g/l during the A, NA, and D periods respectively. Protein and energy intake were, nonetheless, lower than that of the normal subjects.

Figure 1 depicts leucine kinetics of the study subjects. Leucine release from protein breakdown (\(Q\)) and leucine incorporation into body protein (\(S\)) were reduced, and leucine oxidation (\(C\)) was increased in uraemic and acidic patients (CRF-A). Correction of acidosis led to a reduction in leucine oxidation. Dialysis treatment resulted in an increase in leucine flux, both protein degradation and synthesis were increased, the latter to a greater extent, and leucine oxidation rate was lower than that of the normal subjects.

Figure 2 illustrates the adaptive changes in CRF patients. When acidosis was corrected, the fraction of leucine appearance that went into oxidation, \(C/Q\),
was reduced, and that into protein synthesis, S/Q, increased.

For ease of the readers, we have created Table 5 summarizing the directional changes of the different components of leucine flux in ESRD patients as compared to normal subjects. Before initiation of dialysis whether acidosis was present or not, leucine release from endogenous protein degradation was reduced. Leucine oxidation rate was not different from the normals in ESRD patients when acidic and before dialysis (CRF-A), but was reduced following correction of acidosis and initiation of dialysis. Protein synthesis, strikingly, was not statistically different between the ESRD patients and normal subjects. The readers may, however, like to refer back to Table 4 showing that protein synthesis was significantly increased in the ESRD patients after maintenance dialysis. The fraction of leucine flux that went into leucine oxidation (C/Q) was lower, and that went into protein synthesis (S/Q), higher after correction of acidosis and initiation of dialysis.

### Discussion

Using the technique of leucine flux measurement, we found that uraemia per se was not a catabolic state.
The effects of uraemia, acidosis, and dialysis on leucine kinetics

Table 5. Directional changes in leucine kinetics in ESRD patients following correction of acidosis and initiation of maintenance dialysis as compared to normal subjects

<table>
<thead>
<tr>
<th>Group/period</th>
<th>Degradation</th>
<th>Oxidation</th>
<th>Synthesis</th>
<th>C/Q</th>
<th>S/Q</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>117</td>
<td>23</td>
<td>94</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>CRF-A</td>
<td>↓</td>
<td>=</td>
<td>=</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>CRF-NA</td>
<td>↓</td>
<td>↓</td>
<td>=</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>CRF-D</td>
<td>=</td>
<td>↓*</td>
<td>=</td>
<td>↓*</td>
<td>↑*</td>
</tr>
</tbody>
</table>

*CRF-D values that are statistically different from normal values.

Fig. 1. Leucine kinetics (means ± SEM) in normal subjects (N) and CRF patients during A, NA, and D representing, respectively, uraemic/acidotic, uraemic/non-acidotic and dialysis periods. Ra is the rate of leucine released from endogenous protein breakdown, which is also equal to Q or total leucine flux. S is leucine incorporation into protein or protein synthesis, and C, leucine oxidation; * and ‡ indicate statistically significant differences comparing A vs NA, A and NA vs D; § depicts significant differences between normal subjects and CRF patients at designated period.

Fig. 2. Percentages (means ± SEM) of leucine appearance that went to protein synthesis (S/Q) and oxidation (C/Q) in normal subjects (N) and in CRF patients during A, NA and D representing respectively uraemic/acidotic, uraemic/non-acidotic, and dialysis periods; *and ‡ indicate statistically significant differences comparing A vs NA, A and NA vs D; § depicts significant differences between normal subjects and CRF patients at designated period.

Not only was there no evidence of augmented catabolism, but protein turnover was actually downregulated. This finding of reduced protein breakdown is contrary to the prevailing view that uraemia is protein catabolic [7,10]. In uraemic rat models there is abundant documentation of increased protein degradation and reduced protein synthesis during muscle incubation and hindleg perfusion studies [8,9,11–13]. In humans, Reaich et al. [24] reported that in predialysis patients, both protein degradation and leucine oxidation increased in the presence of metabolic acidosis. In haemodialysis patients they found that protein degradation was reduced from 181 to 131 μmol/kg/h when plasma CO₂ rose from 19 to 25 mmol/l[25]. Not all human data, however, are consistent with hypercatabolism. In another six predialysis patients, whose serum creatinines ranged from 2 to 6 mg/dl, presumably mildly acidotic, Goodship et al. did not find increased protein degradation or increased leucine oxidation; in fact those patients adapted to low protein intake similarly to the normals by reducing feeding-induced amino-acid oxidation [26]. The same group of authors also found mild, but statistically insignificant, reduction in leucine flux and leucine oxidation in ESRD patients before and after peritoneal dialysis treatment as compared to normal subjects [27].

Conley et al. and Berkelhammer and colleagues reported that protein turnover was decreased in children and adults with ESRD [28,29]. Using nitrogen balance techniques, many investigators showed that both chronic renal failure and ESRD patients are able to maintain nitrogen balance despite significantly lower protein intake [30,31]. In fact urinary urea nitrogen excretion and peritoneal dialysate urea nitrogen removal decreased proportionately with reducing dietary protein consumption [30,32]. Furthermore, Deferrari et al. found that total amino-acid release from the leg in the post-absorptive state is similar in CRF patients and normal subjects, indicating the absence of exaggerated proteolysis [33]. Most importantly, many long-term diet protocols designed to examine the effects of low protein diet on the progression of renal insufficiency have uniformly showed little adverse effects of protein restriction on the nutritional status of the studied populations [34–38].

Metabolic acidosis, independent of uraemia, accelerates protein catabolism. In the rats, NH₄Cl-induced acidosis resulted in augmented net protein degradation and increased amino-acid oxidation [39,40]. In man, NH₄Cl administration also increases protein breakdown and amino-acid oxidation [41]. As for uraemic acidosis, bicarbonate supplementation reduced net protein degradation in both muscle incubation preparations and in hindquarter perfusion in the rats. While augmented protein breakdown in NH₄Cl-induced acidosis is abolished by adrenalectomy, uraemic acidosis-
related protein degradation appears not to be gluco-
corticoid-dependent [42,43]. In humans with uraemic
diabetic, Goodship and his colleagues found increases
in all parameters of leucine flux in one study, and
increases in only protein degradation and protein syn-
thesis without affecting leucine oxidation in another
study [24,25]. In the current report comparing uraemic
patients with and without bicarbonate treatment, leuc-
ine oxidation was unequivocally higher when acidosis
was present, protein degradation and synthesis both
increased minimally, and these changes did not reach
statistical significance. Thus, in our hands uraemic
acidosis increased primarily leucine oxidation resulting
in a significantly elevated C/Q fraction of leucine
release from protein breakdown that went into
irreversible oxidation. Reciprocally, S/Q, the fraction
of leucine release that went into protein synthesis,
was significantly reduced.

Following initiation of maintenance dialysis, the two
sides of mass balance equation (refer to Subjects and
methods, Q = C + S) changed. On the one hand, protein
turnover (Q) increased towards normal level, on the
other hand, amino acid oxidation (C) rose to a lesser
degree, resulting in a greater rise in protein synthesis
[5]. As shown in Table 4, leucine-protein incorporation
rose from 85 to 101 μmol/kg/h. These data, at first
stance, may appeared contrary to the current belief
that dialyses are catabolic events. It should, however,
be emphasized that the catabolic nature and dialysis is
based on data obtained during single dialysis proced-
ures showing obligatory amino acid and protein loss
[14–16] and, perhaps, increased protein breakdown
when using bioincompatible dialysers [17]. Our conclu-
sion pertains to the longitudinal effects of maintenance
dialysis treatment. These data showing improved pro-
tein synthesis are in agreement with the commonly
observed clinical feature of weight gain, increased
vigor and functional capacity following initiation of
dialysis. Since dietary intake was constant in the CRF
patients during all three study periods, the improve-
ment following dialysis could only be explained by
more efficient substrate and energy utilization.

The fact that both blood pH and total CO\textsubscript{2}
were higher following initiation of maintenance dialysis
cannot exclude the possibility that the enhanced protein
synthesis observed might be related, in part, to the
mild metabolic alkalosis. None of the medication could
account for the change in metabolic state following
dialysis. The single patient who was receiving thyroid
replacement had been on the same dosage for many
years. No patient was taking glucocorticoid or andro-
gen during the three study periods. Because the effect of
Erythropoietin on protein metabolism is unknown, we
were careful not to add Epo during dialysis. All
the three patients who received Epo were started with
this medication before and stayed on the same doses
during the dialysis period. We waited for a minimum
of 6 weeks after the start of Epo injections before
conducting the first leucine flux measurement. This
precaution was observed in order to avoid picking
up any increase in protein synthesis associated with
enhanced erythropoiesis during the initial response to
Epo.

One might argue that in situations of stress such as
sepsis, burns, and trauma, protein flux (Q) is also
increased. In those conditions, amino-acid oxidation
(C) rate is unequivocally high, and protein synthesis
[5], measured by leucine flux, was reduced [44–46]. In
stress, amino acids derived from muscle proteolysis
are oxidized for energy supply, utilized as substrate
for hepatic gluconeogenesis and protein synthesis. The
nitrogenous components of the amino acids are channe-
lled to the liver for urea synthesis [47]. Accelerated
urea genesis is not seen in stable chronic uraemia on
a constant diet, as was the case in our patients.

It could be said that a flaw in this study is the higher
protein intake in the normal subjects. This flaw has no
bearing on the differences amongst the CRF patients
themselves studied longitudinally during treatment.
The observed changes of increased protein flux and
protein synthesis following maintenance dialysis were
unrelated to dietary intake, which was fixed in all three
periods. In contrast to most published reports, which
consist of different patients in different stages of renal
insufficiency, our study is unique in that the same
patients were followed longitudinally from immediately
before to 8–10 weeks after initiation of dialysis, and
were ingesting a constant diet during all periods. This
is important because metabolic status varied widely
from subject to subject, but is relatively constant within
the same person.

If neither uraemia nor dialysis are catabolic, why is
it that virtually every nutritional survey of CRF
patients revealed extensive evidence of malnutrition?
First, the literature favours reporting of malnutrition.
Clinical experience suggests that there are as many
dialysis patients who are robustly nourished as there
are undernourished. The USRDS showed that in 1996,
20 and 19% respectively, of peritoneal and haemodi-
alysis patients were reported as undernourished [48].
Second, malnutrition may be attributable to poor dietary
intake and not necessary increased protein breakdown.

In summary, the current study showed that when
metabolic acidosis was corrected, uraemic patients
adapted successfully to the lower dietary protein/energy
intake by downregulation of amino-acid oxidiza-
tion and protein degradation with preservation of
protein synthesis capacity. After initiation of mainten-
ance dialysis treatment, all components of protein flux,
especially protein synthesis, were accelerated, sug-
gesting an improved body protein economy. These
current findings, together with a body of literature
showing that CRF and dialysis patients are able to
adapt to low protein intake by reducing urea genera-
tion [31–33,49], collectively provide an argument
against the conventional concept that uraemia and
dialysis are catabolic events.

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