Chronic Protein Undernutrition and an Acute Inflammatory Stimulus Elicit Different Protein Kinetic Responses in Plasma but Not in Muscle of Piglets1,2

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ABSTRACT The changes in protein metabolism of severe childhood malnutrition are generally perceived as a metabolic adaptation to chronic protein undernutrition. However, severe malnutrition is invariably accompanied by infections which also have profound effects on protein metabolism. This study aimed to distinguish the effect of protein undernutrition from that of an inflammatory stimulus on muscle and plasma protein synthesis rates. Two groups of five piglets consumed diets containing either 23% or 3% protein for 4 wk. They then were infused intravenously with ³H³-leucine before and 48 h after subcutaneous injections of turpentine to measure the fractional synthesis rates (FSR) of muscle protein and both the FSR and the absolute synthesis rates (ASR) of albumin and fibrinogen. Prior to turpentine injection, compared to control piglets, protein-deficient piglets had significantly lower muscle FSR and plasma concentrations of both albumin and fibrinogen, although only albumin had lower FSR and ASR. Turpentine injection decreased muscle FSR but increased the FSR, ASR and plasma concentrations of both albumin and fibrinogen in control piglets. In protein-deficient piglets, the inflammatory stress caused a further decrease in muscle protein FSR and in plasma albumin concentration despite marked increases in albumin FSR and ASR. Fibrinogen FSR, ASR and plasma concentration were increased. We conclude that protein undernutrition and inflammation elicit the same kinetic response in muscle protein but different kinetic responses in plasma proteins. Furthermore, whereas protein deficiency reduces the plasma albumin pool via a reduction in albumin synthesis, inflammation reduces it through a stimulation of catabolism and/or loss from the intravascular space. J. Nutr. 129: 693–699, 1999.

KEY WORDS: • protein undernutrition • inflammatory stimulus • stable isotope • piglets

• muscle protein • plasma protein

The underlying derangements of protein metabolism in severe protein-energy malnutrition (PEM)4, which are thought to be pivotal in the pathogenesis of the disease, have not been clearly elucidated. This is because of the fact that PEM is invariably accompanied by infections; hence, the protein metabolic response to chronic protein and energy under-

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4 Abbreviations used: ASR, absolute synthesis rate; FSR, fractional synthesis rate; PEM, protein-energy malnutrition; RIA, radioimmunoassay; TCA, trichloroacetic acid; VLDL, very low density lipoprotein.

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had an increased rate of synthesis of gut mucosal protein (Hirschfeld and Kern 1969), suggesting that the utilization of dietary amino acids by the muscle bed is reduced during protein deficiency, thereby enabling dietary amino acids to be directed towards the maintenance of splanchnic protein synthesis. On the other hand, some workers (McNurlan and Garlick 1981, McNurlan et al. 1982) have reported decreased rates of protein synthesis in all the major organs and tissue beds of rats fed a protein-free diet, which suggests that all the organ and muscle systems are involved in the adaptation to a chronic reduction in protein intake. In two previous studies (Jahoor et al. 1996, Wykes et al. 1996), we found that young pigs fed a protein-deficient diet for 8 wk had a reduction in their whole body protein turnover rates that included decreased rates of protein synthesis in all the major organs and tissue beds of the body. However, the responses among plasma proteins were not uniform. Whereas protein deficiency lowered the plasma concentration and rate of synthesis of some plasma proteins, others were unchanged or increased (Jahoor et al. 1996).

The metabolic response to the stress of infection, inflammation, or trauma, on the other hand, is generally characterized by an increased rate of whole body protein turnover resulting in a net loss of body protein primarily from skeletal muscle (Cuthbertson 1932, Jahoor et al. 1988). The response also includes an increased rate of release of amino acids from the muscle bed and a simultaneous increase in uptake by the splanchnic bed (Clowes et al. 1980). It has been hypothesized that this redistribution serves the beneficial purpose of facilitating the transfer of amino acids from the peripheral tissues to the liver for the synthesis of rapidly turning over proteins that are critical for survival (Fleck 1989). Thus, there is a redistribution of protein synthetic activity away from the synthesis of muscle and towards synthesis of splanchnic proteins, such as the positive acute phase proteins.

There is evidence that children with PEM when infected have higher plasma concentrations of positive acute phase proteins and lower concentrations of negative acute phase proteins compared to when they are free of their infections (Schelp et al. 1979). It was shown that infected PEM children have higher protein turnover rates than uninfected children with PEM (Tomkins et al. 1983). Furthermore, the N loss of well-nourished children with infection does not occur in infected malnourished children (Tomkins et al. 1983). Together, the findings of these studies suggest that the protein metabolism of children with PEM is profoundly affected by the response to concurrent infections. To distinguish the effect of chronic protein deficiency on the rate of synthesis of albumin, fibrinogen, and muscle protein. At the end of the infusion, an antibiotic [0.1 mL Baytril/kg (enrofloxacin), Miles; Shawnee Mission, KS] was administered intramuscularly. Four days later, when the pigs were 5 wk old, 1.5 mL of turpentine/kg was injected subcutaneously along the back and right hindquarter of all the piglets. Two days after the turpentine injections, the second isotope infusion was performed to determine the effect of inflammation on the rate of synthesis of the proteins. Each piglet was fed 1/12 of its known daily feed intake at 2-h intervals starting 2 h before the isotope infusion. At the end of the infusion, the piglets were killed with an intravenous injection of 0.33 mL Beuthanasia-D/kg (129 mg sodium pentobarbital, 16.5 mg sodium phenytoin) obtained from Schering-Plough Animal Health; Kenilworth, N.J.

**Isotope infusion.** The rates of synthesis of albumin, fibrinogen, and muscle protein were calculated from the rate of incorporation of $^2H_2$-leucine into the proteins. The average isotopic enrichment of muscle-free leucine was used as an estimate of leucine enrichment in the muscle precursor pool, and the plateau enrichment of apoB-100 bound leucine in plasma was used to represent the enrichment of the intrahepatic leucine pool from which other plasma proteins are synthesized.

There were two isotope infusions. The first was performed after 4 wk of dietary treatment, and the second after 2 d of turpentine administration. A sterile solution of $^2H_2$-leucine (Cambridge Isotope Laboratories, Woburn, MA), was prepared in 4.5 g saline/L and infused through the jugular vein catheter. The piglets were given a priming dose of 30 μmol/kg, followed by a constant infusion of the isotope for 6 h at 30 μmol·kg$^{-1}$·h$^{-1}$. A 5-mL arterial blood sample was drawn before the infusion started and at 1-h intervals throughout the infusion. A 50–100 mg sample of muscle tissue was obtained from the longissimus dorsi before the isotope infusion started and at 3 and 6 h after the infusion started.

**Sample collection and preparation.** Blood was drawn in prechilled tubes (containing Na$_2$EDTA and a cocktail of sodium azide, mercaptoethanol, and soybean trypsin inhibitor), immediately centrifuged for 1000 × g for 15 min at 4°C, and plasma was removed and stored on ice until the end of the infusion. The muscle tissue samples were obtained by scalpel dissection under local anesthetic and aseptic conditions and immediately frozen in liquid nitrogen. The incision was closed with two sutures and covered withProvidone-iodine ointment (Professional Disposables, Orangeburg, NY). All samples were stored at −70°C for later analysis.

**Sample analyses.** Plasma albumin concentration was measured, as previously described (Wykes et al. 1996), and fibrinogen concentration was measured using a Fibrinogen Clotting Assay Kit (Sigma Chemical, St Louis, MO) and a BBL Fibrometer (Becton Dickinson, Rutherford, N.J.). Briefly, plasma was diluted 1 to 10 with Owren’s buffer (28 mmol sodium barbital/L, 125 mmol sodium chloride/L, pH 7.35) and 0.2 mL was added to a fibrometer cup. After incubation for 2 min at 37°C, 0.1 mL of thrombin (100,200 NIH U/mL) was added, and the timer started immediately to determine clotting time. In this reaction, the fibrinogen concentration was rate limiting and was inversely proportional to clotting time, yielding a curvilinear relationship. Plasma fibrinogen concentrations were determined from a standard curve. Plasma insulin and cortisol concentrations were measured by radioimmunoassay (RIA) using kits from ICN (ICN Biomedicals, Costa Mesa, CA). Plasma urea and glucose concentrations and the activities of plasma alanine aminotransferase and aspartate aminotransferase were measured on a Ciba-Corning 550 (Ciba-Corning Diagnostics, Oberlin, OH). Urea and glucose concentrations were measured using the urease and glucose oxidase reactions, respectively;
aspartate aminotransferase activity was measured by the oxidation of NADH in the coupled reactions in which oxaloacetate is first derived from the deamination of aspartate by aspartate aminotransferase and then reduced to malate by malate dehydrogenase. Similarly, alanine aminotransferase activity was determined by the oxidation of NADH in the coupled reactions in which pyruvate is first derived from the deamination of alanine by alanine aminotransferase and then reduced to lactate by pyruvate dehydrogenase.

The plasma proteins were extracted as previously described (Jahoor et al. 1994). Briefly, fibrinogen was isolated as fibrin by thrombin precipitation, and albumin was extracted with acidified ethanol from the fibrinogen-free serum (Jahoor et al. 1994). The very low density lipoprotein (VLDL) was separated from plasma by ultracentrifugation (100,000 × g for 1 h) and apoB-100 was extracted with isopropanol (Egusa et al. 1983).

The frozen muscle tissue samples were homogenized in 5 mL of ice-cold 0.6 mol trichloroacetic acid (TCA)/L and centrifuged. The TCA supernatant containing tissue-free amino acids was removed by washing with 0.5 mol trichloroacetic acid (TCA)/L, twice, and finally centrifuged. The TCA precipitates were washed with ice-cold 0.6 mol trichloroacetic acid (TCA)/L and centrifuged. The dried protein precipitates were hydrolyzed in 6 mol HCl/L at 110°C for 24 h then dried. After several washings, the protein pellet was dried.

The dried protein precipitates were hydrolyzed in 6 mol HCl/L at 110°C for 24 h then dried. Both free and protein-bound amino acids were resuspended in 1 mol acetic acid/L, purified by cation exchange chromatography, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafluorobutyric acid (HFB) with a Finnigan MAT 8200 gas chromatograph, and converted to the n-propyl ester, heptafl...
In this study, we have used the FSR and ASR of fibrin as estimates of fibrinogen FSR and ASR. Although the FSR and ASR of fibrinogen were modestly faster in the protein-deficient group than in the control group, the plasma concentration of fibrinogen was significantly lower \((P < 0.01)\) in the protein-deficient group (Fig. 2). After turpentine administration, the plasma concentration, FSR, and ASR of fibrinogen increased significantly \((P < 0.01)\) in both groups. Plasma fibrinogen concentration, however, was still significantly lower \((P < 0.05)\) in the protein-deficient group compared to the controls.

The FSR of longissimus dorsi protein was significantly slower \((P < 0.01)\) in the protein-deficient group compared to the control group (Fig. 3). After turpentine administration, there were significant reductions \((P < 0.01)\) in the FSR of muscle protein in both groups of piglets, and the FSR of the protein-deficient group was still significantly slower \((P < 0.05)\) than in the control group.

DISCUSSION

This study aimed to distinguish the effect of protein deficiency from that of an inflammatory stimulus on the rate of synthesis of muscle protein and two plasma proteins, a positive (fibrinogen) and a negative (albumin) acute-phase protein. Compared to controls, the slower albumin and muscle protein FSR of the protein-deficient piglets suggest that protein deficiency reduces the pools of these proteins by reducing their

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control group, and, whereas the administration of turpentine significantly lowered \((P < 0.05)\) the plasma urea concentrations of the controls, it significantly raised \((P < 0.05)\) the plasma urea concentrations of the protein-deficient group. Although there was no difference between the two groups in the plasma concentrations of two enzymes involved in amino acid metabolism, alanine aminotransferase and aspartate aminotransferase, the administration of turpentine had opposite effects in the two groups of piglets. Whereas turpentine administration caused significant reductions \((P < 0.05)\) in the plasma concentrations of both enzymes in the control group, it caused modest increases in concentrations in the protein-deficient group.

After 31 d of dietary treatment, the plasma albumin concentration, FSR, and ASR of the protein-deficient group were significantly lower \((P < 0.01)\) than those of the control group (Fig. 1). Although turpentine administration elicited significant increases in the FSR and ASR of albumin in both control and protein-deficient groups, only the control group had a significant increase \((P < 0.01)\) in plasma albumin concentration. In the protein-deficient group, there was a significant reduction in the plasma concentration of albumin in response to turpentine administration. After turpentine administration, there was no difference between the groups in albumin FSR, but albumin concentration and ASR remained significantly lower \((P < 0.01)\) in the protein-deficient group compared to those of the control group.

![FIGURE 1](https://example.com/figure1.png)

**FIGURE 1** Plasma concentration and the fractional (FSR) and absolute (ASR) synthesis rates of albumin in control and protein-deficient piglets before and after turpentine administration. Values are means ± SEM, \(n = 5\) pigs. \(* P < 0.01, \) significantly different from the control value; † \(P < 0.01, \) significantly different from the pre-treatment value.

![FIGURE 2](https://example.com/figure2.png)

**FIGURE 2** Plasma concentration and the fractional (FSR) and absolute (ASR) synthesis rates of fibrinogen in control and protein-deficient piglets before and after turpentine administration. Values are means ± SEM, \(n = 5\) pigs. \(* P < 0.01, \) significantly different from the control value; † \(P < 0.01, \) significantly different from the pre-treatment value.
rates of synthesis. On the other hand, although the plasma concentration of fibrinogen was lower, the FSR of fibrinogen was not slower, suggesting that protein deficiency caused a reduction in the size of the fibrinogen pool through a different mechanism. The reduction in muscle protein FSR in both control and protein-deficient piglets in response to turpentine injection together with the slower muscle FSR of the protein-deficient pigs before turpentine treatment, suggests that both protein deficiency and the inflammatory stimulus had similar effects on muscle protein synthesis rate. On the other hand, the inflammatory stimulus had the opposite effect on the rates of synthesis of the two plasma proteins, as it stimulated their rates of synthesis. However, whereas the increase in the synthesis rate of fibrinogen was associated with an increase in its plasma pool in both groups of pigs, the increased rate of synthesis of albumin was associated with an increase in the plasma albumin concentration only in the control group. The protein-deficient piglets actually had a reduction in total plasma protein and of albumin concentration, suggesting that the inflammatory stimulus caused a concomitant increase in the rate of catabolism or loss of albumin and other proteins from the intravascular compartment. Thus, protein deficiency and an acute inflammatory stimulus elicit similar responses in muscle protein synthesis rates but opposite responses in plasma protein synthesis rates.

In two previous studies (Jahoor et al. 1996, Wykes et al. 1996), we showed that the response to a chronic deficiency of dietary protein is associated with a reduction in whole body protein turnover, which includes slower rates of protein synthesis in most organs and tissues. With respect to plasma proteins, although the concentration and rate of synthesis of total plasma proteins were reduced, the concentration and rate of synthesis of some individual proteins were either increased or unaffected by protein deficiency. Similar findings have been reported in other studies that showed that there was a marked reduction in the rate of synthesis of muscle proteins in rats fed a low protein diet (Tawa et al. 1992, Waterlow and Stephen 1968) and of proteins in muscle and other organs and tissues in rats fed a protein-free diet (McNurlan et. 1982). Together, these findings suggest that chronic protein deficiency leads to an overall reduction of protein synthesis that may not include all of the plasma proteins. Our present finding, that 31 d of protein deficiency lead to a marked suppression of muscle protein and albumin synthesis rates in young pigs, further supports such a proposal.

Of interest were the different responses of albumin, a negative acute-phase protein, and fibrinogen, a positive acute-phase protein, to protein deficiency. The pool size of a plasma protein is determined by the balance between its rates of synthesis and catabolism or loss from the vascular compartment. Pool size could be reduced by one of two potential mechanisms: either a decrease in FSR unbalanced by a change in the rate of catabolism or loss or an increase in the rate of catabolism/loss relative to the synthetic rate. The lower fibrinogen concentration of the protein-deficient pigs was not associated with slower FSRs and ASRs, suggesting that the lower plasma concentration was caused by increased catabolism and/or loss of fibrinogen from the intravascular space. This finding is similar to our recent observation in severely malnourished children when they were free of their infections. We found that, compared to values at recovery, fibrinogen concentration was modestly lower, but FSR and ASR modestly faster in the severely malnourished children when their infections were treated (Morlense et al. 1998). Together, these findings suggest that the reduced pools of individual plasma proteins induced by protein deficiency are not all caused by reduced synthesis rates. On the other hand, in a previous study (Jahoor et al. 1996) we showed that piglets fed a protein-deficient diet for 8 wk had normal concentrations of fibrinogen but slower FSRs and ASRs, suggesting that the response of fibrinogen kinetics to protein deficiency changes with the degree of chronicity.

The decrease in muscle protein synthesis rate and the increased rate of synthesis of fibrinogen elicited by the inflammatory stimulus were not surprising, as it is well documented that the metabolic response to the stress of infection, inflammation, or trauma is characterized by an increased net loss of body protein, primarily from skeletal muscle (Cuthbertson 1932); by higher plasma concentrations of the positive, acute-phase proteins, including fibrinogen; and lower plasma concentrations of total plasma proteins and of the negative, acute-phase proteins, including albumin (Fleck 1989). For example, Mansoor et al. (1997) recently reported that the protein metabolic response to head trauma was characterized by a 50% decrease in skeletal muscle protein synthesis rate and a twofold increase in fibrinogen FSR. The positive, acute-phase proteins are of clinical relevance because they serve a variety of important functions related to restoration of homeostasis when the integrity of the animal organism is perturbed by injury or infection (Kushner 1982). These functions include the containment and destruction of infectious agents by assisting and promoting the immune response, the repair of damaged tissues and the protection of healthy tissues, and the indirect alteration of substrate metabolism via the induction of cytokine production (Kushner 1982, Schreiber 1988). Thus, there is a redistribution of protein synthetic activity away from the synthesis of muscle and negative, acute-phase proteins towards the synthesis of the positive, acute-phase proteins that are critical for survival (Clowes et al. 1980, Cuthbertson 1932, Fleck 1989, Kushner 1982). A surprising finding, therefore, was the increased rate of synthesis of albumin in both groups of severely malnourished children, and the higher concentration of total plasma proteins in the control group versus a lower plasma concentration in the protein-deficient group in response to the inflammatory stimulus.
In the past it was believed that the lower concentration of the negative, acute-phase proteins induced by stressed states was caused by a reduced rate of synthesis of these proteins (Aldred and Schreiber 1993). However, the faster rate of synthesis of albumin in both groups of piglets suggests that this is not the case. This finding is in agreement with our previous finding that the lower albumin concentration of marasmic children was accompanied by a faster albumin FSR when the children were also stressed by infections compared to when their infections were cleared (Morlese et al. 1996). Similarly, Mansoor et al. (1997) reported that the hypoalbuminemia of head trauma subjects was accompanied by a 60% increase in albumin synthesis during the acute response to head trauma. Together, these findings suggest that the stress of infection, inflammation, and injury do not suppress the rate of synthesis of albumin. In all likelihood, total protein and albumin concentrations decrease precipitously in infection and in trauma because of an increased transcapillary escape rate and an increased catabolic rate (Davies et al. 1982, Fleck et al. 1985, Grossman et al. 1960). Whereas this seemed to be the case in the protein-deficient animals whose albumin and total plasma protein concentrations were decreased by the inflammatory stimulus, it was not so in the control pigs, as both the albumin and total plasma protein concentrations of this group increased in response to the inflammatory stimulus. Hence, the stress of the inflammatory stimulus was of a sufficient magnitude to suppress muscle protein synthesis and to stimulate plasma protein synthesis in both groups of animals. However, it was not sufficient to elicit an increase in albumin and total plasma protein catabolism or intravascular loss in the control animals.

It has been proposed that the protein metabolic response to the stress of infection, inflammation, or trauma represents a redistribution of amino acids from the peripheral tissues to the liver for the synthesis of rapidly turning over proteins that are critical for survival (Clowes et al. 1980, Fleck 1989). We have made the observation, however, that this redistribution of amino acids seems to be an inefficient process as it is accompanied by a net loss of body nitrogen (Reeds et al. 1994). Our data from the present study provides indirect evidence that the stress of inflammation caused by injections of turpentine may have elicited an increased loss of body protein in the protein-deficient group, but not in the controls. For example, whereas the plasma concentrations of urea and the two transaminating enzymes of the protein-deficient pigs were higher after turpentine administration, they were lower in the control pigs, suggesting that the controls reacted to the stress by switching to a protein anabolic mode and conserved protein, but the protein-deficient piglets were unable to mount such a response and entered into a state of protein catabolism. Much evidence suggests that the increased protein catabolism of infections and trauma is mediated by the increased counterregulatory hormones, including cortisol, hypothalalminemia, and increased cytokines elicited by the stress response (Fleck 1989, Hardin 1993). In the present study, however, turpentine administration elicited a decrease in plasma cortisol concentrations in the control and protein-deficient pigs, as was the case in the control, but not in the protein-deficient piglets. The protein-deficient piglets also had markedly lower plasma insulin concentrations compared to the control piglets. Because insulin is a major protein anabolic hormone (Millward 1990), it is reasonable to postulate that the chronic hypoinsulinemic state of the protein-deficient pigs does not favor attenuation of protein loss despite the turpentine-induced reductions in cortisol levels.

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LITERATURE CITED


