Protein synthesis in liver and extra-hepatic tissues after partial hepatectomy

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Effects of partial hepatectomy on protein synthesis were defined in liver and extra-hepatic tissues of the mature rat. Studies were performed at 24 h and 48 h after surgery in the absence of the dietary input. Protein accretion in the regenerating liver preceded mitosis, but was accompanied by increases in RNA content and fractional rates of protein synthesis (k_s). A positive relationship existed between protein-synthetic capacity and k_s over the period of study. Increases in k_s also bore a positive relationship with increases in translational efficiency. Extra-hepatic tissues showing decreased rates of protein synthesis after liver resection included kidney, striated muscles and brain. Effects were observed mainly at 24 h after surgery and resulted from decreased translational efficiency. Partial hepatectomy increased k_s in diaphragm and tibia at both 24 h and 48 h after surgery. In diaphragm, there was net protein accretion, and, as in liver, increases in k_s were due to increases in both protein-synthetic capacity and efficiency.

INTRODUCTION

The regenerating liver after partial hepatectomy may be used as a model for investigating the mechanisms responsible for liver cell growth in normal, as opposed to cancerous, tissue. Restoration of the liver mass occurs as a consequence of both hypertrophy and hyperplasia. We have observed that stimulation of hepatic protein synthesis is a primary event relating to liver re-growth, even preceding the first mitosis (Preedy *et al.*, 1989). Remarkably, increase in rates of protein synthesis during liver regeneration can occur in the absence of nutritional support (see, e.g., Schofield *et al.*, 1985), implying that the biosynthetic pathway can be sustained by precursors of endogenous origin derived from body protein. The predominant sources of the amino acids used for liver re-growth have not yet been defined. Furthermore, it is not known whether mobilization of amino acids from extra-hepatic tissues results from changes in rates of protein synthesis or degradation.

In the present study, we have examined the time course of protein accretion in the regenerating liver after two-thirds partial hepatectomy in relation to changes in hepatic biosynthetic capacity and translational efficiency and in relation to protein turnover in extra-hepatic tissues. Studies were performed over the first two post-operative days, the period of most rapid liver re-growth, and in the absence of dietary input. A preliminary report of some aspects of this work has been published (Preedy *et al.*, 1989).

EXPERIMENTAL

Animals and materials

Female albino Wistar rats (age about 8–9 weeks) were bred in the animal house of the London Hospital Medical College. They were maintained on a 12 h-light/12 h-dark cycle, with the light phase beginning at 08:00 h. Rats were allowed free access to a

normal laboratory diet (22% protein) before two-thirds partial hepatectomy (Schofield *et al.*, 1985) or the sham-operation (laparotomy and liver manipulation; see Preedy *et al.*, 1988). Surgery was performed at 08:30–09:30 h. Food was not provided post-operatively, and the rats were housed in grid-bottomed cages before use. Water was provided *ad libitum*. Materials were obtained from the sources described previously (Preedy *et al.*, 1984).

Experimental groups

The effects of partial hepatectomy on protein synthesis and degradation *in vivo* were examined in conjunction with the effects of starvation and surgical stress without liver resection (the sham operation). Significant effects of both starvation and the sham operation alone were identified: these data have been reported and discussed separately (Preedy *et al.*, 1988). We have therefore restricted the present study to the specific effects of partial hepatectomy. Values for unoperated and sham-operated rats have been included in the Figures in order to facilitate direct comparison between the groups.

Measurement of rates of protein synthesis

Rates of protein synthesis were measured by the flooding-dose method using [4-³H]phenylalanine (Garlick *et al.*, 1980) in conscious rats at 24 h or 48 h after surgery. The methodology employed is described in detail in Preedy *et al.* (1988). Because of the short period of exposure to [4-³H]phenylalanine, the method measures exported as well as resident protein.

Other methods

Protein was measured by the method of Gornall *et al.* (1949), RNA as described by Munro & Fleck (1969) and DNA as described by Burton (1956). The projected initial protein, RNA and DNA contents of livers of partially hepatectomized rats were taken to be 427 mg, 17.1 mg and 8.5 mg respectively.

Abbreviations used: k_s , fractional rate of protein synthesis (%/day); k_{RNA} , efficiency of protein synthesis, i.e. rate of protein synthesis relative to RNA (g of protein synthesized/day per g of RNA); k_d , fractional rate of protein degradation; k_g , fractional rate of growth; C_s , capacity for protein synthesis, i.e. RNA/protein ratio (μ g of RNA/mg of protein).

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RESULTS AND DISCUSSION

Liver weights and protein contents

Liver weights of the partially hepatectomized rats were restored to 82% of the sham-operated values within 48 h of resection (Table 1). The rats subjected to the sham operation lost approx. 19% of their hepatic protein over the 48 h period of starvation, with the major loss occurring during the first post-operative day (Table 1). Despite fasting, partially hepatectomized rats gained hepatic protein (Table 1).

Protein accretion in relation to DNA and RNA

Protein accretion in the regenerating liver is independent of mitotic activity (Preedy *et al.*, 1989). The accumulation of protein in the regenerating liver is, however, accompanied by a net increment in hepatic RNA content (Table 1). A 51% increase in the RNA content of the regenerating liver was observed during the first 24 h after partial hepatectomy, with a further 32% increase over the next 24 h (Table 1). The lack of co-ordination between changes in the DNA and RNA contents of the regenerating liver is emphasized by the increased RNA/DNA ratio at both 24 h and 48 h after liver resection (Table 1). Since the increase in the total DNA content of the liver reflects mitosis and the bulk of hepatic RNA is ribosomal, it may be concluded that the ribosome contents of the cells of the regenerating liver are increased.

Mechanisms underlying increased hepatic protein accretion after partial hepatectomy

Hepatic protein accretion after partial hepatectomy is associated with increased fractional rates of protein synthesis (k_s) (Preedy *et al.*, 1989). There are two distinct mechanisms by which k_s can be varied, either a change in the capacity for protein synthesis (C_s), which may involve alterations in rates of RNA synthesis and degradation (Brown *et al.*, 1983), or a change in the translational efficiency of protein synthesis (k_{RNA}), which involves altered rates of peptide-chain initiation and/or peptide-chain elongation or termination (Garlick *et al.*, 1983). However, it is important to appreciate that care must be taken in interpreting alterations in k_{RNA} , since it is theoretically possible that there may be preferential loss of mRNA over other forms of RNA.

The relationship between increases in k_s and increases in the capacity for protein synthesis in the regenerating liver is shown in Fig. 1(a). Results obtained for sham-operated rats are also shown. By comparing these results with data obtained in fasted

unmanipulated rats, it becomes clear that the normal positive relationship between protein-synthetic capacity and the protein-synthetic rate is unperturbed by surgery or liver resection.

Increased rates of hepatic protein synthesis after liver resection are also facilitated by significant increases in the translational efficiency of protein synthesis (Preedy *et al.*, 1989). Again, a positive relationship is observed between the rate of protein synthesis and the efficiency of translation, and again the relationship appears to be unperturbed by surgery or liver regeneration (Fig. 1b).

Degradation versus synthesis

Decreased protein degradation has been demonstrated as a factor contributing to protein accumulation in the regenerating liver in the fed state (Scornik & Botbol, 1976). As it is known that starvation normally increases the degradation of hepatic protein (Mortimore & Ward, 1976), it was important to investigate the relative contributions of increased protein synthesis and decreased protein degradation in effecting net protein accretion in the regenerating liver in the fasted state.

In sham-operated rats, the absolute rate of protein synthesis (including both secreted and non-secreted proteins) over the first 24 h after surgery is 863 mg (mean value; see Table 1). As there is net loss of 149 mg of hepatic protein, this rate of protein synthesis does not compensate for protein degradation and export. The combined rates of protein degradation plus export thus approximate to 1012 (863 + 149) mg. A decrease in liver mass to that observed immediately after partial hepatectomy would be predicted to decrease the rate of hepatic protein degradation and export to 337 mg, increasing with increases in liver weight to 569 mg at 24 h after partial hepatectomy.

The absolute rate of protein synthesis during the first 24 h after partial hepatectomy (468 mg) exceeds that of degradation plus export by 113 mg (Table 1): the combined rates of protein degradation and export therefore approximate to 354 mg. At 24 h after surgery this is approx. 62% of that which would be predicted from rates observed after the sham operation. The ratios of synthesis to degradation plus export in the two situations are 0.85 (sham-operation) and 1.32 (partial hepatectomy). It may be concluded that increases in protein synthesis in the regenerating liver are accompanied by reciprocal decreases in protein degradation and/or export, even in the fasted state. Consistent with this conclusion, the fractional rate of protein degradation (k_d , calculated from k_s and k_g) at 24 h after partial hepatectomy was decreased by 27% relative to the sham-

Table 1. Effects of partial hepatectomy on liver protein synthesis in starved rats

Fed rats were subjected to partial hepatectomy (PH) or sham operation (SO), starved post-operatively and sampled after 24 h or 48 h as indicated. Body and liver weights in fed control (unoperated) rats were 214 ± 3 g and 8.05 ± 0.20 g wet wt. respectively. Protein, RNA and DNA contents of livers of fed control rats were 1282 ± 32 mg, 51.5 ± 1.8 mg and 25.5 ± 0.8 mg respectively: projected protein, DNA and RNA contents immediately after two-thirds partial hepatectomy are one-third of these values. Results are means $\pm$ S.E.M. for 10–12 rats. Statistically significant effects of PH are indicated by: ^a $P < 0.001$; ^b $P < 0.01$; ^c $P < 0.05$.

Parameter	24 h		48 h	
	SO	PH	SO	PH
Body wt. (g)	204 ± 3	200 ± 4	197 ± 4	191 ± 4
Liver wt. (g)	6.30 ± 0.16	3.54 ± 0.09^a	5.92 ± 0.12	4.86 ± 0.25^a
Protein content (mg)	1133 ± 27	540 ± 19^a	1039 ± 20	659 ± 30^b
RNA content (mg)	51.7 ± 1.4	25.9 ± 1.0^a	45.4 ± 0.8	34.1 ± 1.5^a
RNA/DNA	1.98 ± 0.4	3.09 ± 0.07^a	1.80 ± 0.03	2.95 ± 0.12^a
Absolute rate of protein synthesis (mg/day per rat)	863 ± 44	468 ± 24^a	687 ± 31	582 ± 46
k_s (%/day)	–10.32	+22.62	–9.22	+26.11
k_d (%/day)	85.4	62.4	76.8	63.8

Fig. 1. Relationship between the fractional rate of protein synthesis (k_s) and (a) the capacity for protein synthesis (C_s) or (b) the efficiency of protein synthesis (k_{RNA}) in livers of starved rats

Rats subjected to partial hepatectomy ($\blacktriangle$, $\bullet$) or sham operation ($\triangle$, $\circ$) were sampled at 24 h ($\triangle$, $\blacktriangle$) or 48 h ($\circ$, $\bullet$) after surgery. Rats were fasted post-operatively. Data obtained from unoperated rats fasted for 24 h ($\triangle$) or 48 h ($\circ$) (Preedy *et al.*, 1988) are included for comparison.

operated value (Table 1). A relatively low fractional rate of protein degradation continued to be observed at 48h after liver resection (Table 1).

Although it is not excluded that there may be changes in rates of protein export from the liver as regeneration proceeds, the ratio of export to resident protein is generally maintained constant. The present results therefore indicate significant effects of liver resection both to increase hepatic protein synthesis (via increases in C_s and k_s) and to decrease hepatic protein degradation and export.

Fractional rates of protein synthesis in extra-hepatic tissues after partial hepatectomy

We have reported previously that laparotomy under ether anaesthesia (the sham operation) elicits changes in tissue rates of protein synthesis which vary between individual tissues (Preedy *et al.*, 1988). The response to partial hepatectomy also exhibited a considerable degree of tissue specificity, not only in terms of the direction and magnitude of the observed changes, but also in the mechanisms by which they were achieved. Absolute values for

Table 2. Protein-synthesis rates in various extrahepatic tissues after partial hepatectomy

Values are mean $\pm$ S.E.M. for 7–12 rats. Values for the control (sham-operated rats) are given in Preedy *et al.* (1988). Statistically significant effects of partial hepatectomy as compared with sham-operated rats fasted for the same length of time are indicated: ns, not significant ($P > 0.05$).

Tissue group	Rats ... k_s (%/day)	24 h-fasted/partially hepatectomized		48 h-fasted/partially hepatectomized	
		% change versus control	Significance versus control	% change versus control	Significance versus control
Thoracic tissues					
Heart	7.34 $\pm$ 0.21	−0.7	ns	6.73 $\pm$ 0.29	+0.9 ns
Diaphragm	10.14 $\pm$ 0.47	+61.9	$P < 0.001$	13.25 $\pm$ 0.95	+122.9 $P < 0.001$
Lung	18.41 $\pm$ 1.33	+13.6	ns	16.22 $\pm$ 1.74	+7.13 ns
Skeletal muscles					
Soleus	5.11 $\pm$ 0.24	−11.6	$P < 0.05$	5.71 $\pm$ 0.29	−4.4 ns
Plantaris	2.53 $\pm$ 0.19	−17.6	$P < 0.05$	2.57 $\pm$ 0.07	−3.5 ns
Gastrocnemius	2.25 $\pm$ 0.18	−18.5	$P < 0.05$	2.46 $\pm$ 0.12	−0.8 ns
Smooth muscles					
Stomach	40.00 $\pm$ 1.84	−10.9	$P < 0.05$	41.42 $\pm$ 2.54	−13.9 ns
Small intestine	71.07 $\pm$ 2.61	−0.7	ns	64.49 $\pm$ 2.19	−20.6 $P < 0.05$
Uterus	25.78 $\pm$ 2.89	+7.7	ns	22.79 $\pm$ 2.22	−6.0 ns
Non-muscle tissues					
Kidney	27.64 $\pm$ 1.28	−17.7	$P < 0.05$	31.54 $\pm$ 1.63	−9.9 ns
Spleen	37.91 $\pm$ 1.84	−13.8	ns	46.60 $\pm$ 1.96	+3.7 ns
Brain	10.61 $\pm$ 0.28	−9.0	$P < 0.05$	11.13 $\pm$ 0.25	−4.7 ns
Tibia	21.43 $\pm$ 1.60	+23.4	$P < 0.05$	21.22 $\pm$ 1.54	+31.4 $P < 0.05$

fractional rates of protein synthesis in a range of extra-hepatic tissues of the partially hepatectomized rat are shown in Table 2, in which we have also indicated the direction and magnitude of the changes in k_s elicited by partial hepatectomy as compared with the control (sham-operated) rats, values for which are given in Preedy *et al.* (1988).

Tissues showing decreased rates of protein synthesis. In most of the tissues studied, fractional rates of protein synthesis decreased during the first post-operative day (Table 2). Statistically significant decreases in k_s were observed in skeletal muscles (soleus, plantaris and gastrocnemius), stomach, kidney and brain. Neither cardiac nor uterine protein synthesis was affected by partial hepatectomy. The tissues showing the greatest decline in k_s in response to partial hepatectomy (decreases of approx. 18%) included the striated muscles containing relatively high percentages of Type II glycolytic fibres (the plantaris and gastrocnemius) (see Ariano *et al.*, 1973, for details of fibre composition) and the kidney, of which the medulla has an obligatory requirement for glucose. The fractional rate of protein synthesis in the brain, whose metabolism is also dependent on the use of glucose, was also decreased by partial hepatectomy (Table 2). Except for the small intestine, where a significant effect of partial hepatectomy was observed only after 48 h (Table 2), effects of liver resection to decrease k_s were restricted to the first post-operative day (Table 2). The predominant mechanism underlying the observed decreases in k_s was decreased translational efficiency (Table 3), as opposed to decreased protein-synthetic capacity (Table 4): indeed, in certain tissues (notably small intestine, stomach, kidney and spleen), there was some indication that protein-synthetic capacity might even be increased after partial hepatectomy.

It is possible that diminished protein synthesis is related to the small yet significant decreases in glycaemia which are observed after liver resection in the fasted state (Schofield *et al.*, 1985; see also Katz, 1979). Partially hepatectomized rats exhibit only modest ketonaemia after starvation (Schofield *et al.*, 1985), and

it is reasonable to suggest that there may be an increased requirement for glucose as an energy substrate in the fasted state. [Although the brain can adapt to utilize ketone bodies as alternative energy substrates to glucose after prolonged starvation, there is not a significant decrease in arterio-venous glucose concentration differences across the brain after starvation for 48 h (Hawkins *et al.*, 1971) and glucose phosphorylation is only slightly decreased (Issad *et al.*, 1987).]

Tissues showing increased rates of protein synthesis. In two tissues (diaphragm and tibia), partial hepatectomy was associated with a significant increase in k_s (Table 2). These effects were marked, even greater in magnitude than the responses observed in the regenerating liver itself (see Preedy *et al.*, 1989). In contrast with the relatively transient inhibition of protein synthesis in most extra-hepatic tissues, stimulatory effects of partial hepatectomy on protein synthesis in diaphragm and tibia were sustained over the period of study (48 h) (Table 2). In the diaphragm, where, as in the liver, net protein accretion is observed (Table 5), a salient feature of the response was a significant increase in the capacity for protein synthesis (Table 4; see also Fig. 2), as well as in the translational efficiency (Table 3). Protein accretion may therefore be partly attributable to changes in RNA turnover.

Increases in k_s and C_s in the diaphragm are not necessarily specifically related to partial hepatectomy. We have reported previously that the sham operation (laparotomy and liver manipulation under ether anaesthesia) will, even in the absence of liver resection, induce significant increases in protein synthesis in this constantly contracting muscle (Preedy *et al.*, 1988). Although it is possible that the response to abdominal surgery may be a consequence of anaesthesia (with associated changes in respiratory rates, tidal volumes etc.), it is remarkable that the effects are observed as late as 48 h after surgery.

Increases in fractional rates of protein synthesis in tibia are not observed in response to laparotomy in the absence of liver resection (Preedy *et al.*, 1988). These effects are therefore

Table 3. Translational efficiencies in extra-hepatic tissues after partial hepatectomy

See legend to Table 2 for details.

Tissue group	Rats ...			24 h-fasted/partially hepatectomized			48 h-fasted/partially hepatectomized		
	k_{RNA} (g of protein/day per g of RNA)	% change versus control	Significance versus control	k_{RNA} (g of protein/day per g of RNA)	% change versus control	Significance versus control	k_{RNA} (g of protein/day per g of RNA)	% change versus control	Significance versus control
Thoracic tissues									
Heart	10.78 ± 0.28	-3.4	ns	10.22 ± 0.23	-6.8	ns			
Diaphragm	13.97 ± 0.49	+13.4	$P < 0.05$	12.19 ± 0.44	+7.4	ns			
Lung	21.78 ± 0.84	-0.9	ns	24.46 ± 0.78	+7.1	ns			
Skeletal muscles									
Soleus	16.21 ± 0.71	+1.1	ns	16.25 ± 1.06	-4.4	ns			
Plantaris	10.44 ± 0.59	-13.6	$P < 0.05$	11.45 ± 0.30	-3.5	ns			
Gastrocnemius	10.51 ± 0.78	-20.0	$P < 0.01$	12.76 ± 0.73	-0.8	ns			
Smooth muscles									
Stomach	17.34 ± 0.82	-8.1	ns	16.26 ± 0.82	-13.9	$P < 0.05$			
Small intestine	13.20 ± 4.38	-9.4	ns	11.93 ± 0.47	-20.6	$P < 0.001$			
Uterus	9.82 ± 0.54	-3.5	ns	9.84 ± 0.69	-6.6	ns			
Non-muscle tissues									
Kidney	12.66 ± 1.11	-17.6	ns	13.55 ± 0.57	-9.9	ns			
Spleen	12.31 ± 0.65	-10.9	ns	12.26 ± 0.47	-3.7	ns			
Brain	8.60 ± 0.18	-7.4	$P < 0.05$	9.09 ± 0.16	-4.7	ns			
Tibia	6.99 ± 0.29	+11.5	ns	7.15 ± 0.99	+31.4	ns			

Table 4. Protein-synthetic capacities in extra-hepatic tissues after partial hepatectomy

See legend to Table 2 for details.

Rats ...	24 h-fasted/partially hepatectomized			48 h-fasted/partially hepatectomized		
	C_s (μg of RNA/mg of protein)	% change versus control	Significance versus control	C_s (μg of RNA/mg of protein)	% change versus control	Significance versus control
Tissue group						
Thoracic tissues						
Heart	6.87 ± 0.11	+4.7	ns	6.60 ± 0.13	-8.9	$P < 0.01$
Diaphragm	7.29 ± 0.17	+43.8	$P < 0.001$	10.84 ± 0.47	+113.8	$P < 0.001$
Lung	8.75 ± 0.45	+12.5	ns	6.71 ± 0.66	-18.4	ns
Skeletal muscles						
Soleus	3.32 ± 0.11	-8.0	ns	3.60 ± 0.19	-7.1	ns
Plantaris	2.41 ± 0.11	-1.2	ns	2.34 ± 0.07	-3.5	ns
Gastrocnemius	2.10 ± 0.81	-1.9	ns	1.95 ± 0.06	0	ns
Smooth muscles						
Stomach	22.93 ± 0.48	-4.9	ns	25.57 ± 0.73	+11.2	$P < 0.05$
Small intestine	54.22 ± 1.15	+7.7	$P < 0.05$	55.09 ± 1.43	+10.8	$P < 0.01$
Uterus	26.60 ± 1.59	+6.7	ns	23.14 ± 1.19	+3.6	ns
Non-muscle tissues						
Kidney	22.22 ± 0.35	+2.9	ns	23.14 ± 0.93	+9.0	$P < 0.05$
Spleen	33.60 ± 1.80	+1.7	ns	40.75 ± 1.74	+18.1	$P < 0.01$
Brain	12.29 ± 0.12	-0.6	ns	12.30 ± 0.08	-1.1	ns
Tibia	29.94 ± 1.37	+6.5	ns	30.32 ± 0.97	+10.2	ns
Skin	9.60 ± 0.70	-1.8	ns	8.36 ± 0.33	+3.9	ns

Table 5. Protein contents of extra-hepatic tissues after partial hepatectomy

See legend to Table 2 for details.

Rats ...	24 h-fasted/partially hepatectomized			48 h-fasted/partially hepatectomized		
	Protein content (mg)	% change versus control	Significance versus control	Protein content (mg)	% change versus control	Significance versus control
Tissue group						
Thoracic tissues						
Heart	127.4 ± 2.7	-0.8	ns	126.7 ± 3.4	-3.7	ns
Diaphragm	77.9 ± 1.6	+12.5	$P < 0.01$	71.6 ± 2.3	+6.4	ns
Lung	317.0 ± 34.1	-8.7	ns	421.9 ± 43.4	+20.6	ns
Skeletal muscles						
Soleus	17.2 ± 0.6	-2.5	ns	16.9 ± 0.7	-3.3	ns
Plantaris	40.2 ± 0.8	-0.6	ns	37.1 ± 1.1	-9.8	$P < 0.05$
Gastrocnemius	208.4 ± 8.2	-3.4	ns	209.5 ± 3.6	-0.5	ns
Smooth muscles						
Stomach	149.7 ± 4.4	+9.4	ns	140.9 ± 3.9	+5.9	ns
Small intestine	672.1 ± 35.5	-6.3	ns	649.9 ± 39.8	+2.2	ns
Uterus	44.7 ± 3.4	+0.9	ns	36.9 ± 2.5	+12.4	ns
Non-muscle tissues						
Kidney	118.1 ± 2.5	+8.05	$P < 0.05$	116.0 ± 3.3	+4.2	ns
Spleen	103.7 ± 5.7	-4.9	ns	103.3 ± 5.3	+3.8	ns
Brain	189.9 ± 2.4	-0.5	ns	188.5 ± 2.2	-0.8	ns
Tibia	31.4 ± 1.3	+6.5	ns	31.2 ± 1.7	-0.6	ns
Skin	3328 ± 222	-2.6	ns	3578 ± 171	-5.2	ns

specifically related to liver regeneration. Increases in k_s in the tibia are not associated with net protein accretion (Table 5), possibly because of protein export from the bone. It will be of considerable interest to determine whether the effects of partial hepatectomy on bone protein-synthesis rates are restricted to the long bones, which are active in haematopoiesis, or are more generally observed.

Protein accumulation or loss after partial hepatectomy

Because of the significant increases in rates of protein synthesis, it might be expected that liver regeneration would impose a substantial drain on amino acid precursors for protein synthesis. However, by virtue of the decreased liver mass, the absolute rate of protein synthesis in the regenerating liver is, in fact,

Fig. 2. Relationship between the fractional rate of protein synthesis (k_s) and the capacity for protein synthesis (C_s) in diaphragms of starved rats

Details of the experimental groups and the notations used are given in the legend to Fig. 1.

significantly decreased compared with the sham-operated controls (Table 1). Except for the plantaris at 48 h, decreases in k_s were not generally accompanied by significant decreases in protein content (Table 5).

The total protein content of the plantaris, a representative white muscle, was decreased from an initial value of 40.9 ± 0.8 mg in the fed state to 37.1 ± 1.2 mg ($P < 0.001$) at 48 h after partial hepatectomy, but was not decreased by the sham operation (Table 5). This loss of muscle protein may be of physiological

significance in terms of whole-body protein turnover after partial hepatectomy. The skeletal-muscle mass constitutes 40 % of body weight, and white fibres represent 50 % of the fibre population. Thus the projected loss of skeletal-muscle protein (approx. 700 mg over the 48 h period) exceeds the net requirements for amino acid precursors for protein synthesis. Excess amino acids may be used as precursors for gluconeogenesis, supplementing starvation-induced amino acid release from visceral tissues.

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