ORIGINAL ARTICLE

Metabolic changes in the liver and thymus of rats with chronic liver failure

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Abstract. *We compared substrate utilisation in liver fibrosis or cirrhosis using microdialysis to follow interstitial concentration changes of urea, glucose, lactate and glycerol in peritoneal cavity, liver and thymus. Material and methods: Male Wistar rats (n = 18) were divided into 3 groups. Group I: INT - intact rats. Group II: BDL – rats 14 days after bile duct ligation. Group III: CIRH - liver cirrhosis induced by chronic CCl_4 administration. Microdialysis probes CMA 20 was inserted into organs, perfused by Ringer's solution (75 µl/h), samples were collected after 6 hours. Surgical procedures were carried out under pentobarbital anaesthesia. Results: Periodical degradation of sodium pentobarbital by intact liver and fluctuating depth of anaesthesia increases interstitial blood perfusion. Glucose concentration (mmol/l) decreased especially intraperitoneally in BDL (0.80…0.61). Glucose in the liver was higher in INT (1.11…0.90) in comparison with BDL (0.56…0.38) or CIRH (0.95…0.36). Thymic lactate (mmol/l) did not decrease in INT (0.30…0.25 – signifies thymocyte proliferation) in comparison with CIRH (0.22…0.10). Glucose in thymus was stable in INT (0.81…0.71) but not in BDL (0.80…0.45) and CIRH (0.63…0.47). Lower availability of glucose and lactate production was in BDL and CIRH (thymocytes are not able to proliferate). Conclusions: Liver damage influenced interstitial metabolism of basal metabolites in distant organs. Glucose, lactate and glycerol are essential for cell proliferation. Fluctuation or decrease of interstitial concentrations of these metabolites could be explanation of pathophysiological changes in distant organs. The impairment of glucose metabolism may be the cause of pathophysiological changes in thymus.*

Key words: *microdialysis, glucose, lactate, liver, thymus, rat, cirrhosis*

Živná H, Živný P, Nožička J, Hrubá P. Metabolické změny v játrech a thymu potkanů s chronickým jaterním selháním. Folia Gastroenterol Hepatol 2005; 3 (3): 80 – 91.

Souhrn. *Sledovali jsme s využitím metody mikrodialýzy změny koncentrací močoviny, glukózy, laktátu a glycerolu v intesticiu fibrotických nebo cirhotických jater a thymu a v peritoneální dutině. Materiál a metody: Potkani - samci kmene Wistar (n = 18) byli rozděleni do 3 skupin. Skupina I: INT – intaktní potkani. Skupina II: BDL – potkani 14 dní po provedení podvazu ductus choledochus. Skupina III: CIRH – potkani s jaterní cirhózou navozenou opakovanou aplikací CCl_4 p.o. Všechny operační zákroky byly provedeny v pentobarbitalové anestezii. Mikrodialyzační sondy CMA 20 byly implantovány do orgánů a následně perfundovány Ringerovým roztokem rychlostí 75 µl/h, vzorky byly kontinuálně sbírány po dobu 6 hodin. Výsledky: Periodické odbourávání aplikovaného pentobarbitalu intaktními játry snižovalo hloubku anestezie a naopak zvyšovalo krevní průtok intersticiem. Koncentrace glukózy (mmol/l) klesala zvláště intraperitoneálně u BDL (0,80…0,61), glukóza byla vyšší v játrech u INT (1,11…0,90) ve srovnání s BDL (0,56…0,38) nebo CIRH (0,95…0,36). Koncentrace laktátu v thymu (mmol/l)*

neklesaly u INT (0,30…0,25 – známka proliferace thymocytů) ve srovnání s CIRH (0,22…0,10). Koncentrace glukózy v thymu se neměnily u INT (0,81…0,71), ale klesaly u BDL (0,80…0,45) i CIRH (0,63…0,47). Nižší dostupnost glukózy a nižší produkce laktátu je u BDL a CIRH, kdy thymocyty nejsou schopné u potkanů s poškozenými játry proliferovat. Závěry: Jaterní poškození ovlivňuje metabolismus bazálních metabolitů i v intersticiu vzdálených orgánů. Glukóza, laktát a glycerol jsou nezbytné pro buněčnou proliferaci. Chybění nebo nedostatek těchto metabolitů může vysvětlovat patofyziologické změny ve vzdálených orgánech. Narušení metabolismu glukózy může být příčinou patofyziologických změn v thymu.

Klíčová slova: *mikrodialýza, glukóza, laktát, játra, thymus, potkan, cirhóza*

The aim of our study was to compare substrate utilisation in rats with initial liver fibrotic changes after bile duct ligation (3,9) and in rats with advanced liver cirrhosis with ascites after chronic tetrachlormethane administration (19). The microdialysis method enabled us to follow metabolic changes directly in interstitial space of selected organs – liver and thymus.

General anaesthesia is needed for the microdialysis process of visceral organs. General anaesthesia lasting for 6 hours leads necessarily to cessation of food and water consumption and then leads to changes in basic metabolic substrates utilisation too. We suppose, based on literature, that intraperitoneal changes of substrate concentrations imitate plasma changes. Urea concentration changes in microdialysate can give basic indirect information concerning tissue perfusion, glucose, lactate and glycerol concentration give indirect information about the rate of interstitial saccharide and fat metabolism. According to literature, the effect of pentobarbital anaesthesia induces the following changes in the organism: decrease in arterial blood pressure and increase in pulse rate (23), decrease in perfusion of peripheral tissue (13,20), decrease in glucose utilisation (11,12), increase in blood lactate concentration (23,24).

Material and methods

Male Wistar strain rats obtained from Velaz (Praha, Czech Republic) were maintained under controlled temperature (22 – 24 °C) and a constant twelwe-hour light-dark cycle. The animals were housed in hanging plastic cages and fed using commercial pelleted food (ST 1-TOP, Velaz (Praha, Czech Republic), total energy content was 15.18 kJ/g, fat – 1.13 kJ, protein – 4.17 kJ, saccharides 9.89 kJ) and drinking water *ad libitum*.

Microdialysis was performed by using microdialysis (MD) probes CMA 20 (CMA Microdialysis, Solna, Sweden) with a linear perfusion pump LD 20 (Tesla, Přelouč, Czech Republic). MD probes were perfused with Ringer's solution, perfusion speed was constantly 75 µl per hour. Microdialysis samples were collected every hour.

Protocol and all experimental procedures were approved by the local Animal Care Committee of the Faculty of Medicine. All surgical procedures were carried out under pentobarbital anaesthesia.

Rats were anesthetized with sodium pentobarbital for 6 hours (the first dose was 40 mg/kg b.w. i.p., the next serial doses only in group INT: 15 mg/kg of b.w. i.p. into the pelvic region) and 6 microdialysate samples were collected during general anaesthesia at room temperature (20 – 22 °C).

MD probes were inserted simultaneously: 1) into the constant part of the liver; 2) into the peritoneal space near the right kidney (the reason was to avoid interference of microdialysis with sodium pentobarbital administration) after skin and abdominal muscle incision; and 3) into the thymus through short skin incision in the region of the superior part of sternum. MD probes were exactly inserted using a special guide and the appropriate probe position was confirmed after the rats were sacrificed.

Rats were sacrificed after six hours of running microdialysis by exsanguination from their abdominal aorta. We have to acknowledge that intraperitoneal sodium pentobarbital administration could influence concentrations of all analytes in microdialysate. To minimize these factors thirty minutes equilibration period was reserved for recovery.

At random, 18 male rats were divided into 3 groups after institutional approval.

Group I: INT (n = 6, body weight at the time of microdialysis – b.w. 287 ± 15 g) intact Wistar rats.

Group II: BDL (n = 7, b.w. at the time of microdialysis 253 ± 10 g) the rats underwent surgical bile duct ligation (BDL) according to Kountouras et al. (9) and 14 days after BDL microdialysis was implemented for 6 hours and then the rats were sacrificed. BDL was

carried out as follows: laparotomy was performed, and the common bile duct was isolated, doubly ligated, and resected between the ligatures.

Group III: CIRH (n = 5, b.w. at the time of microdialysis 336 ± 20 g). Liver cirrhosis was induced by chronic peroral tetrachlormethane administration (tetrachlormethane was diluted with olive oil 1:1, and administered 2 ml/kg b.w. twice a week during 12 weeks). Microdialysis was performed during the 13th week and then rats were sacrificed.

Samples

Urea, glucose, and lactate concentrations were estimated using standardised kits on a Hitachi 917 (Roche GmbH, Mannheim, Germany) automatic analyser. Glycerol concentrations were estimated by colorimetric method with a kit from Randox (μmol/l, Randox, Crumlin, UK).

Histological examinations

The liver tissue for the histopathological examination was obtained from one standard site *(processus caudatus lobi caudati)*, fixed in 10% buffered formalin, embedded in the paraffin and sectioned at 3 μm. The sections were stained with haematoxylin and eosin.

Statistical evaluations

SigmaStat software (Jandel Scientific Corporation, San Rafael, California, USA) was used. Tests used were: unpaired t-test, one way ANOVA. The data is presented as the mean ± S.E.M. (standard error of the mean). The statistical significance was expressed by the number of signs: one sign = $p < 0.05$, two signs = $p < 0.01$, three signs = $p < 0.001$.

Results

Histologically we have evaluated changes in liver tissue from all the three groups of rats.

In the INT group we found preserved intact liver parenchyma. Lobular architecture was intact without any change (Fig 1).

In the BDL group portal tracts were expanded by oedema and biliary type of fibrosis. The outlines of the portal tracts were irregular. The typical proliferation of bile ducts set in oedematous and inflamed fibrous stroma was seen mainly on the periphery of the portal tract (Fig 2).

In the CIRH group we found established micronodular cirrhosis of liver parenchyma. Nodules of hepatocytes were affected by the moderate steatosis. Hepatocytes alone display dystrophic changes mainly. There was oedema of hepatocytes and some hepatocytes display oncocytic transformation. Apoptotic cells and single mitoses of hepatocytes were scattered throughout the nodules (Fig 3).

We found the rat thymus with a preserved structure of cortical and medullar parts in INT (Fig 4). The thymic lobule with atypical architecture was in CIRH.

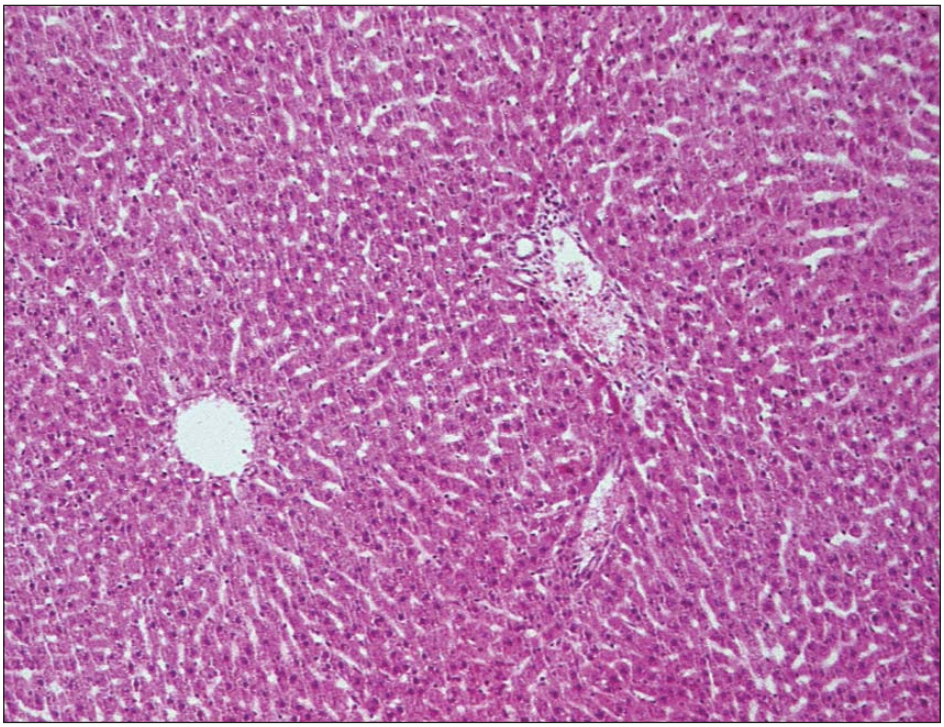

Fig. 1
Intact liver parenchyma with regular lobular architecture (haematoxylin-eosin, magnification 200x).

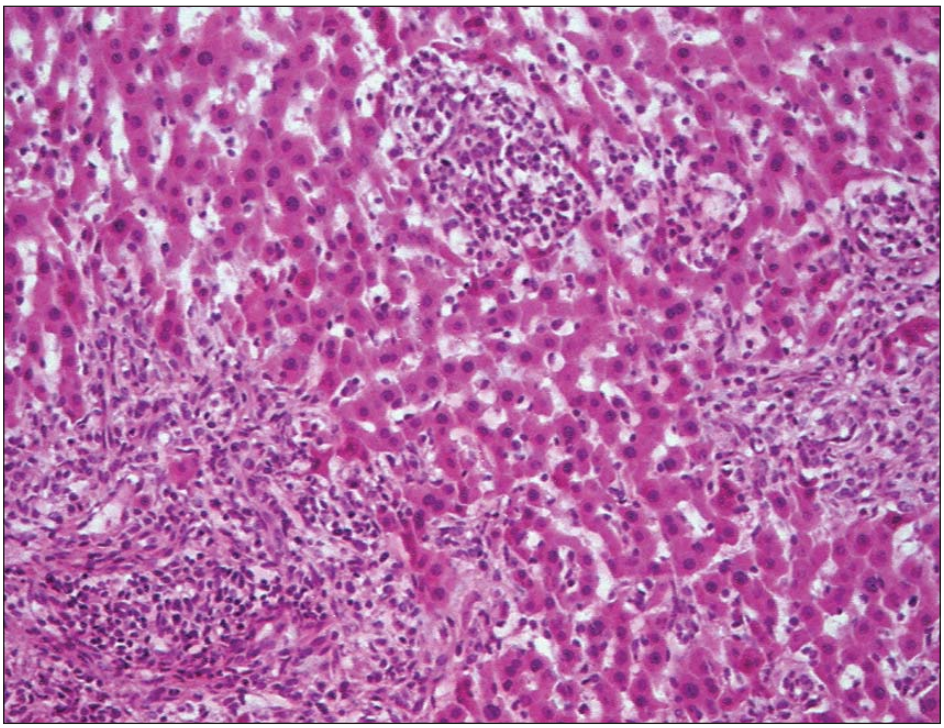

Fig. 2
Portal tract is expanded by oedema and fibrosis 14 days after bile duct ligation. The outlines of the portal tract are irregular. Proliferated bile ducts set in oedematous and inflamed fibrous stroma are seen mainly on the periphery of the portal tract (haematoxylin-eosin, magnification 400x).

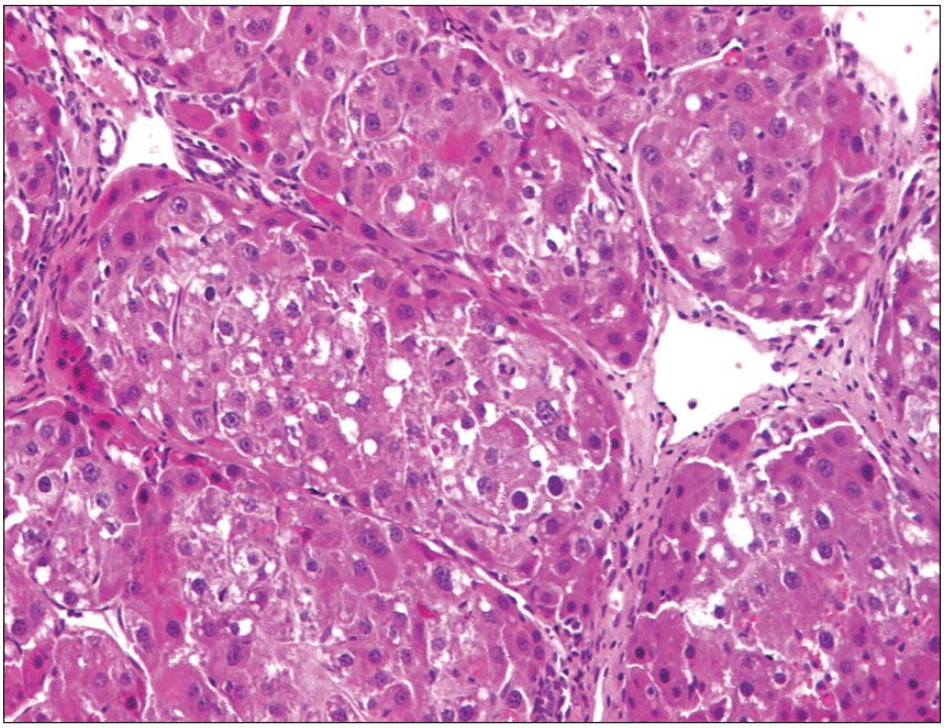

Fig. 3
Histology of liver tissue after 12 weeks tetrachlormetane aplication. Effacement of the liver architecture by the obvious cirrhosis of the parenchyma. Multiple fibrotic bridges separate regenerating nodules of hepatocytes (haematoxylin-eosin, magnification 400x).

There is loss of sharp border between the cortical and medullar portions. A considerable decrease of cellularity (about 70 % in comparison with normal thymus) and increased amount of fibrotic tissue within the medulla was seen (Fig 5). Changes in thymus of BDL group were very similar (not presented).

There were time dependent changes in urea concentrations in dialysate from the peritoneal cavity in the intact rats (but not significant with one another), in spite of this fact, these results are presented as a sign of interstitial concentrations of molecules freely diffuse through all membranes. There were no time dependent changes in interstitial urea concentrations in the liver and the thymus (Table 1).

Glucose concentrations in microdialysate of intact rats from the peritoneal cavity were significantly higher in comparison with liver and thymus interstitial urea concentrations with the exception of 5th and 6th hour interval. The dynamics of concentration changes is similar to urea changes. There was moderate decrease in glucose microdialysate concentrations in all compartments during anaesthesia in rats after BDL. Gluco-

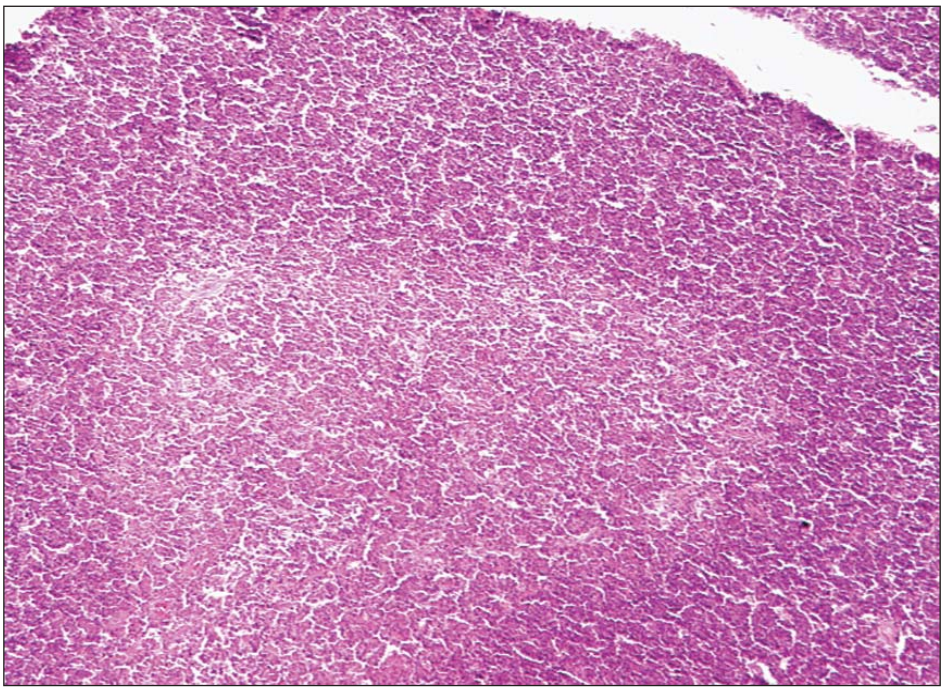

Fig. 4
Histology of intact thymus with the preserved stucture of cortical and medullar parts (haematoxylin-eosin, magnification 200x).

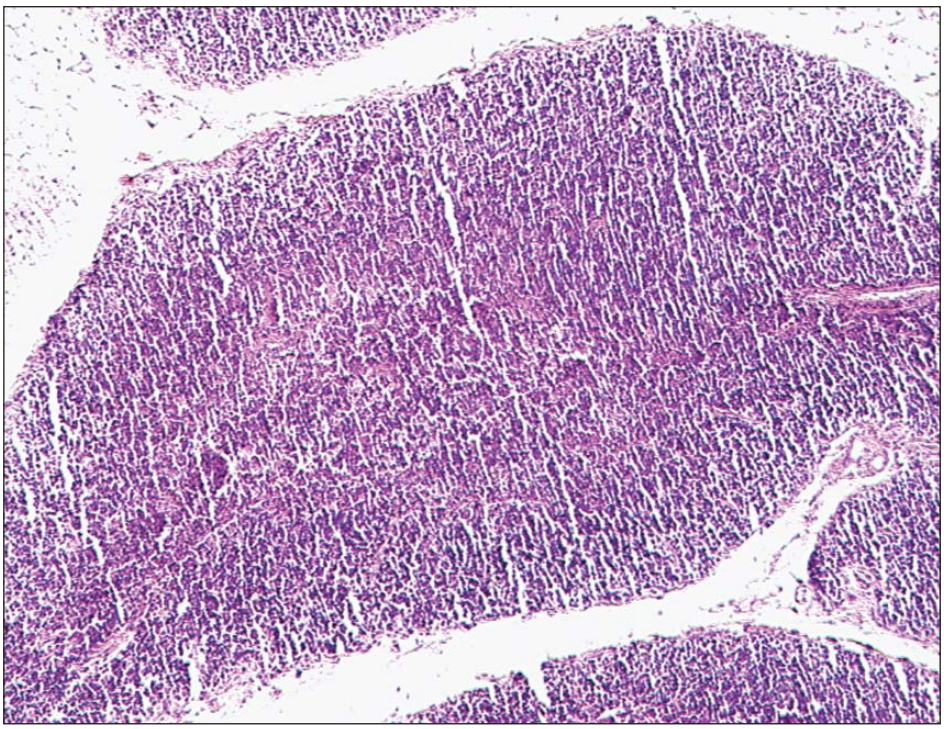

Fig. 5
Histology of thymus in liver cirrhosis: the erased architecture of thymic lobule with considerable reduction in the number of thymocytes and condensation of stroma (haematoxylin-eosin, magnification 200x).

se concentrations in microdialysate from the peritoneal cavity in CIRH rats were significantly higher in comparison with glucose concentrations from the liver and the thymus. The liver and thymus interstitial glucose concentrations decrease during anaesthesia. There were significantly lower glucose liver and thymus interstitial concentrations in liver impairment model rats in comparison with intact rats since the 3rd hour of microdialysis. Significantly lower glucose concentrations were intraperitoneally in rats with BDL in comparison with intact rats since the 3rd hour of microdialysis (Table 2).

The microdialysate concentrations of lactate in intact rats had similar dynamic changes during anaesthesia in peritoneal cavity as well as in liver and thymus. There was a moderate decrease in lactate microdialysate concentrations in all compartments during anaesthesia in BDL and CIRH, markedly in the thymus in CIRH. There were significant differences in interstitial lactate concentration between intact rats and rats with liver impairment in the thymus since the 4th hour of microdialysis (Table 3).

Summaries of glycerol concentrations were pre-

Table 1
Urea concentration in dialysate in rats (mmol/l)

		1st hour	2nd hour	3rd hour	4th hour	5th hour	6th hour
Peritoneum	**INTACT**	2.10±0.28	2.07±0.34	2.25±0.21	2.23±0.14	1.70±0.21	2.14±0.35
	BDL	2.01±0.41	2.03±0.41	1.97±0.35	1.99±0.35	1.87±0.29	1.90±0.39
	CIRH	1.67±0.33	2.43±0.78	2.70±0.91	2.80±1.20	2.70±0.90	2.75±0.95
Liver	**INTACT**	1.40±0.42	1.18±0.54	1.33±0.20	1.53±0.24	1.90±0.39	1.36±0.22
	BDL	1.20±0.29	1.10±0.23	1.04±0.11	1.11±0.13	1.10±0.15	1.13±0.14
	CIRH	1.53±0.85	1.57±0.67	1.47±0.37	1.15±0.05	1.40±0.20	1.45±0.24
Thymus	**INTACT**	1.53±0.15	1.47±0.15	1.60±0.19	1.50±0.17***	1.45±0.16	1.30±0.15
	BDL	1.43±0.34	1.33±0.25	1.30±0.22	1.28±0.23	1.20±0.22	1.17±0.18
	CIRH	1.17±0.21	1.37±0.41	1.50±0.40	1.20±0.10***	1.20±0.10	1.20±0.05

Table 2
Glucose concentration in dialysate in rats (mmol/l)

		1st hour	2nd hour	3rd hour	4th hour	5th hour	6th hour
Peritoneum	**INTACT**	1.27±0.17	1.19±0.21	1.31±0.13	1.37±0.12	1.04±0.10	1.29±0.20
	BDL	1.02±0.11	0.89±0.10	0.80±0.09	0.78±0.06	0.71±0.06	0.61±0.06
	CIRH	0.87±0.12	1.16±0.35	1.10±0.34	1.08±0.41	0.91±0.31	0.94±0.38
Liver	**INTACT**	1.11±0.38	0.74±0.14	0.77±0.09	0.93±0.10***	1.15±0.29	0.90±0.12
	BDL	0.56±0.09	0.44±0.06	0.39±0.06	0.38±0.05***	0.37±0.06	0.38±0.07
	CIRH	0.95±0.41	0.65±0.28	0.54±0.20	0.33±0.03	0.37±0.04	0.36±0.03
Thymus	**INTACT**	0.81±0.09	0.80±0.09	0.91±0.12	0.81±0.10	0.85±0.08	0.71±0.05
	BDL	0.80±0.05	0.63±0.08	0.58±0.03	0.58±0.03	0.49±0.03	0.45±0.05
	CIRH	0.63±0.11	0.68±0.17	0.63±0.14	0.47±0.02	0.46±0.01	0.47±0.03

Table 3
Lactate concentration in dialysate in rats (mmol/l)

		1st hour	2nd hour	3rd hour	4th hour	5th hour	6th hour
Peritoneum	**INTACT**	0.44±0.08	0.22±0.04	0.22±0.02	0.25±0.07	0.34±0.11	0.28±0.05
	BDL	0.50±0.10	0.36±0.10	0.33±0.10	0.32±0.09	0.28±0.06	0.26±0.07
	CIRH	0.29±0.03	0.26±0.03	0.24±0.05	0.17±0.02	0.17±0.02	0.16±0.03
Liver	**INTACT**	0.45±0.18	0.20±0.06	0.18±0.03	0.20±0.03	0.36±0.07	0.25±0.03
	BDL	0.35±0.09	0.25±0.04	0.24±0.05	0.24±0.03	0.21±0.03	0.20±0.02
	CIRH	0.52±0.21	0.31±0.10	0.26±0.10	0.17±0.07	0.19±0.07	0.17±0.06
Thymus	**INTACT**	0.30±0.04	0.20±0.03	0.22±0.02	0.29±0.06***	0.33±0.07	0.25±0.03
	BDL	0.35±0.04	0.29±0.07	0.18±0.03	0.20±0.04***	0.20±0.04	0.18±0.05
	CIRH	0.22±0.06	0.22±0.08	0.22±0.12	0.09±0.01	0.09±0.01	0.10±0.00

sented from all microdialysis samples during 6 hours of anaesthesia (the reason was lack of material for analysis). Both groups with impaired liver function had lower interstitial liver glycerol concentrations in comparison with intact rats. On the other hand there were higher interstitial glycerol concentrations in the thymus of BDL or CIRH in comparison with INT (Table 4).

Table 4
Summary of glycerol concentrations in dialysate during 6 hours of microdialysis (μmol/l) and thymus weight in rats (mg)

	Peritoneum	Liver	Thymus	Thymus weight
INTACT	1.67±0.61	1.83±0.70	0.50±0.21*	345±27
BDL	1.71±0.63	1.00±0.69	0.86±0.22	226±41
CIRH	2.33±0.62	1.00±0.70	2.00±0.24*	232±17

Discussion

Body weight of all three groups was similar at the onset of experiment. The decrease of body weight in BDL was caused by experimental surgery and following maldigestion due to lack of bile, liver impairment and inflammatory changes within the liver. The increase of body weight in CIRH was caused by ascites and fluid retention associated with liver cirrhosis.

Effect of anaesthesia on metabolism

In our study we used sodium pentobarbital anaesthesia during 6 hours (40 mg per kg of b.w. intraperitoneally). The effects of pentobarbital anaesthesia are: arterial blood pressure decreased and pulse rate increased (23), decreased liver perfusion (20), decreased blood flow in subcutaneous tissue (13) and in adipose tissue, where glucose utilisation is decreased (decrease in glucose concentration and increase in lactate concentration – ref. 12). Lang et al. (11) demonstrated in rats that the rapid reduction in glucose metabolism is caused by hypothermia, not by pentobarbital anaesthesia alone. On the other hand, other authors showed the participation of sodium pentobarbital in the increase of blood lactate concentration (by developed hypercapnia and acidosis in spite of good oxygenation), and cortisol increased (23) or mainly through circulating epinephrine – partially through sympathetic nervous stimulation (24). We found the increase of lactate in the 5th hour of experiment in INT rats. The anaesthesia probably could be the cause of lactate increase; for instance Taylor (23) stated that hypercapnia and acidosis were developed in anaesthetized sheep (but they were well oxygenated).

In our study, rats without metabolic substrates and/or water supplementation were covered with aluminium foil during the period of anaesthesia to prevent decrease in body temperature. We did not observe indirect signs of haemoconcentration in parenchyma interstitium (urea concentrations were stable), but the concentrations of glucose, lactate and glycerol changed during anaesthesia. We supposed a periodical decrease of sodium pentobarbital concentration in INT rats with intact liver and following mild anaesthesia which leads to increased blood perfusion (urea, glucose and lactate concentration decrease especially intraperitoneally). The initial dose of sodium pentobarbital was sufficient for maintaining deep anaesthesia during 6 hours in rats with severe liver damage.

Metabolism in impaired liver

Liver cirrhosis (induced by tetrachlormethane administration) produces fibrotic tissue and new formation of regenerative nodi, whereas 14 days after BDL increased mixed inflammatory infiltration within portal tracts was found and mild incipient fibrosis only. We suppose that higher liver interstitial concentrations of urea and glucose in the 5th hour of microdialysis in INT reflects an increase of gluconeogenesis and indicates higher metabolic turnover of glucose. These described changes were not found in BDL and CIRH rats, probably due to inability of the liver to increase the gluconeogenesis. Higher urea concentrations in peritoneal cavity in CIRH group may give evidence about kidney damage by tetrachlormethane (16).

Glucose and lactate

Glucose, lactate and glycerol plasma concentrations are not significantly different in cirrhotic and healthy people (10) that is why microdialysis is the only one effective method for metabolic change monitoring in a particular organ. Microdialysis of the peritoneal cavity gives no real analyte concentrations (there is no absolute recovery of the microdialysis probe). Nevertheless with regard to the large area of the peritoneum and significant resorption capability, concentration changes of analytes in microdialysate from this site are very similar to plasmatic concentrations changes, these concentrations could be disturbed in groups with impaired liver functions. Glucose liver interstitial concentrations were higher in INT then in rats with liver damage. That is in accordance with the recent findings of Petersen et al. (18). He showed that the low hepatic glycogen content may be due to a net loss of functioning hepatocytes (there are replaced by fibrosis and immature hepatocytes are malfunctioned), and it may be due to porto-systemic shunting. Absorbed carbohydrates from the gut are disposed of peripherally. The highest individual concentrations of glucose were found in microdialysate from peritoneal cavity of CIRH. Probably due to high glucagon concentrations (18). Perdigoto et al. (17) showed that hepatic glycogen synthesis and hydrolysis are impaired. They stated that early stages of cirrhosis in humans where significant and substantial reductions in glycogenolytic flux (lower sensitivity to glucagon) are compensated for by increased rates of glu-

coneogenesis (by chronically elevated plasma concentrations of glucagon). The dominance of the gluconeogenesis in overnight-fasted cirrhotics is similar to healthy subjects fasted for an extended period (18).

Glycerol metabolism

Cirrhosis is in usually associated with a significant shift from carbohydrate to fat utilization (15), with elevated plasma concentrations of nonesterified fatty acids (4, 5), by increased lipolysis with releases more glycerol and free-fatty acids (18) or an impairment of free-fatty acids re-esterification into triglyceride within the adipocyte (22).

Johansson (7) demonstrated using of the microdialysis higher interstitial adipose tissue glycerol concentrations as well as higher arterial glycerol concentrations in cirrhotic patients than in the control subjects. The authors presume an increased rate of lipolysis (7). In our study we found an increase of glycerol concentration in the peritoneum and the thymus interstitium in CIRH rats. On the other hand, Shangraw et al. (22), Kaye et al. (8) and Nosadini et al. (14) assume that plasma free fatty acid and glycerol concentrations are elevated in patients with end-stage liver disease, because glycerol flux and hepatic clearance were lower than in control. Our results in accordance with recent literature showed that elevated interstitial concentration of glycerol in the peritoneum and thymus are seen entirely in rats with liver cirrhosis (end-stage liver disease). Both CIRH and BDL groups had lower liver interstitial concentrations of glycerol in comparison with INT. We suppose that CIRH rats had an increased rate of lipolysis as well as decrease of hepatic glycerol clearance in contradistinction to entirely lower hepatic glycerol clearance in BDL rats.

Metabolism in the thymus

We did not prove any fluctuation of urea thymic interstitial concentrations (status indicative for stable milieu /environment/ in thymus). The absence of a decrease in interstitial thymic glucose concentrations during entire microdialysis time in INT suggest that the glucose metabolism in the thymus is very stable, importantly for thymic metabolism (6). Thymic interstitial glucose concentrations were significantly lower in rats with liver damage compared with intact rats since the 3rd hour of microdialysis. Brand & Hermfisse (2) declared that glucose is essential for glycolytic enzyme induction and proliferation of mitogen-activated rat thymocyte. Resting thymocytes meet their ATP demand mainly by oxidative glucose breakdown, whereas proliferating thymocytes produce 86 % by glycolytic degradation of glucose to lactate and only 14 % by oxidation to CO_2 and water (2).

Thymic interstitial lactate concentrations in INT tend to increase since the 3rd hour of microdialysis (thymocytes possibly proliferate), on the other hand we can see lower availability of glucose (and subsequent lower lactate production) in thymus in BDL and especially in CIRH rats (thymocytes are in resting state - not able to proliferate). There is strong link between the thymus and the liver influencing T cell functions. The liver significantly enhanced extrathymic T cell pathway. Impaired hepatocytes (fibrotic or cirrhotic liver) are not able to ensure good metabolic conditions for thymocytes and *vice versa* thymocytes are the source of cytokines, growth factors and in addition nucleotides for hepatocytes so that their number in the thymus declines in the case of severe liver impairment (21).

There were higher interstitial thymic glycerol concentrations in rats with liver damage compared with INT (namely in CIRH vs. INT, $p < 0.02$). It could lead to lipoperoxidation increase (1). They stated that this could have a negative influence on thymic microenvironments where lipoperoxidation processes are minimalized. These changes influenced thymus weights, which were significantly lower in rats with liver damage.

Conclusion

Liver damage influenced interstitial metabolism of basal metabolites in distant organs. A balanced concentration of glucose, lactate and glycerol is essential for cell function and proliferation. Fluctuation of interstitial concentrations of these metabolites could be explanation of pathophysiological changes in distant organs. The impairment of the metabolism may be the cause of pathophysiological changes in the thymus.

Acknowledgements

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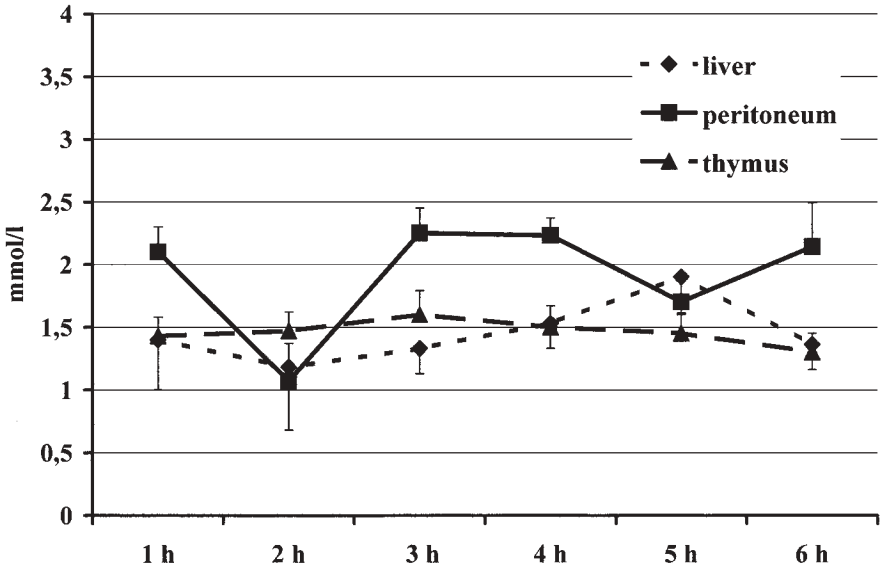
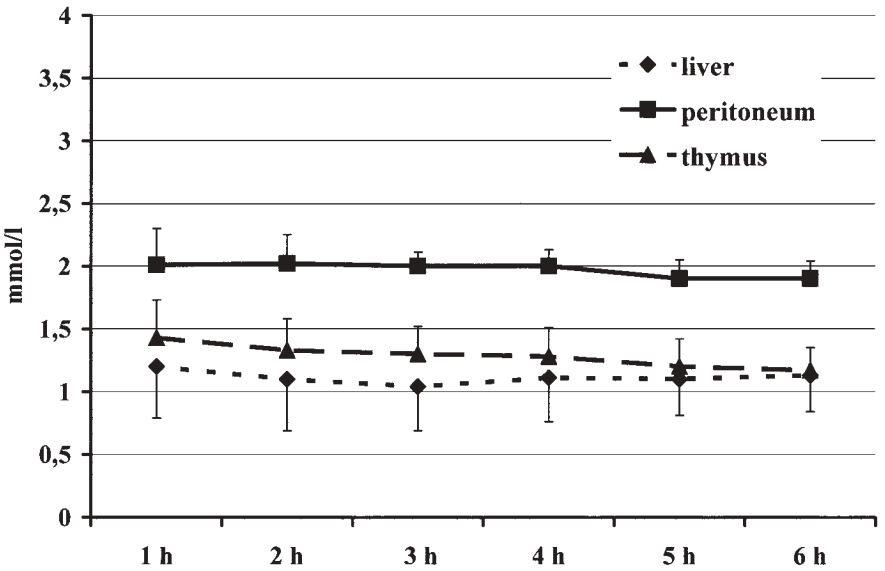
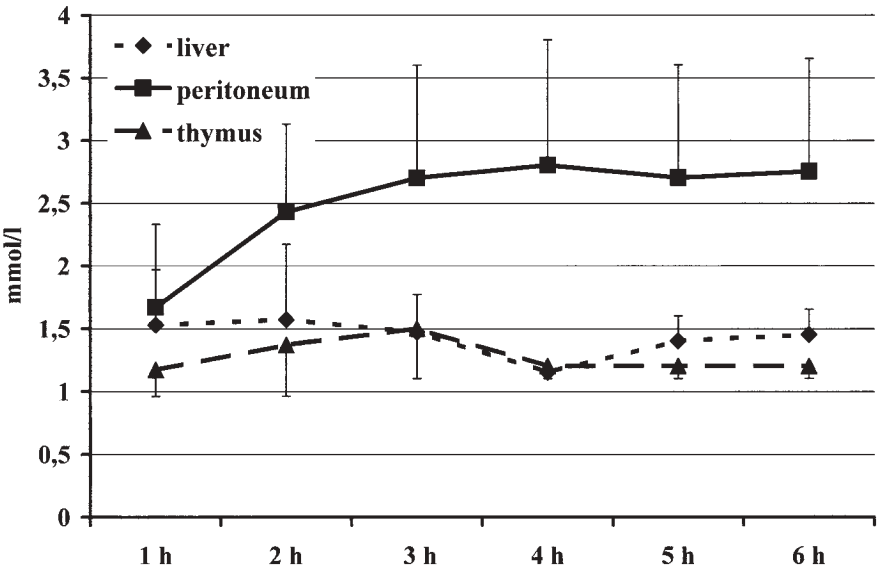
Urea concentration in dialysate in intact rats (mmol/l).



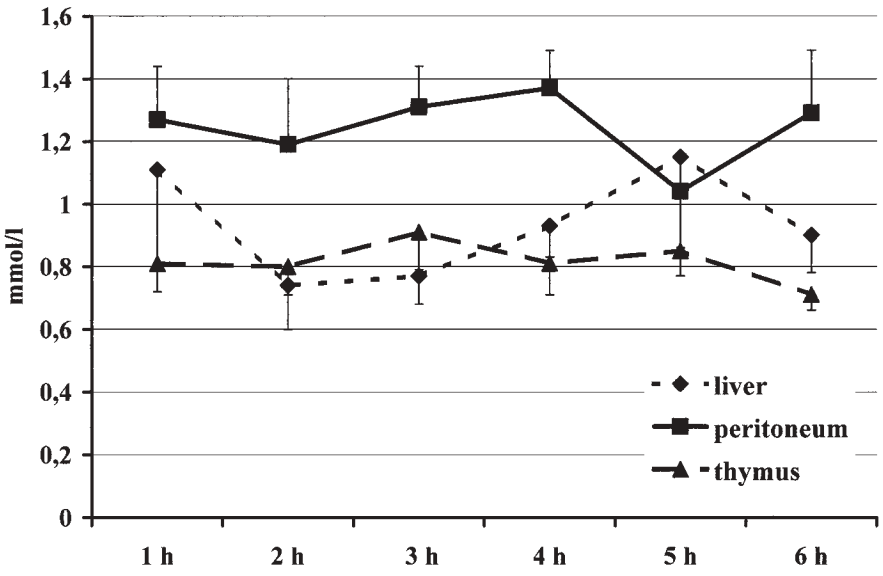
Urea concentration in dialysate in rats with BDL (mmol/l).



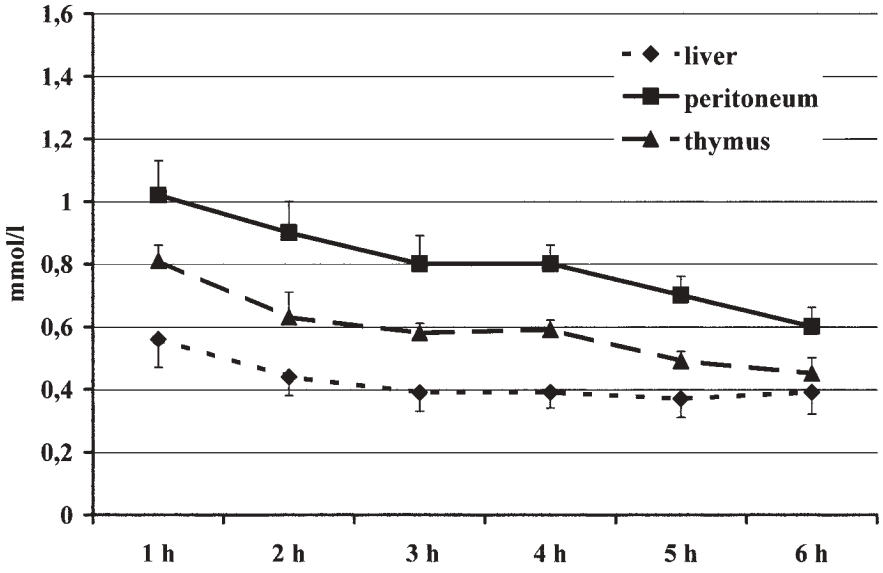
Urea concentration in dialysate in cirrhotic rats (mmol/l).



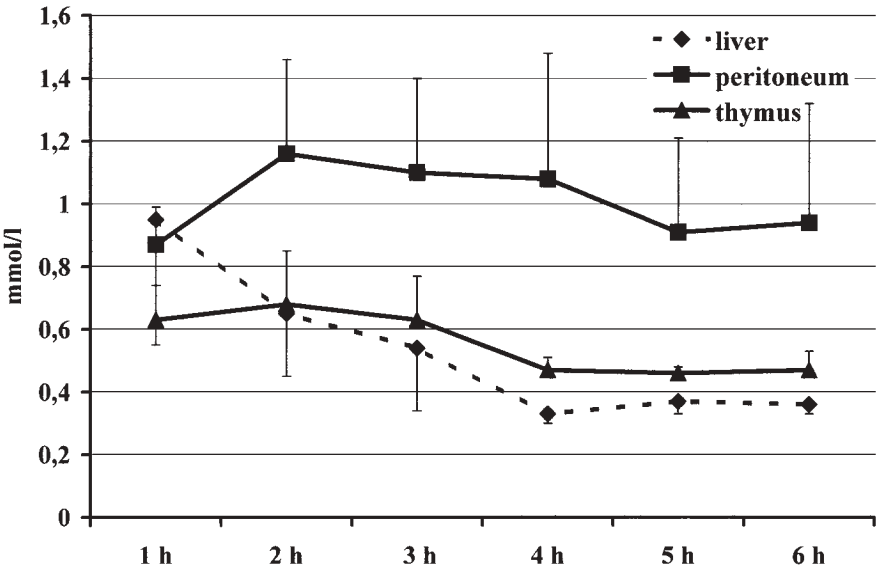
Glucose concentration in dialysate in intact rats (mmol/l).



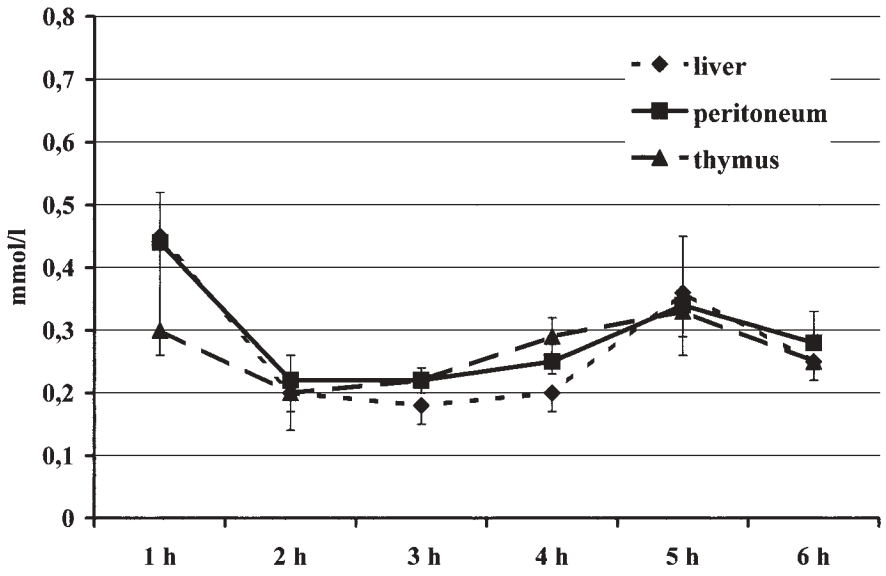
Glucose concentration in dialysate in rats with BDL (mmol/l).



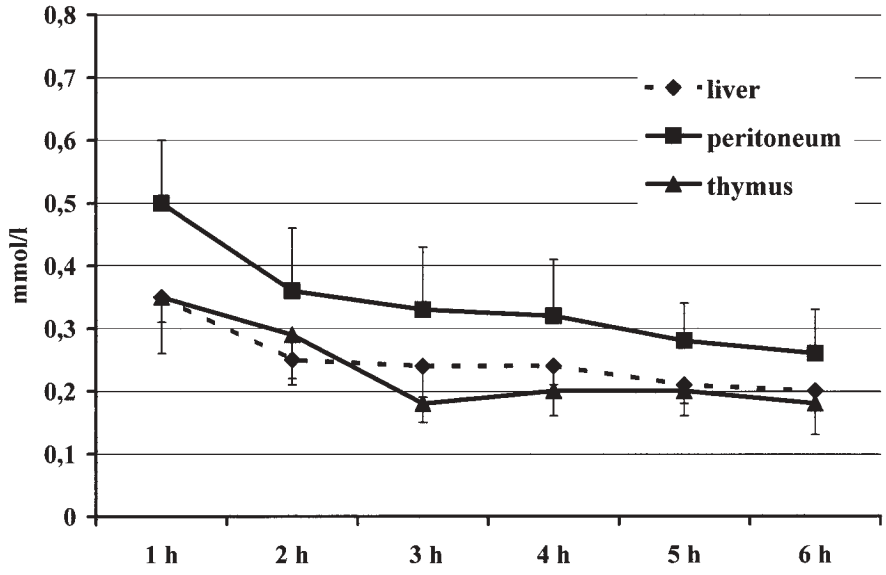
Glucose concentration in dialysate in cirrhotic rats (mmol/l).



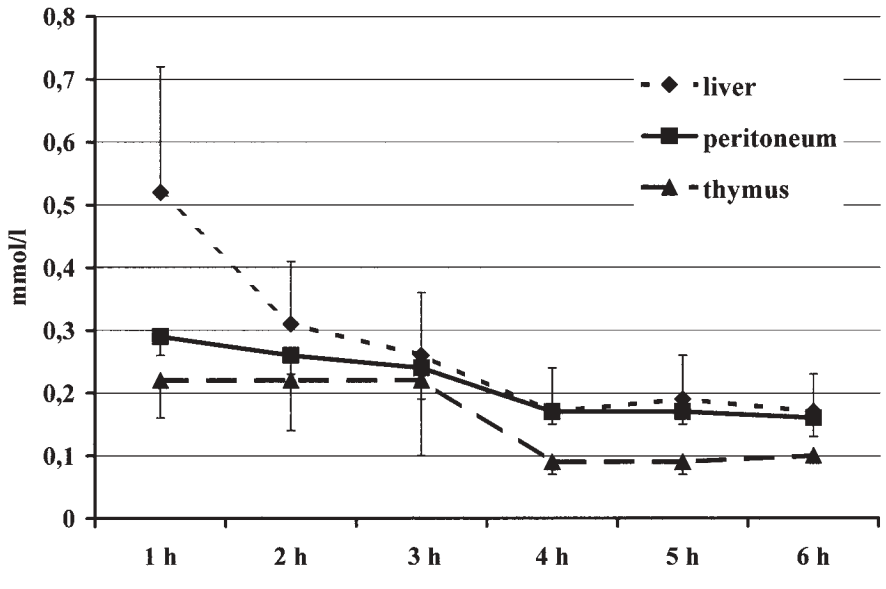
Lactate concentration in dialysate in intact rats (mmol/l).



Lactate concentration in dialysate in rats with BDL (mmol/l).



Lactate concentration in dialysate in cirrhotic rats (mmol/l).



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