31 Henze, M., Hoppe-Seyler's Z. physiol. Chem. *213* (1932) 125.
32 Fieser, L. F., J. Am. chem. Soc. *46* (1924) 2639.
33 Shriver, D. F., in: The Manipulation of Air-sensitive Compounds, p. 195. McGraw-Hill, New York 1969.
34 Rinehart, K. L., Kishore, V., Bible, K. C., Sakai, R., Sullins, D. W., and Li, K.-M., J. nat. Prod. *51* (1988) 1.
35 Ireland, C., and Scheuer, P. J., J. Am. chem. Soc. *102* (1980) 5691.
36 Ireland, C. M., Durso, A. R., Newman, R. A., and Hacker, M. P., J. org. Chem. *47* (1982) 1807.
37 Hamamoto, Y., Endo, M., Nakagawa, M., Nakanishi, T., and Mizukawa, K., J. chem. Soc., chem. Commun. (1983) 323.
38 Hochachka, P. W., and Somero, G. N., in: Biochemical Adaptation, pp. 24, 132, 145, 161. Princeton University Press, Princeton 1984.
39 Dingley, A. L., Kustin, K., Macara, I. G., and McLeod, G. C., Biochim. biophys. Acta *649* (1981) 493.
40 Cantley, L. C., Resh, M. D., and Guidotti, G., Nature *272* (1978) 552.
41 Mitchell, P., Nature *191* (1961) 144.
42 Mitchell, P., and Moyle, J., Eur. J. Biochem. 9, (1969) 149.
43 Tzagoloff, A., in: Mitochondria, p. 199. Plenum Press, New York 1982.
44 Federov, S. N., Chumak, A. D., Denisenko, V. A., Stonik, V. A., and Isakov, V. V., Chem. nat. Comp. *18* (1982) 634; translation of 1982 Khim. Prir. Soedin. 664.
45 Pollack, J. R., and Neilands, J. B., Biochem. biophys. Res. Commun. *38* (1976) 989.
46 Harris, W. R., Carrano, C. J., Cooper, S. R., Sofen, S. R., Avdeef, A. E., McArdle, J. V., and Raymond, K. N., J. Am. chem. Soc. *101* (1979) 6097.
47 Goodbody, I., Adv. mar. Biol. *12* (1974) 1.
48 Smith, M. J., Biol. Bull. *138* (1970) 354.
49 Robinson, W. E., Kustin, K., and Cloney, R. A., J. exp. Zool. *237* (1986) 63.
50 Kustin, K., Robinson, W. E., and Smith, M. J., Int. J. Invert. Reprod. Devl. (1989) in press.
51 Chaga, O. Y., Tsitologiya *22* (1980) 287, 619.
52 Stoeker, D., Ecology *6* (1980) 1327.
53 Scofield, V. L., and Nagashima, L. S., Biol. Bull. *165* (1983) 733.
54 Smith, M. J., and Neilands, J. B., in: Molecular Strategies for Crop Protection, p. 157. A. R. Liss, Inc. 1987.
55 Smith, M. J., Tetrahedron Lett. *30* (1989) 313.
56 Hochachka, P. W., and Guppy, M., in: Metabolic Arrest and the Control of Biological Time, p. 10. Harvard University Press, Cambridge 1987.
57 Hochachka, P. W., and Mommsen, T. P., Science *219* (1983) 1391.
58 Lee, S., Kustin, K., Robinson, W. E., Frankel, R. B., and Spartalian, K., J. inorg. Biochem. *33* (1988) 183.
59 Lee, S., Nakanishi, K., Chiang, M. Y., Frankel, R. B., and Spartalian, K., J. chem. Soc., chem. Commun. (1988) 785.
60 Deck, J. D., Hay, E. D., and Revel, J.-P., J. Morph. *120* (1966) 267.
61 Cloney, R. A., and Grimm, L., Z. Zellforsch. *107* (1979) 157.
62 Myers, C. R., and Nealson, K. H., Science *240* (1988) 1319.
63 Neilands, J. B., Microbiol. Sci. *1* (1984) 9.
64 Simoncini, L., Block, M. L., and Moody, W. J., Science *242* (1988) 1572.
65 Meedel, T. H., and Whittaker, J. R., Proc. natl Acad. Sci. *80* (1983) 4761.

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Research Articles

Subcutaneous transposition of the spleen enhances the survival rate following 90% hepatectomy in rats

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Summary. The effects of subcutaneous transposition of the spleen (STS) on the survival rate following 90% hepatectomy were investigated in rats. The survival rate was significantly higher in the STS group than in the non-STS group. Light microscopy enabled us to note that congestion in the terminal portal veins and sinusoids occurred either slightly earlier or to a higher degree in the non-STS group.
Key words. 90% hepatectomy; spleen transposition; portal congestion; portal-systemic shunt; hepatic failure.

Ninety percent hepatectomy in rats is fatal within 40 h without regeneration of the liver remnant[1]. When rats are given 20% glucose to prevent hypoglycemia[2], or given testosterone to enhance protein synthesis[3], the survival rate is over 80%.

Subcutaneous transposition of the spleen (STS) was attempted, to produce portal-systemic shunting for the decompression of the portal blood flow[4,5]. An overload of metabolites in the liver remnant has been considered to be one of the main factors causing the high mortality rate following 90% hepatectomy in rats[6]. The effect of STS in increasing the survival rate following 90% hepatectomy is reported.

Materials and methods. Male Wistar rats, weighing 250–300 g at the time of 90% hepatectomy, were used. They were fed a standard laboratory chow and water ad libitum. The animals were divided into 2 groups with or without the subcutaneous transposition of the spleen (STS).

STS was undertaken as follows: A left-sided longitudinal abdominal incision was made under light ether anesthesia. The fine peritoneal attachments between the stomach and the spleen were divided. Through a split in the abdominal muscle the spleen was pulled out and placed under the skin. The muscle was approximated carefully and the skin closed. The splenic artery and vein were not damaged[4,5].

Ninety percent hepatectomy was performed as follows: The rats of both groups were deprived of solid food for the 12 h prior to surgery and 5% glucose was given ad libitum. 90% hepatectomy consisted of Higgins-Anderson's partial hepatectomy[7] plus a resection of the lower

part of the right lateral lobe and finally the upper part of the right lateral lobe, leaving only the caudal (accessory) lobe[2]. In the STS group, hepatectomy was performed one week following STS. All operations were performed under light ether anesthesia between 09.00 h and 11.00 h. After surgery, the animals were provided with 5% glucose on the first postoperative day. From the second postoperative day, 5% glucose and a regular diet were given.

When the rats died, the abdominal cavity was opened and the abdominal viscera were carefully examined. The liver was removed, weighed and fixed in 10% formalin for the purpose of light microscopic examination. The liver tissues examined included two rats in each group with or without STS at the 12th hour, on the 1st and 2nd day, respectively. Sections of liver tissue, 5-µm-thick, were embedded in paraffin and stained with hematoxylin and eosin. The survival rates of both groups were analyzed using Kaplan-Meier's test and the generalized Wilcoxon test. P values of less than 0.05 were considered to be statistically significant.

Results. The weight of the resected liver was 7.9 ± 1.2 g (mean ± SD, N = 10), the remnant liver weight was 0.97 ± 0.26 g (mean ± SD, N = 10), thus the percentage of liver resected was 89.2 ± 1.6% (mean ± SD, N = 10) of the total liver weight. The survival rates of the groups with or without subcutaneous transposition of the spleen (STS) are shown in figure 1. The survival in both the STS and the non-STS groups dropped remarkably on the first day following 90% hepatectomy, and in the latter group it declined further on the second day. The survival in the STS group was significantly higher after the second day, compared with the non-STS group ($p < 0.01$). The former was significantly higher than the latter ($p < 0.05$) during the entire period following 90% hepatectomy, as judged by the generalized Wilcoxon test.

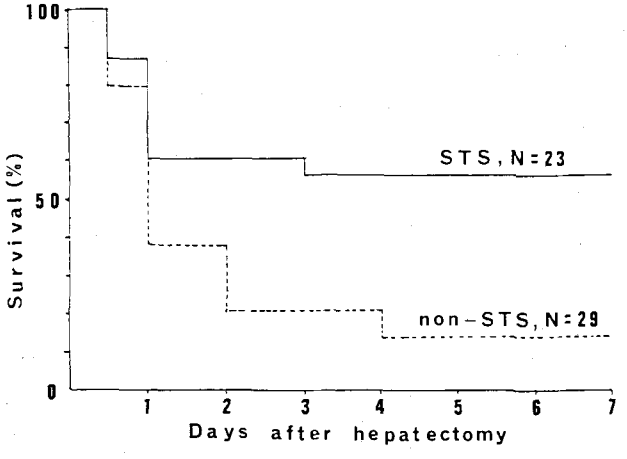

Figure 1. Kaplan-Meier survival curves. Solid and broken lines indicate the survival rates of the STS and the non-STS groups, respectively. The survival rate in the STS group is significantly higher between days 2 and 7, compared with the non-STS group ($p < 0.01$).

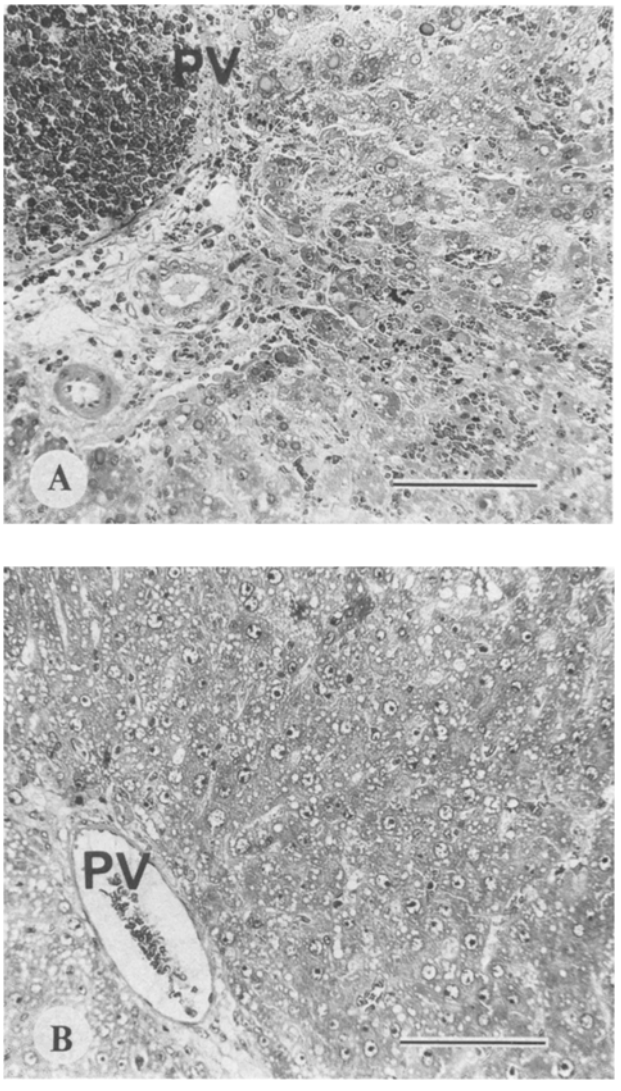

Figure 2. Light micrographs of the livers 12 h following 90% hepatectomy in the non-STS rats (*A*) and 1 day following 90% hepatectomy in the STS rats (*B*). Congestion in the portal veins and sinusoids is conspicuous in *A*. Though congestion in the portal vein and sinusoids is also present in *B*, it is less marked than in *A*. PV, portal vein. Scale bar: 100 µm.

The light microscopic findings for the livers in both groups were compared. Massive steatosis was found in both groups from the early period following 90% hepatectomy. Congestion in the terminal portal veins and sinusoids appeared either slightly earlier or deeper in the non-STS than in the STS group. Typical microscopic findings for the two groups are shown in figure 2A and B.

Discussion. The present study showed that the subcutaneous transposition of the spleen (STS) significantly improved the survival rate following 90% hepatectomy. Portography five days after STS shows a rich collateral circulation around the spleen[5]. Since 90% hepatectomy was performed seven days after STS in the present study, the rats in the STS group were considered to have a rich

collateral circulation around the spleen at the time of hepatectomy. The congestion which was found in the terminal portal veins and sinusoids of the non-STS group occurred either slightly earlier or to a higher degree than in the STS group by light microscopy. Though the abdominal viscera were carefully examined immediately after all rats died, neither gastrointestinal hemorrhage nor small bowel infarction was observed macroscopically. Therefore, it was tentatively speculated that the high portal blood flow into the liver remnant was one of the important factors causing such a high mortality rate following 90% hepatectomy.

Massive steatosis was also found in both groups from the early period soon after the 90% hepatectomy. In our previous study, where the fine structure of hepatocytes in the early period after 90% hepatectomy was investigated, lipid accumulation was first observed soon after surgery and the increase after 12 h was progressive[6]. When the rats were given testosterone to enhance protein synthesis, the survival rate and liver remnant weight following 90% hepatectomy were significantly improved[3]. Therefore, hepatic steatosis did not appear to be a primary factor for survival. It was tentatively concluded that the improvement of the survival rate following 90% hepatectomy in the STS group was likely to be due to the decompression of the portal blood flow. The precise mechanism, however, still awaits further elucidation.

1 Tuczek, H. V., and Rabes, H., Experientia *27* (1971) 526.
2 Gaub, J., and Iversen, J., Hepatology *4* (1984) 902.
3 Vic, P., Saint-Anbert, B., Astre, C., Bories, P., Bonardet, A., Descomps, B., Humeau, C., and Joyeux, H., Hepatology *2* (1982) 247.
4 Bengmark, S., Borjesson, B., Olin, T., Sakuma, S., and Vosmic, J., Scand. J. Gastroent. (Suppl. 7) *12* (1970) 175.
5 Bengmark, S., Borjesson, B., and Olin, T., Am. J. Surg. *125* (1973) 757.
6 Koga, A., Fukuyama, T., and Momii, S., J. clin. Electron Microscopy *21* (1988) 365.
7 Higgins, G. M., and Anderson, R. M., Archs Path. *12* (1931) 186.
8 Kaplan, E. L., and Meier, P., J. Am. Stat. Ass. *53* (1958) 457.

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Spontaneous rhythmic contractions of human saphenous veins isolated from old subjects are sensitive to cyclooxygenase inhibitors

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Summary. Spontaneous rhythmic contractions were observed in some preparations of human isolated saphenous veins from old (> 60 years) subjects. These contractions were insensitive to adrenergic and histaminergic blockers, but were abolished by the cyclooxygenase inhibitors, aspirin and indomethacin, indicating the participation of endogenous eicosanoids.
Key words. Human saphenous vein; spontaneous rhythmic contractions; cyclooxygenase inhibitors.

Rhythmic contractile activity has been shown to occur spontaneously in various vessels isolated from humans[2-8] and animals[9-13]. In some instances, this activity has been associated with pathological states[11-13] and/or aging[6-8].

Here we report on spontaneous contractions of human isolated saphenous veins. This phenomenon could only be observed in veins from old subjects and disappeared in the presence of cyclooxygenase inhibitors.

Materials and methods. Fragments of human saphenous veins, obtained from patients undergoing aortocoronary bypass operations, were immediately transferred to Krebs' physiological solution (composition in mM: NaCl 112, KCl 5, $NaHCO_3$ 25, $MgSO_4$ 1.2, KH_2PO_4 1, $CaCl_2$ 1.25 and glucose 11.5) at 4 °C. Tissues were kept at this temperature for maximally 24 h before being used. Rings, 2–3 mm in length (internal diameter 2–3 mm) were prepared. In some of them, the intimal surface was deliberately rubbed with the ends of small forceps in order to remove the endothelial lining. Rings were then mounted between two L-shaped holders in 50-ml organ-chambers containing Krebs' solution bubbled with a mixture of 95% O_2–5% CO_2, pH 7.4 at 37 °C. Isometric changes in tension were recorded. Tissues were suspended under a tension of 2 g and allowed to relax. 15 min later the tension was readjusted to 2 g. During the following equilibration period, the baseline tension stabilized at about 1.5 g. Because the donor patients were generally being treated for coronary artery disease by various drugs, tissues were extensively washed for 4 h, and also stimulated by histamine (0.2 mM) or by noradrenaline (1 μM). Those of the preparations which did not contract in response to these stimuli were discarded.

Preparations in which spontaneous rhythmic activity developed after this equilibration period were used for testing a series of drugs. Drugs used were (-)-noradrenaline (Fluka), histamine dihydrochloride (Merck), prazosin