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.

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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

hydrochloride (Pfizer), phentolamine mesylate (Ciba-Geigy), mepyramine hydrochloride (Specia), aspirin (Bayer), indomethacin (Sigma) and nifedipine (Bayer). Noradrenaline was prepared as a stock solution (10 mM) in 7.9 mM Na_2SO_3 supplemented with 34 mM HCl and kept at 4 °C. Prazosin was dissolved in absolute ethanol to provide a stock solution of 1 mM. Stock solutions (10 mM) of nifedipine and indomethacin were prepared in absolute ethanol and 50 mM Na_2SO_3, respectively. Other drugs were prepared daily in distilled water.

Results. Fragments of human saphenous veins from 42 patients (34 males, 8 females, mean age ± SEM: 61 ± 1 years) were responsive to noradrenaline or histamine. Among them, most of the fragments originating from 6 of the patients (4 males, 2 females) showed clearcut signs of spontaneous contractile activity. The table gives the age distribution of these patients and that of the total patients. The incidence of the activity was zero in fragments from patients less than 60 years old (table). The venous fragments prepared from the older (> 60-year-old) patients were all 'spontaneously active', except for one case (female, 64-year-old) in which only 1 among 4 preparations was active. Figure 1 illustrates various patterns of activity. Spontaneously rhythmic activity occurred regardless of the presence or absence of the endothelium in the preparation. The mean (± SEM) amplitude and frequency of the oscillations were 1.20 ± 0.20 g and 15 ± 3/h, respectively, in 17 venous rings. The amplitude of the spontaneous contractions amounted to about 75% of that of contractions induced by noradrenaline 1 μM, and 33% of that of those induced by histamine 0.2 mM. The rhythmic activity was insensitive to phentolamine 10 μM (n = 3), prazosin 10 nM (n = 2) or mepyramine (n = 2), but was nearly abolished in the presence of the cyclooxygenase inhibitors, aspirin 0.1 mM (n = 4) or indomethacin 5 μM (n = 4). The effect of indomethacin was concentration-dependent, as cumulative doses of the cyclooxygenase inhibitor given at 30-min intervals produced increasing inhibition of the activity (fig. 1c). The IC_{50} value of indomethacin was close to 1 μM (fig. 2). Indomethacin did not significantly alter the frequency of oscillations. After

Age distribution of the total number of patients whose human saphenous veins were studied and of those whose veins exhibited spontaneous rhythmic contractile activity

Age (years)	Number of patients Total	With activity
41–45	2	0
46–50	1	0
51–55	7	0
56–60	11	0
61–65	8	3
66–70	6	1
71–75	6	1
76–80	1	1
	42	6

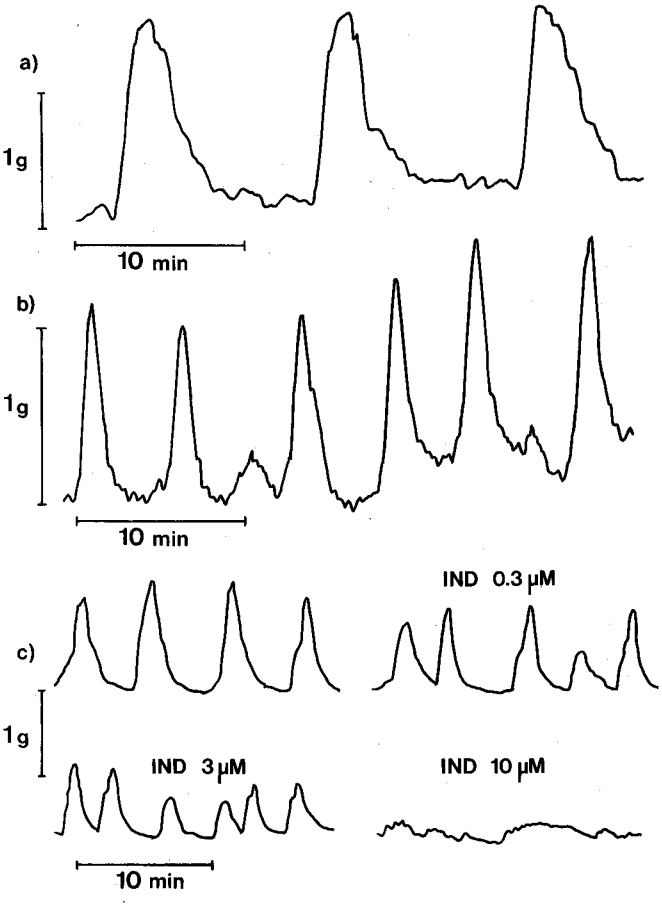

Figure 1. Various patterns of spontaneous rhythmic contractions of human isolated saphenous veins. *a*, *b* and *c* show recordings from three different vascular preparations; *c* also illustrates the effect of cumulative addition of indomethacin (IND).

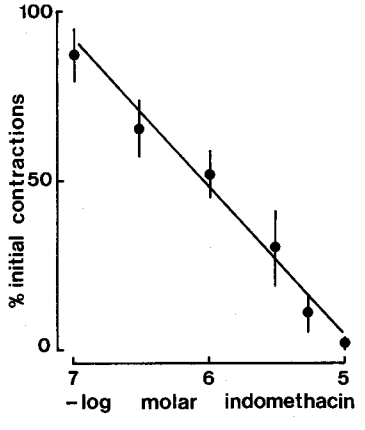

Figure 2. Indomethacin-induced decrease in the amplitude of spontaneous contractions of human saphenous veins. Data are the means ± SEM (represented by vertical bars) of 3 observations, expressed as percent ages of the amplitude of the initial spontaneous contractions (in the absence of indomethacin).

periodical washing during several hours, spontaneous activity was totally restored. Finally, nifedipine (3 μM) suppressed the activity.

Discussion. Spontaneous rhythmic activity has been reported in some preparations of human isolated saphenous vein[4], as well as in those of other human and animal vessels[2,3,5,9,10]. The appearance of such activity may be related to pathophysiological factors. Evidence has been presented that mechanical activity tends to develop in isolated vessels from hypertensive rats[11,12] or after experimental coronary occlusion[13]. On the other hand, the spontaneous rhythmic activity described in human isolated coronary arteries seems to be age-related, since it did not occur in preparations from young subjects[6-8]. Similarly, the study of a large number of saphenous veins enabled us to show that this phenomenon preferentially developed in vessels from old patients. As is the case in other isolated vessels[9,14], spontaneous activity of human saphenous vein was insensitive to adrenergic and histaminergic blockers, ruling out the involvement of catecholamines or histamine. By contrast, the inhibitory effect of aspirin and indomethacin strongly supports the idea that some cyclooxygenase products may be involved in the rhythmic contractions of human saphenous veins. It is known that various prostaglandins can induce rhythmic activity in some isolated vessels[14,15]. Human saphenous veins spontaneously release prostacyclin and thromboxane A_2[16]. Thromboxane A_2 is a potent vasoconstrictor and prostacyclin, in spite of its vasorelaxant effect on most vessels, appears to induce contraction of the human saphenous vein[17]. Lastly, the rhythmic contractile activity of human saphenous vein could be abolished by nifedipine; this observation is in line with the findings that spontaneous activity of other isolated vessels was inhibited by calcium entry blockers[5,8,13,14,18-20] or in Ca-free medium[5,11,12]. As a whole, our results suggest that, in preparations of human saphenous veins isolated from old subjects, some endogenous eicosanoid makes extracellular Ca^{++} available for spontaneous rhythmic contractions.

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VLDL substrate properties and efficiency of their metabolic transformation by LPL

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Summary. A study was made of the regulation of the triglyceride hydrolysis catalysed by LPL from bovine milk, by the apoproteins from human plasma VLDL. Both isolated apolipoproteins, and those found on the surface of plasma VLDL particles, were investigated. A concentration-dependent activating action of apo C-II on the hydrolysis of emulsified triolein, and uncompetitive inhibition of VLDL triglyceride hydrolysis by apo C-III were found. It is suggested that VLDL lipolysis might be controlled in vivo trough the variation of the relative surface content of these enzymatic activity modulators.
Key words. Human plasma very low density lipoproteins; apolipoproteins C-II and C-III; lipoprotein lipase.

The involvement of lipoprotein lipase (LPL) in a directional transport of triglycerides (TG) from endogenous very low density lipoprotein (VLDL) and chylomicrons, as a part of a general energy storage pathway, suggests that regulation and control of such an ordered system must occur at the sites of hydrolysis of TG[1]. There is