The rise of the α_2-macroglobulin level is also difficult to explain. This protein seems not to belong to the acute phase reactants[16,17] and the possibility of its extrahepatic synthesis has been suggested[18,19]. It is generally assumed that it has more than one biological function, but whether it participates in some manner to the recovery processes after exercise or not, remains unclear.

The possibility was previously discussed that the increase of serum transferrin after exercise and training, with the concomittant rise of plasma iron, is connected with the increased iron requirement for the biosynthesis of Fe-containing proteins in the exercised muscle[5]. OSAKI et al.[20], showed that ceruloplasmin, which has a ferroxidase activity, strongly enhances the incorporation of Fe^{II} into apotransferrin[21]. Animal experiments also showed that an elevation of only 10% of the initial ceruloplasmin level in the blood stream markedly increased the plasma iron values[22]. It can therefore be concluded that the higher level of both ceruloplasmin and transferrin in athletes serum is related to the increased turnover of iron after exercise. In this respect one could think of an increased loss of iron from the fatigued muscle, as well as of an enhanced iron uptake for the biosynthesis of iron-containing compounds. Data obtained in animals by YOSHIMURA et al.[23] seem to favour the latter possibility.

The present results particularly point to 2 facts: repeated, heavy physical exercise has a definite effect – maybe of a cumulative nature – on the level of several serum glycoproteins, very probably connected with the recovery processes after the exercise stress; in studies concerning the normal values of these glycoproteins in man, care should be taken as to the physical activity of the subjects on the days before examination.

Résumé. Les sportifs examinés au repos, après plusieurs jours consécutifs d'entraînement ou de compétitions ont un niveau nettement plus élevé que le groupe de contrôle pour l'α_1-antitrypsine, l'α_2-HS-glycoprotéine, l'α_2-macroglobuline, la transferrine, la céruloplasmine et le cuivre sériques. La signification biologique possible de ces faits est discutée.

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Catecholamine Biosynthesis in Vascular Tissue

Rates of noradrenaline (NA) biosynthesis in heart, spleen, vas deferens and brain are generally reported to lie within the range, 0.1–0.3 $\mu g/g/h$[1–3]. However, with the exception of a recent study[4] from this laboratory, in which pulmonary artery was used, there are no reports of NA biosynthesis in vascular tissue. Yet it is vascular NA biosynthesis that is presumably the target of tyrosine hydroxylase inhibitors now receiving increasing attention as potentially useful drugs in the treatment of human hypertension[5]. Lack of knowledge concerning vascular synthesis of NA and its regulation may underlie the unexpected ineffectiveness of one such inhibitor, α-methyl tyrosine, in essential hypertension[5]. As a preliminary to detailed study of the relationship of sympathetic transmission and NA biosynthesis in vascular tissue, we examined the conversion of the amino-acid precursor, tyrosine, to catecholamine in a variety of blood vessels of the rabbit. It was our goal to identify a vascular bed with a catecholamine biosynthesis rate sufficiently high to permit its use as a model in our future work.

Rabbits (1.5–2.5 kg) were killed by cervical fracture. Descending thoracic aorta, right femoral artery, main pulmonary artery, superior mesenteric artery and portal vein were rapidly removed, cleared of adherent non-vascular tissue as far as possible and incubated for 15, 30 or 60 min in a total of 2.5 ml of oxygenated Krebs medium (37 °C) containing $4 \times 10^{-5} M$ uniformly labelled tyrosine C^{14} (New England Nuclear Corporation; Final specific activity = 50 mc/mmole). After incubation, vascular segments were removed, blotted dry and immediately frozen on dry ice. They were then weighed and homogenized in 10% trichloro-acetic acid. After centrifugation of homogenates in the cold (4 °C) at 15,000 $\times$ *g* for 10 min, supernatant portions were decanted and either analyzed immediately or frozen for subsequent analysis of catecholamine-C^{14} and endogenous NA by methods described earlier[4]. In previous experiments[4] it was found that over 80% of the radioactive catecholamine was in fact NA. Initial experiments in the present study showed that the rate of tyrosine to NA conversion was not consistently linear if incubation was prolonged beyond 15 min. Accordingly all subsequent experiments involved only 15 min incubation periods. The Table documents the calculated catecholamine-C^{14} synthesis rate and endogenous NA content of the blood vessels used. It can be seen that the superior mesenteric artery had a surprisingly high synthesis rate which was more than 3 times that reported[1,3] in heart or brain, while rates in pulmonary artery and portal vein fell within limits previously reported. The rapid NA biosynthesis

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rate of mesenteric artery was paralleled by its high endogenous amine content (Table).

These data focus attention on the unexpectedly high catecholamine biosynthetic capacity of the superior mesenteric artery. In addition, our results point to the potential value of this blood vessel for further study of adrenergic transmitter biosynthesis in vascular tissue[6].

Catecholamine-C^{14} biosynthesis and noradrenaline content of vascular tissue

Tissue	Catecholamine-C^{14} synthesis[a] (ng/g per h ± S.E.M.)		Endogenous noradrenaline (µg/g ± S.E.M.)	
Aorta	67.5 ± 7.3	(10)[b]	0.51 ± 0.12	(4)[b]
Femoral artery	106.1 ± 26.2	(6)	0.64 ± 0.14	(3)
Pulmonary artery	208.5 ± 14.7	(6)	0.52 ± 0.10	(4)
Mesenteric artery	629.8 ± 55.3	(7)	2.02 ± 0.24	(3)
Portal vein	261.9 ± 39.6	(7)	0.72 ± 0.16	(4)

[a] Values extrapolated from synthesis rates determined during 15 min incubation periods. [b] Number of samples.

Zusammenfassung. Die Umwandlung von Tyrosin in Katecholamin wurde in verschiedenen Blutgefässen untersucht. Die Katecholamin-Biosynthese erfolgte am schnellsten in der Arteria mesenterica sup. (0,6 µg/g/h), was zehnmal höher liegt als diejenige in der Aorta oder in der Arteria pulmonalis.

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The Effect of Theophylline on the Actions of Pancreozymin and Secretin

In recent years, cyclic AMP has been implicated as an intracellular mediator of hormonal action[1]. Administration of theophylline, a methyl xanthine which inhibits the breakdown of cyclic AMP[2], has been shown to augment or mimic the action of several hormones[3–5]. The possibility that the hormones of the G.I. tract exert their actions by means of this cyclic AMP mechanism has received scant attention. It was reported in 1968[6] that theophylline enhanced the action of histolog on gastric secretion in man, but the mechanism involved was not explored. Case et al.[7] in 1969, using an isolated perfused cat pancreas, demonstrated that a flow of pancreatic juice which contained enzymes, could be stimulated by the introduction of N6-2′-*O*-dibutyryl-adenosine 3′ 5′-monophosphate (dibutyryl cyclic AMP) and theophylline into their perfusate. This group states that although dibutyryl cyclic AMP and theophylline can mimic the action of secretin on the flow rate of pancreatic juice, these agents do not mimic the effects of pancreozymin. They attributed the apparent stimulation of pancreatic enzymes to a washout phenomenon secondary to the increased flow of juice.

The purpose of the present study was to determine whether the administration of theophylline could augment the flow rate, and enzyme output of pancreatic juice secreted in response to exogenous secretin and pancreozymin. Because of the known pepsin stimulatory action of secretin[8], this parameter was also monitored.

Materials and methods. Experiments were performed on unfed cats, anaesthetized with chloralose (80 mg/kg, i.v.). Splanchnic nerves were cut extraperitoneally, and the vagus nerves sectioned in the neck. The pancreatic duct was cannulated as it passed through the duodenal wall, and the pylorus was ligated. Gastric secretions were collected by means of a rubber tube inserted through an oesophageal incision in the neck.

Isosmolar glycine (pH 6.4) was used as a gastric washout fluid and the pepsin content of the washout was determined by the method of Anson[9], the output of pepsin being expressed as mg of tyrosine/15 min. The volume and protein output of pancreatic juice were measured in 15 min periods, protein output being determined spectrophotometrically assuming a standard of O.D. 1.8 = 10 mg free protein/ml of pancreatic juice.

Secretin (SN) and Pancreozymin (PZ) were obtained from GIH Laboratory Sweden (Secretin batch No. 16931; Pancreozymin batch No. 26841). These hormones were administered as constant i.v. infusions in doses of: PZ: 24 Crick Harper Raper U/kg/h; SN: 11.6 clinical U/h, irrespective of body weight. Infusion of both hormones continued for the duration of the experiment. When the flow rate and protein output of pancreatic juice had reached relatively constant levels (2–2.5 ml/15 min, 1.0 – 1.5 mg protein/15 min), theophylline (Schwarz Bioresearch Inc.) was administered as a constant i.v. infusion (6 mg/kg over 20 min).

Results and discussion. Infusion of theophylline resulted in a significant increase in pancreatic protein output ($p < 0.001$), which was not accompanied by a significant augmentation of flow rate ($p > 0.05$) (Figure 1). The latter result appears to disagree with the observations of Case et al.[7] who reported that their isolated pancreas preparation which produced no basal secretion, could be stimulated to secrete by administration of dibutyryl cyclic AMP and theophylline. A possible explanation for our

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