Results and discussion. The identification of PGs in blood has been limited by the lack of sensitivity in available chemical methods. The blood-bathed organ technique which was used to detect Prostaglandin-like substances (PLS) in these experiments possesses the required sensivity for detection of nanogram quantities of PGs. GADDUM[4] considered the evidence provided by parallel pharmacological assay to be more important in the identification of a substance than that provided by same biochemical procedures.

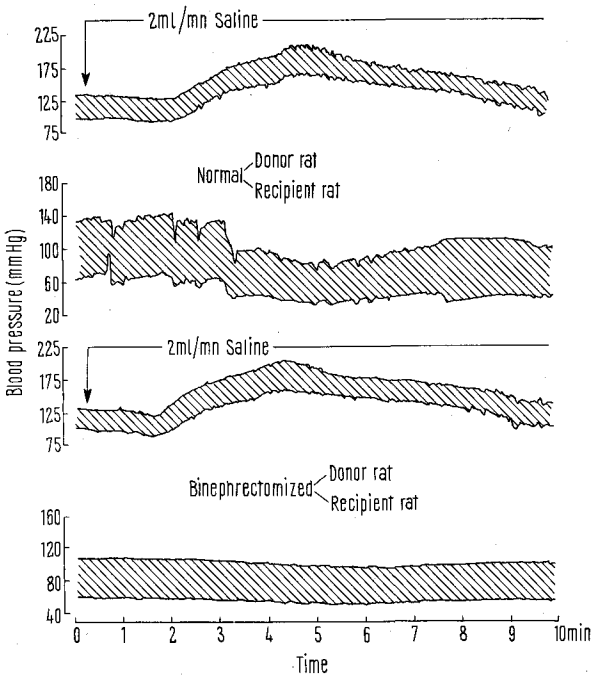

Fig. 2. Cross-circulation experiments. The changes of blood pressure (BP) of normal and binephrectomized rats. Diminution of the BP of the normal recipient rat, while the BP of the donor increased following expansion of the extracellular space. This phenomenon was almost imperceptible on binephrectomized rats.

In all the experiments, expansion of the extracellular and/or of the intravascular space produced the release of PLS which contracted the assay organs (Figure 1). No other known circulating hormones in physiological concentration will produce the same pattern of response as PGs in the 3 specially chosen assay organs[2,3]. The results of changes observed in the animals in cross-circulation show (Figure 2) that the arterial pressure (AP) of the donor was increased during the expansion, while the AP of the recipient diminished. The phenomenon could be repeated during all the experiments.

It is clear that a very active vasodepressor substance was released into the circulation of the donor during the expansion which was capable of diminishing the AP of the recipient. This phenomenon was almost imperceptible when the rats were binephrectomized. This observation suggests a close relationship between the vasodepressor factor and the kidney. Perhaps the kidney is the main organ which produces this vasodepressor factor.

Further investigation by chromatographic methods must take place for identification and separation of PGs which are released through this particular mechanism.

Résumé. Des substances qui semblent être des prostaglandines, détectées par des méthodes de bioassay, se libèrent dans la circulation des rats anesthesiés lors de l'expansion soit de l'espace extracellulaire, soit du volume intravasaculaire. Lors de l'expansion du donneur, en circulation-croisée, il se libère une substance capable de produire une baisse de la tension artérielle du receveur.

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Resistance to Flow Through the Pancreatic Duct by the Isolated Cat Sphincter of Oddi

In cat the principal pancreatic duct and the common bile duct share a common entrance into the duodenum (reviewed by HALLENBECK[1]). BOYDEN[2], in his study on muscle arrangement in the cat choledochoduodenal junction, reported that in the proximal part of the intramural sphincter of Oddi the pancreatic and the bile ducts are separated by a muscle septum, which according to him might selectively influence the bile duct. The ducts are then jointed unto the papillary orifice.

It was thought of interest to investigate the effect of various agents known to affect the sphincter on the resistance to flow through the isolated cat sphincter measured both as perfusion pressure through the common bile duct and as perfusion pressure through the pancreatic duct.

Method. 15 adult cats of both sexes fasted 24 h were used. They were anaesthetized with pentobarbitone sodium (Abbot) and bled. The detailed description of cat sphincter of Oddi by BOYDEN[2] was used as dissection guide. The distal pancreatic duct was dissected free from tissue and cannulated with polyethylene catheter (Clay-Adams PE 10). The catheter was gently moved through the sphincter of Oddi into duodenum. Similarly the distal common bile ducts was cannulated (Clay-Adams PE 50). Then the sphincter of Oddi was dissected free from duodenal tissue. The catheters were withdrawn and the perfusion catheters (PE 90) were ligated just before the entrance of the ducts into the sphincter. The preparation was mounted in an isolated organ bath as shown in Figure 1. Both ducts were perfused with Krebs solution at a constant rate, common bile duct 3 ml/h and pancreatic duct 1–3 ml/h (Perfusor B. Braun Melsungen 71100). Longitudinal isometric tension changes in the sphincter (Grass force displacement transducer FT 03 B) and the perfusion pressures (Statham pressure transducers P 23 AC) were recorded on a Grass Polygraph (7 Pl). The tension was initially adjusted to (0.1–0.4 g). The bath (100 ml) contained Krebs solution gassed with carbogen and maintained at 38°C. A small part of the perfusion catheters just distal to the perfusion pump was replaced by a rubber tubing so that drugs could be given in the perfusion fluid as well as in the solution bathing the sphincter preparation.

[1] G. A. HALLENBECK, in *Handbook of Physiology. Alimentary Canal* (Ed. W. HEIDEL; Williams and Wilkins Co., Baltimore 1967), vol. 2, p. 1007.

[2] E. A. BOYDEN, Surgery *41*, 773 (1957).

The following drugs were used: (±) isoprenaline hydrochloride (Sigma Chemical Company, USA), (−) noradrenaline bitartrate (Sigma Chemical Company, USA), Cholecystokinin (Prof. J. E. Jorpes G.I.H. Laboratories, Karolinska institutet, Stockholm), acetylcholine chloride (Calbiochem, USA).

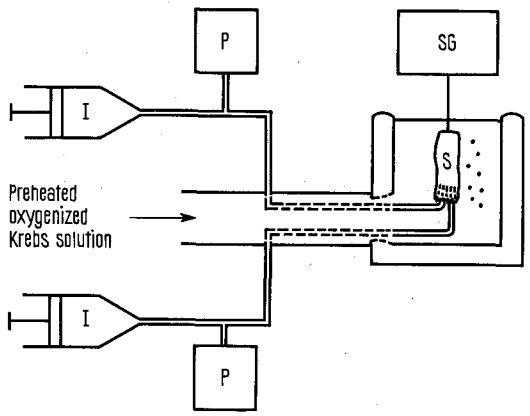

Fig. 1. Experimental set-up for in vitro perfusion of sphicter of Oddi through pancreatic and bile ducts. I, perfusion pump; P, pressure transducer; SG, strain-gauge transducer; S, sphincter.

Results. This isolated sphincter preparation behaved similarly to the preparation where the perfusion took place only through the common bile duct (Persson[3]). The perfusion rates yielded pressures in the bile duct of (8–20) cm H_2O and the pancreatic duct (6–18) cm H_2O. The sphincter exhibited spontaneous activity recorded as longitudinal tension changes and simultaneous pressure changes in the perfused ducts. The spontaneous activity of the sphincter affected the 2 routes of perfusion in the same way Figures 2 and 3. Noradrenaline (0.16 µg/ml) as well as acetylcholine (0.16 µg/ml) given to the bathing solution contracted the sphincter and caused simultaneous increases in resistance to flow through both pancreatic and bile ducts. The contracting effects were recorded as increased amplitude and frequency of the spontaneous activity (Figures 2 and 3). When the agents were given to preparations where the spontaneous activity had ceased, they induced it again. In all cases the contracting agents affected all the recorded parameters in a uniform way. Isoprenaline (0.04 µg/ml) as well as colecystokinin (0.15 iu/ml) in the bathing solution relaxed the sphincter and simultaneously the resistance to flow through both ducts

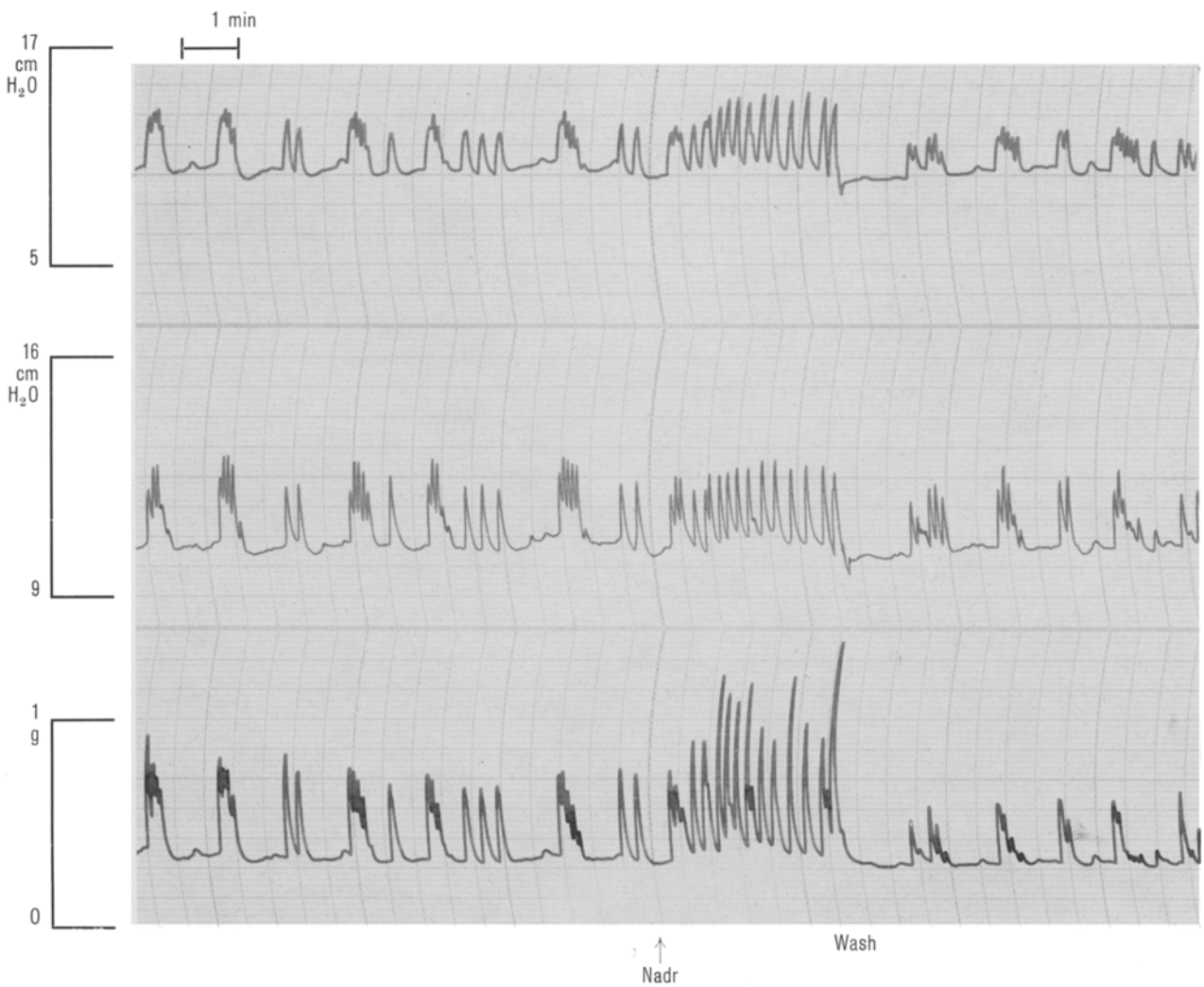

Fig. 2. Effect on the spontaneously active sphincter by noradrenaline 0.16 µg/ml in the bathing solution. Upper curve: Perfusion pressure through the pancreatic duct. Middle curve: Perfusion pressure through the bile duct. Lower curve: Longitudinal tension changes in the sphincter.

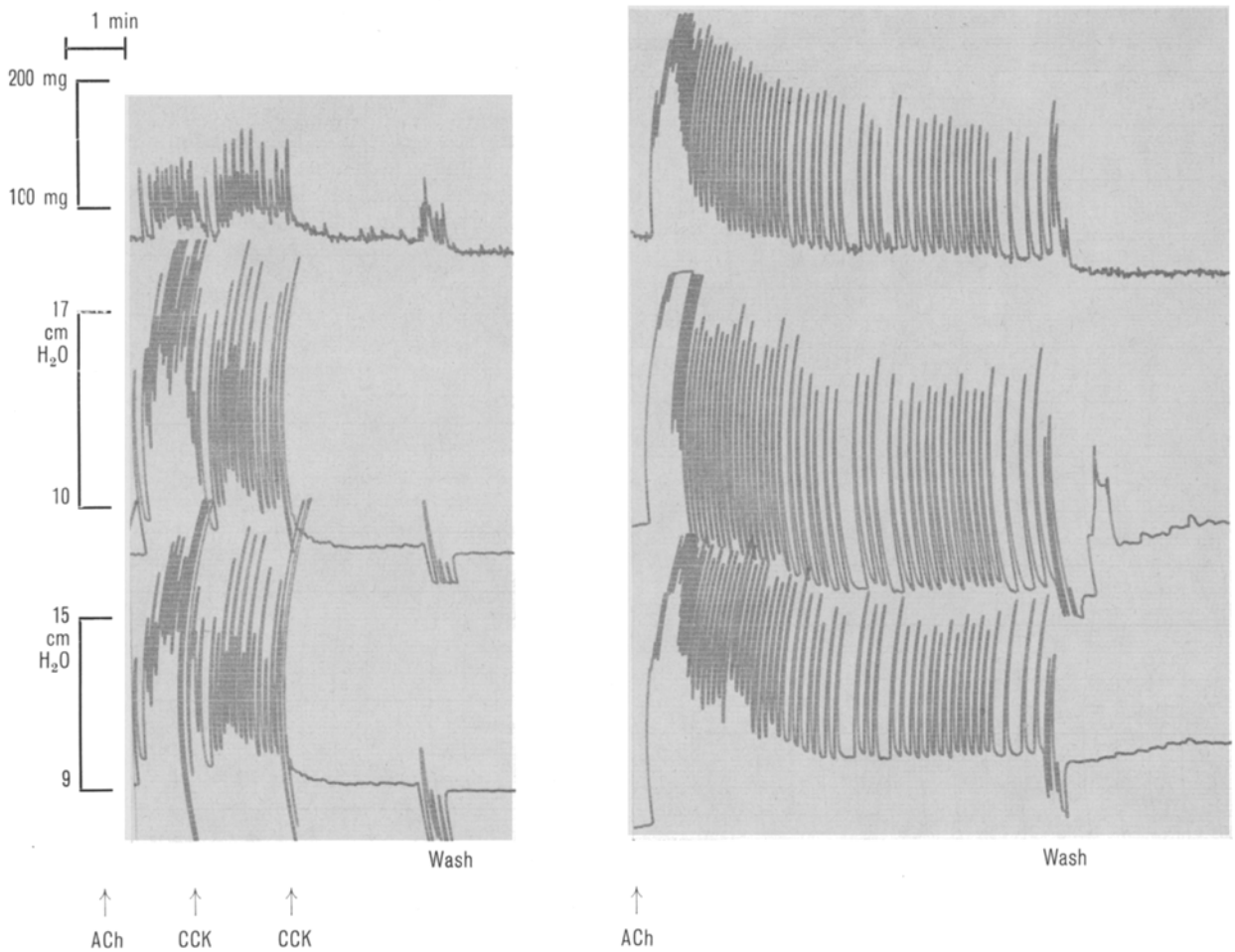

Fig. 3. Effect on a sphincter preparation by acetylcholine (Ach) and cholecystokinin (CCK). Upper curves: Longitudinal tension changes in the sphincter. Middle curves: Perfusion pressure through the pancreatic duct. Lower curves: Perfusion pressure through the bile duct. Left: Effect of 10 μg Ach followed by two 2 IU doses of CCK. The agents are administered in the perfusion fluid to the bile duct. Right: Effect of 0.1 μg/ml Ach given in the bathing solution to the same preparation.

was decreased. Relaxation was shown as inhibition of spontaneous or acetylcholine-induced sphincter activity (cf. Figure 3). In all cases where the sphincter was relaxed, the action on both perfusion pressures closely paralleled the tension changes.

Also when the agents were given in the perfusion fluids the longitudinal tension changes parallelled effects on perfusion pressure through the bile and pancreatic duct (Figure 3). In most cases the manipulation during injection initially disturbed the recording of the pressure changes in the duct injected. After this artefact, both ducts together with longitudinal tension yielded conclusive traces (Figure 3). Saline injection of the same volume as drug solutions (0.05–0.2 ml) into the perfusion fluid only gave initial artefact responses.

Discussion. The investigation has shown that in the isolated cat sphincter of Oddi the spontaneous sphincter activity of myogenic origin (PERSSON[3]) affects the resistance to flow through the pancreatic duct and the bile duct in the same way.

Earlier it was shown that noradrenaline contracted the sphincter due to α-adrenoceptor activation and isoprenaline relaxed due to β-adrenoceptor activation (PERSSON[3]). The effect of α- and β-adrenoceptor stimulation and cholinoceptor stimulation, as well as the effect of cholecystokinin, does not support a functional significance of the possibility pointed out by BOYDEN[2] that pancreatic and bile flow may be selectively affected by the sphincter.

The finding that changes in pressures and tension induced by spontaneous myogenic activity or by the sphincter-active agents occur simultaneously is in concord with the view that the cat sphincter of Oddi is a functional syncytium as discussed by DEWEY and BARR[4] for smooth muscle organs.

Zusammenfassung. Die spontane Aktivität des Sphinkters und die Wirkung von sphinkteraktiven Stoffen zeigen, dass der isolierte Sphinkter Oddi auf dieselbe Weise den Perfusionsdruck durch den Duktus choledochus und durch den Ductus pancreaticus beeinflusst.

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[3] C. G. A. PERSSON, Br. J. Pharmac. *42*, 447 (1971).

[4] M. M. DEWEY and L. BARR, in *Handbook of Physiology. Alimentary Canal* (Ed. W. HEIDEL; Williams and Wilkins Co., Baltimore 1968), vol. 4, p. 1629.

[5] Acknowledgment. The excellent technical assistance of Mrs. M. EKMAN is gratefully acknowledged.