assay with an N-terminal-directed antiserum K4023 (Heding et al., 1976), and increased at least 5-fold after instillation of nutrients. The corresponding plasma concentrations measured with a C-terminally-directed antiserum 30K (Harris et al., 1979) increased only slightly. Consistent with this previous report of Valverde et al. (1970), the glucagon-like polypeptides from both tissues and plasma were separated by gel filtration into poorly resolved peaks in the 800–12000 (peak I) and 3000–5000 (peak II) molecular-weight zones. A peak of immunoreactivity of molecular weight smaller than glucagon was also observed in the chromatograms of plasma and may represent proteolytic-degradation products. As shown in Fig. 1(c), the glucagon-like polypeptides in gut extracts were isoelectrically focussed into components with approximate pl values of 4.7, 5.1, 6.1 and 6.9 (peak I) and 8.7 and 9.6 (peak II), and, as shown in Figure 1(b), the immunoreactive polypeptides isolated from plasma were resolved into major components with pl values of 6.9, 7.8 and 9.4, together with minor components with pl values of 4.8, 5.3 and 5.9. Thus, the molecular heterogeneity of the glucagon-like material in gut extracts is also found in plasma.

Previous studies have demonstrated that larger-molecular-weight glucagon-like polypeptides with pl values in the range 4–8, isolated from gut extracts, are devoid of glucagon-like biological effects on hepatic metabolism (Murphy et al., 1973; Holst, 1977; Conlon et al., 1979), but that the smaller basic (pl > 9) components bind to receptor sites specific for glucagon in hepatic plasma membranes, activate adenylate cyclase and stimulate glycogenolysis with approximately one-tenth of the potency of glucagon (Bataille et al., 1974; Sasaki et al., 1975; Holst, 1977). The present study has shown that small basic components of glucagon-like immunoreactive material are released into the circulation in response to nutrients and may thus be of importance in the regulation of carbohydrate metabolism. These components may play a role, together with pancreatic glucagon, in moderating the insulin-induced hypo-glycaemic response to ingested nutrients and may be of particular importance in pancreatectomized man. The physiological role of the larger more acidic immunoreactive polypeptides, which represent the predominant forms released into the circulation, is unknown, but speculation has arisen that they may exercise an inhibitory effect on gut motility and a trophic effect on gastrointestinal mucosa (Bloom, 1972).

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Mucus in the gastric juice of cats during pentagastrin and secretin infusions: The viscosity in relation to glycoprotein structure and concentration

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Gastric mucus is secreted as a protective gelatinous layer that adheres to the mucosal surface. Changes that occur in luminal mucus with different stimuli should be related to this surface gel. Pig and human gastric-mucus gel is composed of a polymeric glycoprotein (Allen et al., 1972) that can be hydrolysed by pepsin to produce degraded subunits showing greatly decreased viscosity and gel-forming properties. An increase in the glycoprotein output in gastric juice has been reported with various stimuli, including gastrin and secretin (Vagne & Perret, 1976). However, this may not reflect a genuine stimulation of mucus secretion, but an increase in degraded glycoprotein subunit in the gastric juice as a result of peptic erosion of the mucus gel. In the present study we compared changes in the glycoprotein concentration in gastric juice with the specific viscosity of the juice, and relate these to changes in the relative amounts of glycoprotein polymer (characteristic of the gel) and degraded subunit formed by pepsin (Fig. 1).

Experiments were carried out in six conscious cats prepared with gastric fistulae (Hirst et al., 1979). Pentagastrin and secretin were infused intravenously. Gastric secretion was collected continuously by gravity drainage and divided into pooled 15 min samples from all cats.

Pentagastrin infused alone produced pooled gastric-juice volumes of 48, 62, 60, 48, 47, 49 and 40 ml/15 min per six cats. The specific viscosities were below 0.06 for all samples. Addition of secretin to the pentagastrin infusion resulted in a 10-fold rise in specific viscosity (Fig. 1). Secretin did not influence the volume of secretion. The secretion-induced rise in specific viscosity could have resulted from either an increase in glycoprotein concentration and/or an increase in the relative amount of polymeric high-viscosity glycoprotein compared with the pepsin-degraded low-viscosity subunit. Glycoprotein concentrations were similar during infusion of pentagastrin alone, and infusion with pentagastrin plus secretin. However, the specific viscosity was only high when secretin was present (Fig. 1). This signifies that there must be a change in the structure of the glycoprotein, and this is exemplified by the large difference in the reduced specific viscosities (specific viscosity/glycoprotein concentration) for essentially the same glycoprotein concentrations (cf. Fig. 1, 30 and 90 min values).

Gel filtration of gastric-juice samples on Sepharose 2B (Mantle & Allen, 1978) showed all samples to contain high-molecular-weight mucus glycoprotein polymer and lower-molecular-weight pepsin-degraded subunit. However, in samples of high viscosity, i.e., during secretin infusion, the ratio of glyco-
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Several gastrointestinal hormones act on the liver, and in particular on bile flow (Forker, 1977). Somatostatin decreases bile flow and bile acid excretion in the dog (Lin et al., 1977; Holm et al., 1978). The response is rapid and already significant at a dosage of 0.3 μg/kg body wt. per h. As somatostatin inhibits gastrin-induced gastric secretion and secretin-induced pancreatic juice, Holm et al. (1978) have speculated that it might inhibit gut hormone-induced bile secretion, but the mechanism has not been elucidated. In anaesthetized rats somatostatin had no effect on bile flow, yet the effect was observed in the early phase and the increased viscosity due to peptic action. Specific (πsp, □) and reduced specific viscosities (πred, △) are illustrated. Each point is an observation on a pooled sample from six cats.

Quantitative aspects of the effect of somatostatin on bile flow in the rat

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Collection of control bile started 90 min after. Group C (n = 6), receiving only saline, was tested 8 h after the preparation of the biliary drainage, to produce a marked decrease of bile flow and bile acid-secretion rate. In all experiments bile was collected in tared tubes over 10 min periods. The timing of the experiment comprised a 30 min control period, a 60 min somatostatin (Ayerst Laboratories: 20 μg/kg body wt. per h; no priming dose) infusion and a 60 min recovery stage. In the second condition only animals stimulated with a continuous infusion of sodium taurocholate, as in group A, were used. 14C-Erythritol (The Radiochemical Centre, Amersham, Bucks., U.K.) was injected (3 μCi) as priming dose. Followed by an infusion of 0.006 μCi/kg body wt. per min until the end of the experiment. Erythritol was allowed to equilibrate for 90 min before sampling of bile. Experimental animals (n = 7) received somatostatin for 60 min as described above. Blood (300 μl) was obtained through the carotid artery prepared surgically and kept open by a continuous injection of heparin (15 units/kg body wt. per h) in normal saline. It was taken at 15 and 5 min before and at 35, 45 and 55 min after the onset of somatostatin infusion; samples at 65 and 75 min after discontinuation of the infusion (recovery phase) were also obtained. Animals infused only with saline (n = 5) were used as controls (sham infusion).

The overall effect of somatostatin can be divided into two parts: an early phase, already significant at the end of the first 10 min, where the bile flow and bile acid output decreased progressively, and a steady state, from 30 min to the end of the infusion. In the early phase the ratio of bile acid concentration/bile flow remained unchanged. Further data refer only to the steady state, where the maximal display of the cholestatic protein polymer to degraded subunit was much greater than in low-viscosity samples during infusion of pentagastrin alone. Over a period of time, endogenous pepsin split the glycoprotein polymer into subunits, and this was accompanied by a decrease in the viscosity of the juice. The increased viscosity with secretin infusion cannot be explained by a decrease in peptic activity, since this doubled during the secretin infusion; also, the viscosity contribution from the pepsin was negligible.

In conclusion, the mucus glycoprotein seen on infusion with pentagastrin alone is associated with predominately degraded glycoprotein subunits, and a low viscosity. This probably reflects the extra volume of gastric juice washing out previously degraded mucus from the stomach. With secretin, however, there is a large rise in the reduced and specific viscosity, and in the undegraded polymeric glycoprotein characteristic of the gel. This rise in undegraded glycoprotein in the juice, assuming no increase in mechanical erosion, is compatible with a genuine increase in mucus-gel secretion stimulated by secretin. The results also emphasize that measurements of the glycoprotein concentration or output in gastric juice alone cannot be directly equated with changes in the amount of the surface mucus gel.