## The Role of the Autonomic Nervous System in the Control of Glucagon Release During Insulin Hypoglycaemia in the Calf

Results of much recent work indicate that the autonomic nervous system is implicated in the release of glucagon from the pancreas. Histological studies have shown that autononomic nerve terminals may be found in close proximity to α-cells in pancreatic islets[1–3] and that morphological changes occur in these cells in response to nerve stimulation[2,3]. Stimulation of the ventromedial hypothalamus causes a rapid rise in plasma glucagon concentration in adrenalectomized rats[4] and elevated plasma glucagon values have also been observed in monkeys during stress[5]. The experiments described here were devised to determine whether or not the autonomic system is implicated in the release of glucagon which occurs in response to moderate insulin hypoglycaemia in the conscious calf, since stimulation of either the peripheral ends of the vagi, or of both splanchnic nerves, produces a rapid rise in plasma glucagon concentration in this species (S. R. Bloom, A. V. Edwards and N. J. A. Vaughan, unpublished observations).

Pedigree Jersey calves (25–35 kg body weight) were tested with insulin (0.1 units/kg) 20–40 days after birth. Samples of jugular blood were collected at intervals for glucose and glucagon estimations before and after i.v. injection of insulin. Results have been expressed as the change from the values at time = 0 to provide direct comparison between groups. Plasma glucagon was measured by radioimmunoassay according to the principles of Albano, Ekins, Maritz and Turner[6] and glucose with glucose oxidase.

Neither the fall in plasma glucose concentration nor the rise in plasma glucagon, which occurred in response to this small dose of insulin, was significantly different from normal in calves in which both splanchnic nerves had been cut under sterile conditions 3 days previously (Figure 1). In contrast, pretreatment with atropine (0.2 mg/kg body weight) enhanced the hypoglycaemic response to insulin in calves with cut splanchnic nerves. Furthermore, the rise in mean plasma glucagon concentration was significantly delayed in these animals and that which occurred eventually was substantially less than in the control group even though hypoglycaemia was significantly more severe. Thus, 60 min after administration of insulin, mean plasma glucose concentration had fallen by 83.5 ± 5.5 mg/100 ml and plasma glucagon concentration had risen by 97 ± 19 pg/ml in atropine-treated calves with cut splanchnic nerves, whereas the control values were 53 ± 2.5 mg glucose/100 ml and 216 ± 61 pg glucagon/ml respectively (Figure 2).

The finding that the tolerance to insulin was not affected by section of the splanchnic nerves was unexpected in view of the known sensitivity of the hepatic glycogenolytic mechanism to stimulation via the sympathetic innervation[7,8]. Presumably the sympathetic system is


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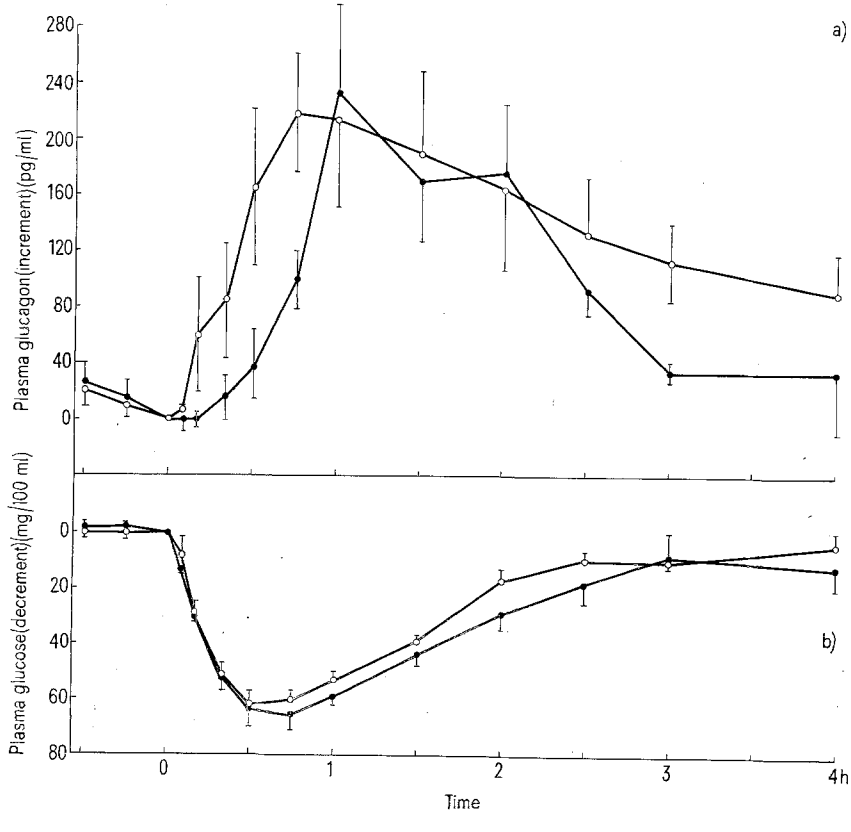


Fig. 1. Comparison of the changes in mean plasma glucagon (a) and glucose concentrations (b) in response to intravenous insulin (0.1 units/kg) at time = 0, in normal calves (○, $n = 4$) and calves with cut splanchnic nerves (●, $n = 4$). Vertical bars: S.E. of each mean value.

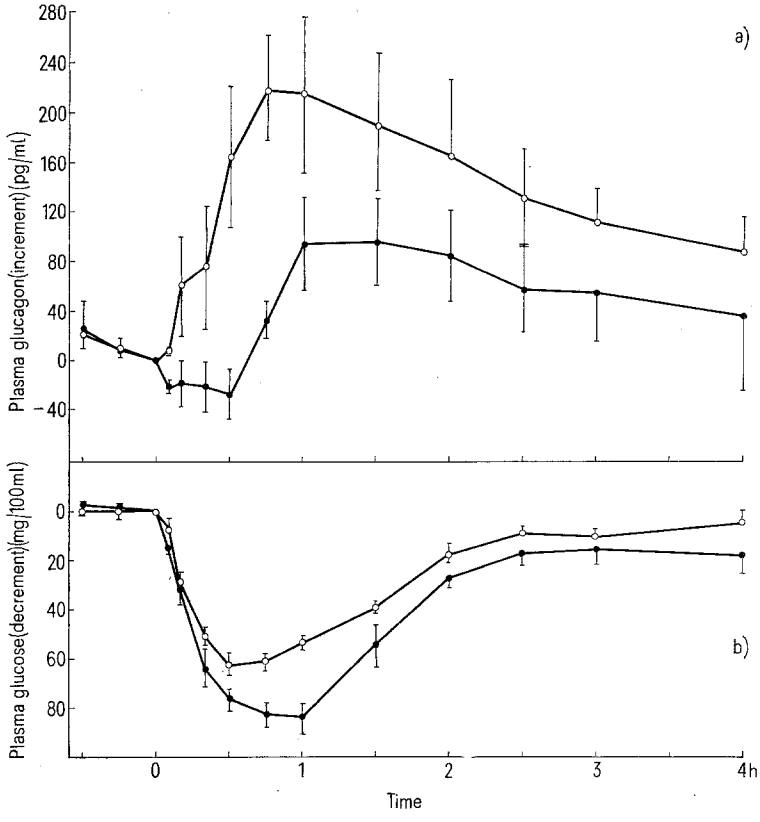


Fig. 2. Comparison of the changes in mean plasma glucagon (a) and glucose concentrations (b) in response to i.v. insulin (0.1 units/kg) at time = 0, in normal calves (○, $n = 4$) and calves with cut splanchnic nerves which were pretreated with atropine (0.2 mg/kg) (●, $n = 4$). Vertical bars: S.E. of each mean value.

relatively insensitive to changes in plasma glucose concentration. These results do, however, support the contention that a cholinergic mechanism is implicated in the release of glucagon which normally occurs in response to hypoglycaemia.

*Zusammenfassung.* Der durch Insulin herbeigeführte hypoglykämische Effekt wurde in Kälbern mit durchtrenntem Nervous splanchnicus durch Atropin verstärkt, wobei sich der Anstieg des Plasma-Glukagonwertes verzögerte und reduzierte. Es wird ein cholinergischer Mechanismus der Glukagonsekretion während der Hypoglykämie vermutet.

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## Changes in Body Temperature Produced by Injecting Prostaglandin $E_1$, EGTA and Bacterial Endotoxins into the PO/AH Region and the Medulla Oblongata of the Rat[1]

Heating and cooling of the medulla oblongata produces changes in body temperature[2,3] and behavior[3] similar to those produced by altering the temperature of the preoptic/anterior hypothalamic (PO/AH) temperature control region. These parallel effects of thermal stimulation of the 2 regions and the finding that the influence of medullary thermoresponsiveness does not depend upon mediation by the PO/AH region[3] suggest that the medulla contains a separate secondary thermosensitive mechanism for body temperature control. It is of interest to know if the 2 brain regions also respond in parallel fashion to certain chemical substances known to influence thermoregulation. Therefore, we compared changes in rectal temperature ($T_r$) produced by injecting prostaglandin $E_1$ ($PGE_1$), which is presumed to act as a mediator in thermoregulation[4,5], into the PO/AH region and medulla. EGTA and bacterial endotoxins, compounds which have been shown to cause hyperthermia after central or peripheral administration, were also injected.

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