

Neonatal secretion of secretin

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Rogers, I. M., Davidson, D. C., Lawrence, J., and Buchanan, K. D. (1975). *Archives of Disease in Childhood*, 50, 120. **Neonatal secretion of secretin.** The plasma levels of secretin have been measured in mothers after labour, and in their babies at birth and on day 4 of life. The mean cord venous level was higher than the maternal level, and there was a significant correlation between the individual maternal and cord values. The level had again increased by day 4, and at this time the secretin level was inversely proportional to the blood glucose level.

It has already been shown that gastric acidity in neonates is lower on day 4 of life than at birth (Miller, 1941). Recent studies, however, have revealed that the fourth day plasma gastrin level is higher than at birth (Rogers *et al.*, 1974). A similar rise in glucagon plasma levels has occurred by day 4 and may act to inhibit the gastric secretory effect of the raised gastrin levels at that time (Rogers *et al.*, 1974).

Secretin also reduces acid response to gastrin (Johnson and Grossman, 1968), and in this study we set out to see if a rise in plasma secretin levels on day 4 might also act to further inhibit the gastrin-induced gastric acid secretion. There have been no previous recordings of secretin levels in the neonate.

Methods and materials

Maternal and cord venous samples were taken at birth from 22 mothers and babies (the same subjects which were studied in an earlier investigation: Rogers *et al.*, 1974). A further 3 ml venous sample was taken from 19 of these babies on day 4 after a 4-hour fast. 2 of the original babies were excluded because regular sedation with phenobarbitone had been required and one was excluded because of early discharge from hospital. The blood glucose was also measured in the cord and day 4 samples and informed consent was obtained from all the mothers studied.

Labour was spontaneous in 11 mothers and was induced by rupture of the membranes and intravenous infusion of oxytocin in 9 mothers. The remaining 2 mothers had an oxytocin infusion during the course of an otherwise spontaneous labour and were included in

the oxytocin group. Pethidine was routinely administered for labour pains.

Radioimmunoassay technique. The blood was removed into a heparinized tube and separated as soon as possible. The plasma was stored frozen at -20°C and transported frozen to Belfast. Plasma for secretin assay was then extracted with ethanol (Heding, 1971).

Pork synthetic secretin (SG 18773, Batch ES XXI-14A, donated by Dr. Michael Donetti, Squibb) was used for standards and labelling. Secretin was labelled with ^{125}I (Radiochemical Centre, Amersham) by the method of Holohan *et al.* (1973) and antibodies were raised to pork natural secretin (Buchanan, Teale, and Harper, 1972) (donated by Dr. V. Mutt). The antibody BB101 was used at a final titre of 1:36 000. The antibody appeared specific for secretin in that no cross-reaction was noted with pancreatic glucagon, large gut glucagon-like immunoreactivity (GLI), human insulin (MRC), gastric inhibitory polypeptide and motilin (both donated by Dr. J. C. Brown), 99% pure cholecystokinin-pancreozymin and vasoactive intestinal polypeptide (both donated by Dr. V. Mutt), and human synthetic gastrin (ICI). Extracts of human jejunum and the neonatal plasma samples cross-reacted in the assay in an identical manner to the standards. Using a highly purified ^{125}I secretin (R. W. J. Flanagan, unpublished observations), a sensitivity of 6 pg/ml, was achieved.

Results

The cord level was higher than the maternal level ($P < 0.001$, no. = 22) (Fig. 1), and there was a correlation between individual maternal and cord values ($P < 0.005$). An increase in the mean plasma secretin level had occurred by day 4 of life ($P < 0.005$, no. = 19) (Fig. 2) but there was no

Received 20 June 1974.

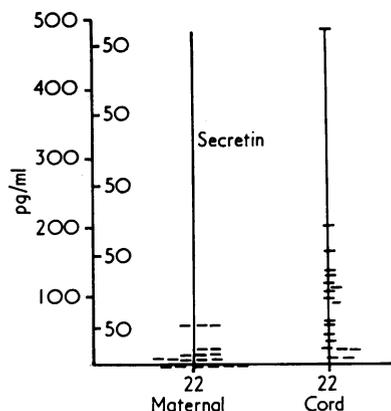


FIG. 1.—Plasma secretin levels in maternal and cord blood. The cord level, mean $91 \text{ pg/ml} \pm 3.6 \text{ SEM}$, was higher than the maternal level, mean $12.5 \pm 3.6 \text{ pg/ml}$, and the individual values were significantly correlated.

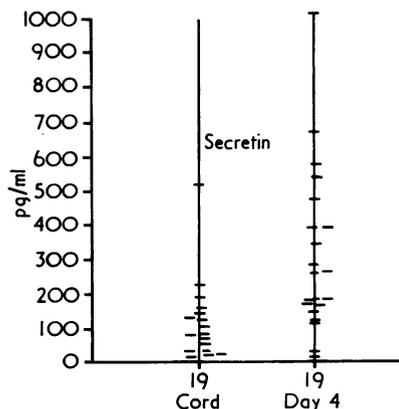


FIG. 2.—Plasma secretin levels in the cord vein as compared with the levels in a peripheral vein on day 4 of life. The day 4 level, mean $299 \text{ pg/ml} \pm 58 \text{ SEM}$, was higher than the cord level of $92.8 \pm 23.9 \text{ pg/ml}$.

individual correlation with the cord level. There was no apparent relation between the blood glucose and plasma secretin level in the cord blood but an inverse correlation had developed by day 4 of life ($P < 0.001$) (Fig. 3).

No relation was apparent between the secretin level either at birth or on day 4 and duration of labour, Apgar score, sex of the baby, birthweight, or type of labour, i.e. spontaneous or induced.

Discussion

It has been shown by several authors that secretin inhibits the gastric acid secretion induced

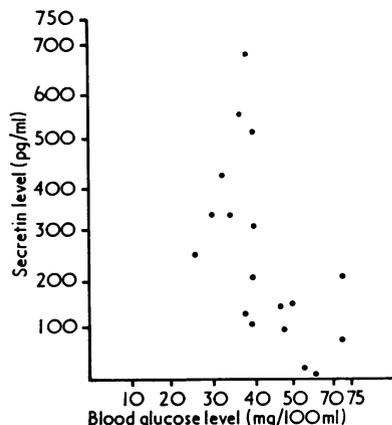


FIG. 3.—Relation between the plasma secretin level and blood glucose on day 4 of life. Blood glucose was measured in $\text{mg}/100 \text{ ml}$.

by gastrin (Nakajima, Nakamura, and Magee, 1969; Johnson and Grossman, 1968). Hence, the higher secretin levels on day 4 may act to inhibit the acid secretory effect of gastrin on day 4. A similar conclusion has been reached with respect to glucagon (Rogers *et al.*, 1974).

The correlation between the maternal and cord levels suggests that secretin may be transferred across the placenta from mother to baby. Further studies are intended to clarify this point.

The inverse correlation between blood sugar concentration and plasma secretin levels on day 4 remains to be explained. There is abundant evidence that secretin stimulates insulin release (Unger *et al.*, 1966; Jarret and Cohen, 1967; Deckert, 1968), and that it may therefore be a hormone of importance in the entero-insular axis for glucose. Further support for this view came from Chisholm, Young and Lazarus (1969), who found that plasma secretin levels rose after the ingestion of glucose. However, work from this laboratory has shown that plasma secretin levels fall after oral glucose in man (Buchanan *et al.*, 1973) and are suppressed after intraduodenal or intravenous infusion of glucose in the dog (K. D. Buchanan unpublished). These conflicting results may be explained by different specificities of the two radioimmunoassays employed in these studies. Chisholm *et al.* raised their antisera against impure pork secretin (Sigma: biological potency 40 clinical units/mg) which also served as their standard, but used pork synthetic secretin as their labelled hormone. Our assay system uses purified materials throughout in antibody production, labelled hor-

mone, and standards. The possibility exists that Chisholm *et al.* produced antisera to secretin or a secretin-like material in their impure antigen which resulted in their assay detecting a cross-reacting secretin-like immunoreactive material which was not identical with secretin.

If secretin is suppressed by glucose then the converse that it is stimulated by hypoglycaemia appears to be logical. The hypoglycaemic stimulus may be mediated through the vagus or by catecholamines or by another mechanism.

The behaviour of secretin with changing glucose concentrations is similar to what would be expected with pancreatic glucagon. Secretin has strong structural similarities with glucagon and has an overlap in biological actions including lipolysis and insulin secretion. Secretion may therefore have to be considered as a hormone of importance in regulating fuels during starvation.

We thank Mr. John Grant, Paediatric Surgeon, Stobhill Hospital for his encouragement, and the sisters and midwives of the labour ward, Stobhill Hospital, for their co-operation.

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