The effect of prolonged pancreatic secretion on blood acid-base balance in the conscious dog

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SUMMARY Prolonged near maximal pancreatic secretion in conscious dogs has been found to result in a metabolic acidosis. This is mild and is accompanied by respiratory and other forms of compensation. Measurements of blood bicarbonate or base-excess changes cannot be used to estimate pancreatic bicarbonate output. The acidosis caused by pancreatic secretion cannot explain the changes in bicarbonate concentration seen in pancreatic juice during prolonged secretion.

The changes in blood acid-base balance resulting from secretion of either gastric or pancreatic juice have been used by some authors to quantitate the secretion. Rune (1966) described a method for estimating gastric acid secretion by measuring the base excess in the blood and allowing for alkali excretion in the urine. The 'volume of distribution of bicarbonate' (F) was previously determined by aspirating gastric juice and measuring urinary alkali and substituting in the equation

\[ F \times \text{body weight} = \frac{\text{net acid loss (m-equivH}\text{\textsuperscript{+})}}{\Delta \text{base excess}} \]

The value obtained was 0.29 ± 0.02 which corresponds closely with a value of 0.31 reported by Singer, Clark, Barker, Crossley, and Elkington (1955) and by Mellemgaard and Astrup (1960) who measured the bicarbonate pool in man using rapid intravenous infusion of bicarbonate solutions. The volume of distribution of bicarbonate also corresponds closely with the volume of the extracellular fluid in man (Wilkinson, 1960) and in the dog (McNeill, Williams, and Moore, 1963).

Anderton, Finlayson, Murray-Lyon, Smith, and Shearman (1968) extended the use of this method to the estimation of pancreatic bicarbonate secretion in man but found that the calculated volume of pancreatic secretion was considerably in excess of the volume obtained by duodenal aspiration.

The results of the present study indicate that plasma bicarbonate or base-excess changes could not be used to estimate pancreatic bicarbonate secretion in the dog. The fall in plasma bicarbonate after an hour of secretion was small and it was only after two hours of secretion that the fall became statistically significant.

During prolonged stimulation of the pancreas the bicarbonate concentration of the secreted juice falls progressively (Komarov, Langstroth, and McRae, 1939; Christodouloupolos, Jacobs, and Klotz, 1961) and it would seem possible that this fall is caused by the acidosis resulting from the prolonged secretion of alkaline juice. Ball (1930) and Rawls, Wistrand, and Maren (1963) observed that the creation of a metabolic acidosis resulted in a fall in bicarbonate concentration and output in the pancreatic juice, but in their experiments the acidosis was severe resulting in a plasma pH of 7.15 and reducing plasma bicarbonate concentration to 16 m-equiv/l. Case et al (1970) have reported that in the isolated perfused cat pancreas bicarbonate output is directly proportional to the concentration of bicarbonate in the perfusate.

It has been shown that during prolonged pancreatic secretion the fall in bicarbonate concentration in the juice is not due to pancreatic exhaustion, as suggested by Christodouloupolos et al (1961), but is due to a dilution of the secreted bicarbonate by an added chloride containing solution, since output of bicarbonate remained constant for up to three hours while bicarbonate concentration fell and the volume and chloride output increased (Fawcett, 1970b). This change could not be prevented even if the secreted bicarbonate were replaced by a separate intravenous infusion.

In the present study, the changes in plasma pH and bicarbonate concentration are small and it is clear that they do not account for the changes in the

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pancreatic juice which occur during prolonged secretion.

The interrelationship between pancreatic secretion and the acid-base balance of the blood has received little attention. Ball (1930) and Rawls, Wistrand, and Maren (1963) studied the effect on pancreatic secretion of alterations in the plasma pH, and Case, Scratcherd, and Wynne (1970) have described the dependence of pancreatic bicarbonate output on the concentration of bicarbonate in the perfusing fluid. No studies have been reported of the effect on plasma acid-base balance of maximal pancreatic secretion in conscious animals over a period of several hours.

Methods

Four dogs were used, three having a Thomas cannula in the duodenum through which the pancreatic duct was cannulated with a fine polythene tube. In the fourth dog the pancreatic juice was collected in a duodenal pouch drained by a cannula of the type described by Fawcett (1970a). Each dog was the subject of three experiments and these were performed in a random order. In two of the three experiments a loading dose of secretin of 1 cu/kg was given by intravenous injection over a period of 20 seconds and this was followed by an infusion of secretin at a dose rate of 2 cu/kg/hr since this dose rate had been found to give near maximal stimulation of pancreatic bicarbonate secretion (Fawcett, 1970b). The secretin was dissolved in 0.15M NaCl solution and infused at a rate of 84 ml/hr, this being approximately equal to the rate of secretion of the pancreatic juice. In one of the three tests in each animal, no secretin was added to the infusion fluid and the volume infused was reduced to match the basal pancreatic secretion.

Arterial blood samples were taken each time before the dog was put in slings and subsequently at hourly intervals after the start of the infusion. To obtain the samples the dog was, in most instances, made to lie on its side and the hind leg was abducted to expose the femoral artery. Direct needle puncture was then performed and blood was withdrawn into heparinized syringes. Occasionally arterial puncture was performed while the dog remained standing in its slings.

Pancreatic juice was collected over periods of 10 minutes in graduated tubes on ice and the chemical estimations were performed immediately the sample was obtained. Plasma pH and pCO₂ were measured on a Radiometer micro-blood gas meter and plasma bicarbonate (as 'standard bicarbonate') and base excess were estimated on the Sigaard-Anderson nomogram.

Results

PLASMA pH
No significant fall in plasma pH occurred during the first hour of secretion (p = 0.3) but there was a significant fall during the second hour (p < 0.01). No further significant fall occurred during the third hour. The mean overall fall in plasma pH was 0.034 (Fig. 1).

![Fig. 1 The changes (mean ± 1 SEM) in plasma pH during prolonged secretin stimulation of the pancreas expressed relative to values before stimulation. Control . . . ; stimulation ———.](http://gut.bmj.com/)

PLASMA pCO₂
Plasma pCO₂ fell by an average of 4 mmHg during the three hours of secretion. During the first two hours the fall was linear but a smaller fall occurred in the third hour (Fig. 2).

PLASMA BICARBONATE
In the first hour of secretion plasma bicarbonate fell by a mean value of 1.2 m-equiv/1 but the values obtained were not significantly different from basal levels (p = 0.1). By the end of the second hour the mean fall was 2.4 m-equiv/1 and these values were significantly lower than initial levels (p < 0.01). In the third hour there was no further significant fall and the mean overall fall was 2.8 m-equiv/1 (Fig. 3).

By measuring the bicarbonate output in the pancreatic juice and assuming a value for the extracellular fluid volume of the dog, it was possible to calculate the change in bicarbonate concentration in the plasma equivalent to the loss of bicarbonate in the juice. This was found to have a mean value of 2.1 m-equiv/l/hr (Fig. 3).
infused, there was no change in plasma pH, pCO₂, bicarbonate, or base excess during the course of the experiment (see Figs 1, 2, and 3).

**Discussion**

The purpose of this study was threefold: (1) to define the effect in a conscious animal of the loss to the body of a substantial volume of alkaline pancreatic juice; (2) to assess the basis for using blood acid-base measurements as an estimate of pancreatic bicarbonate secretory capacity; (3) to see whether the changes in blood acid-base balance could account for the changes in bicarbonate concentration which occur in pancreatic juice during prolonged secretion.

The secretion of pancreatic juice was found to result in a fall of plasma bicarbonate concentration and a mild acidaemia. At the same time plasma pCO₂ fell, indicating that respiratory compensation was active. In the third hour of secretion plasma bicarbonate and base excess did not fall further and it is probable that homeostasis was maintained by renal compensation, but, as the urine was not collected during these experiments, the magnitude of any renal compensation is not known. The changes in plasma pH, pCO₂, bicarbonate, and base excesses were small and did not exceed normal physiological limits.

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This work forms part of a thesis submitted by one of us (A.N.F.) to the University of Cambridge for the degree of Master of Surgery.

**References**

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