THE SITE OF ACTION OF PENTAGASTRIN-INDUCED INHIBITION OF THE RETICULUM

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It is generally assumed that gastrointestinal hormones act peripherally. Since, in the simple stomach, the frequency of contractions is determined by the peripherally-generated basic electrical rhythm, the fact that pentagastrin increases this frequency is consistent with a peripheral mode of action. Reticular contractions however are determined by vagal impulses originating centrally. An alteration of their frequency must therefore be either central or reflex. Pentagastrin inhibits reticular contractions (Ruckebusch, 1971) and an experiment was therefore designed to test the hypothesis that this inhibition is central. If the receptors are peripheral pentagastrin should be no more effective given via the carotid artery than via the jugular vein. If, on the other hand, the receptors are cranial then carotid injections should be more effective.

Method

Under halothane anaesthesia five sheep were fitted with unilateral jugular and carotid cannulae. The contralateral carotid was tied to maximize bilateral distribution of infused material. Previously established ruminal cannulae were used to introduce small balloons (inflated with 5 ml air) into the reticulum, which was identified by the characteristic pattern of contractions. A Physiograph (Narco) was used to record contractions. Experiments commenced 2-4 h after surgery when biphasic reticular contractions were occurring at approximately 60 s intervals.

Pentagastrin (Peptavlon, Ayerst) was infused at 0.6 — 3.0 μg. kg^{-1} h^{-1}. The dose was determined for each sheep in a preliminary trial and was one that, via the jugular, produced a moderate (approximately 10%) reduction in the reticular frequency. Infusions followed an A, B, Recovery, B, A sequence, the initial infusion being randomly via the jugular or the carotid. Infusion and recovery periods lasted 20 min and experiments were terminated if the frequency or amplitude of contractions during the recovery periods declined by more than 50%. In two sheep the dose rate was adjusted during the experiment.

Results and Discussion

There are clearly cranial receptors for the pentagastrin-induced decrease in the frequency of reticular contractions. The effect of carotid infusions on the frequency of contraction was always more than that of jugular infusions (fig. 1). The effect of the infusions on the amplitude of the contractions was less clear. When the contractions were

not abolished by the infusion the amplitude was 77-114% of the control amplitude. The reduction of the amplitude of reticular contractions by pentagastrin may therefore involve peripheral, rather than cranial, receptors.

These results were obtained with doses of pentagastrin that are clearly high. The criterion for a physiological response is that the dose required for the half-maximal response be not greater than that for the identifying action for the hormone (Grossman, 1977). The spectrum of activities of pentagastrin overlaps those of cholecystokinin and gastrin (Walsh and Grossman, 1975) and the effect on reticular motility may therefore, if it is physiological, be associated with either of these hormones. To establish that this is a physiological effect would require the determination in sheep of the dose/response relationships for the two natural hormones for both the reticular effect and for the identifying actions for these hormones. Both gastrin and cholecystokinin decrease reticular motility when infused via the jugular (Grovum, unpublished).

Even if it is established that the dose required for the inhibition of reticular motility is unphysiologically high the phenomenon remains of interest for two reasons. First, the effect may be of pathophysiological importance since it has been reported that the circulating levels of gastrin in sheep infected with *Ostertiagia* are greatly increased (Anderson *et al.,* 1976). More importantly this is the first clear demonstration of a cranial effect of an enterohormone on gastro-intestinal motility.

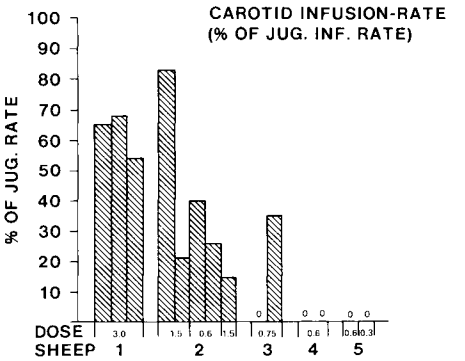

Fig. 1— The effect of carotid infusion of pentagastrin on reticular contractions as a percentage of the effect of the immediately preceding or immediately following jugular infusion. The dose employed in each experiment is shown in $\mu g.kg^{-1}.h^{-1}$.

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