The high DNA content of the uterine artery found in early pregnancy (Table 2) suggests that this artery is undergoing growth. The decrease in DNA content in late pregnancy could be due to a decrease in the number of cells or to a relative increase in the non-nuclear constituents of existing cells. Since a decrease in the number of cells is unlikely, the data indicate that growth has continued into late pregnancy. In the absence of information on the number of cells relative to DNA content, it is not possible to determine whether growth took place by hyperplasis or by hypertrophy. Gestational processes, however, do not appear to affect the other systemic arterias.

The growth indicated by the biochemical measurements is reflected by mechanical measurements. The uterine artery during late pregnancy has a thicker wall (lower r/h value) and is more compliant (higher E_{inc}) than the mesenteric artery. Furthermore, measurements on uterine arteries from non-pregnant dogfish are needed to substantiate these conclusions. The authors acknowledge the assistance of Michael Levy and Francisco Bonilla in obtaining the tissues and Gwen Lech for help with biochemical analyses. This work was supported in part by NIH Grant HD 16899, and by research funds from the Department of Surgery, Mt. Sinai School of Medicine, New York, N.Y., 10029.

THE SIGNIFICANCE OF VASODILATION IN THE SECRETORY RESPONSE OF THE RECTAL GLAND

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Whilst various hemodynamic changes associated with the stimulation of secretion in the rectal gland have been described (Solomon et al., Bull. MDIBL 20:138-141, 1980; Shuttleworth, J. Exp. Biol., 103:193-204, 1983), the physiologically significant parameters have never been specifically defined or their importance in the overall secretory response assessed. The purpose of this study was to investigate the effects of changes in perfusion pressure, perfusion flow and vascular conductance both singularly and "in concert" on secretion rate in isolated perfused glands from Squalus.

Isolated glands were perfused with saline containing dibutyryl cAMP (0.05 mmol l^{-1}) and theophylline (0.25 mmol l^{-1}) using a constant pressure regime, as described previously (Shuttleworth, loc. cit.), and gassed with 99%0_2:1%CO_2. The rectal gland vein and the secretory duct were cannulated and the cannulae led to drop sensors connected to a 2-channel microprocessor-controlled flowmeter (recording flow in $\mu l\ min^{-1}$). This permitted continuous recording of both efferent perfusion flow and secretion flow. The sodium secretion in the secreted fluid was determined from samples collected from the cannula in the secretory duct and from this, and the recorded secretion flow, sodium secretion rate could be calculated.

Glands were initially perfused at the physiological pressure of 20 mm Hg. Under these conditions, efferent perfusion flow was 2802 ± 109 $\mu l\ g^{-1}\ min^{-1}$, secretion concentration (Na) 530.6 ± 2.3 mmol l^{-1}, and the secretion rate 24.6 ± 0.9 $\mu mol\ g^{-1}\ min^{-1}$ (mean ± S.E., N=19 in each case). The effect of changing the afferent perfusion pressure (by raising or lowering the perfusion head) is shown in Figure 1. It is clear that, at perfusion pressures below those normally found in vivo, secretion rate is significantly reduced whilst the concentration of the secreted fluid is maintained. Supranormal pressures however produce only a relatively small increase in secretion rate - an effect apparently limited by a concomitant reduction in the concentration of the secreted fluid. As this represents a reduction in the concentration gradient between the secretion and the perfusion fluid and is accompanied by an increase in the volume of fluid secreted, it probably indicates the onset of damage to the integrity of the epithelium induced by pressures in excess of the physiological range.

Despite the clear effect of a reduced perfusion pressure on secretion rate shown in Figure 1, it must be remembered that other hemodynamic parameters are effected by lowering the afferent perfusion pressure head. Most notable among these is the simultaneous reduction in perfusion flow. In order to investigate whether the observed fall in secretion rate was due to changes in perfusion flow rather than a direct effect of perfusion pressure, experiments were carried out where perfusion flow was reduced whilst maintaining a constant perfusion pressure (20 mmHg).

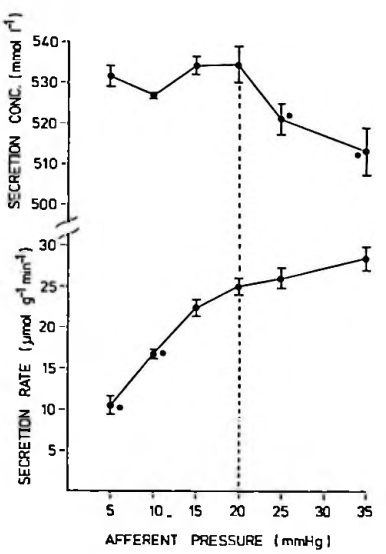

Figure 1.--Effect of afferent perfusion pressure on secretion rate and secretion concentration in the isolated gland. * value significantly different from value at 20 mmHg.

This was achieved by perfusion with the catecholamine norepinephrine (10^{-5} to 10^{-4} mol l^{-1}). High concentrations of norepinephrine are necessitated by the potent vasodilatory effects of cAMP + theophylline contained in the saline, but it is known that, even at these concentrations, norepinephrine has no direct effect on secretory activity in the gland (Shuttleworth, unpublished observations). Perfusion with norepinephrine reduced flow through the gland to 17-55% of control values and also resulted in a reduction in secretion rate. The concentration of the secreted fluid was only slightly affected (controls = 529.6 $\pm$ 1.5 mmol l^{-1}; norepinephrine = 524.1 $\pm$ 1.8 mmol l^{-1}). Figure 2

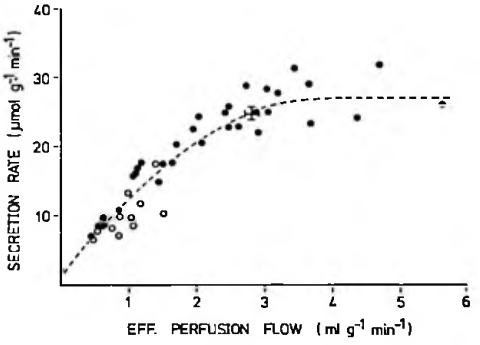

Figure 2.--Relationship between perfusion flow and secretion rate.
(●) Glands perfused at different afferent pressures.
(O) Glands perfused at 20 mmHg with norepinephrine.
(+) Control values. Mean $\pm$ S.E. N=19.

shows the relationship between efferent perfusion flow and secretion rate for individual glands exposed to various perfusion pressures and for those exposed to norepinephrine at a constant (20 mmHg) pressure. It is clear that the data points obtained with norepinephrine lie very close to those obtained with reduced perfusion pressure. Of course, the reduction in perfusion flow induced by norepinephrine at a constant perfusion pressure is associated with considerable changes in vascular conductance within the gland which parallel the observed falls in perfusion flow. However, it is unlikely that vascular conductance per se is a significant factor in determining secretion rate as, in the experiments involving perfusion at a reduced pressure and which produced similarly large reductions in secretion rate, vascular conductance was not significantly different from that seen in controls.

Therefore, the only common hemodynamic variable in the two experimental situations described above is a fall in perfusion flow. It is clear therefore that this must be the specific parameter responsible for the decline in secretion rate observed and that changes in perfusion pressure and vascular conductance are, themselves, of little effect.

It is known that perfusion flow through the gland is dramatically affected by physiological concentrations of circulating catecholamines (Shuttleworth and Thompson, Bull. MDIBL 21:59-62, 1981; Shuttleworth, J. Exp. Biol. 103:193-204, 1983). For example, perfusion flow through the gland was shown to be reduced to approximately 20% of control levels by 3 10^{-7} mol l^{-1} norepinephrine, a value within the range found in vivo. During stimulation of the gland however, the perfusion pathway is vasodilated via a cAMP-mediated processes that is independent of the secretory process itself (Shuttleworth, loc. cit. and Amer. J. Physiol., in press). The data presented in this study permit a quantitative assessment of the significance of this vasodilatory effect in the overall secretory response. At a perfusion flow equivalent to 20% of control levels the maximum secretion rate is approximately 8.0 μmol g^{-1} min^{-1} (see Figure 2) or only 30-33% of that seen in the fully vasodilated controls. Thus, in the presence of only a moderate circulating concentration of catecholamines, the independent, but simultaneous, vasodilation response described above will increase secretion rate some three times. This work was supported by grants from the U.K. Science and Engineering Research Council (GR/B/67063 and GR/C/41777) and the Marshall and Orr Bequest of the Royal Society, London.

STIMULATION OF RECTAL GLAND SECRETION BY AN ENDOGENOUS PEPTIDE

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The involvement of cAMP in regulating ion secretion in the elasmobranch rectal gland implies a hormonal control and, with this in mind, Stoff et al. (Am. J. Physiol. 237:F138-F144, 1979) investigated a range of exogenous peptide hormones and neurohumoral factors for stimulatory activity in the isolated perfused gland of Squalus. Of those tested, only the polypeptide vasoactive intestinal peptide (VIP) was successful in stimulating secretion. However, it has been shown that VIP is totally without effect on ouabain-sensitive oxygen consumption and ouabain binding in the glands of two other elasmobranch species - Scyliorhinus canicula and Raja clavata (Shuttleworth, in preparation). This failure of VIP to affect oxygen consumption or ouabain binding implies that this agent is not able to stimulate secretory activity in the glands of either of these species and thereby raises doubts as to whether VIP is indeed the natural hormone responsible for controlling rectal gland secretion in elasmobranchs in vivo. This report describes some initial success we have had in pursuing an alternative approach, that of isolating the native endogenous secretagogue from elasmobranch tissues.

Extracts of the intestines obtained from freshly sacrificed Scyliorhinus were prepared according to standard procedures for peptide isolation (Mutt, in "Gut Hormones", ed. S. Bloom, pp. 21-27, 1978), involving boiling in water and subsequent acetic acid extraction. Following absorption of peptides to alginic acid and elution with dilute hydrochloric acid (0.2M), sequential purification of polypeptide material was carried out by means of Sephadex gel filtration, ion exchange chromatography and reversed phase high performance liquid chromatography (HPLC). High performance liquid chromatography was performed utilizing an 0.05% trifluoroacetic acid:acetonotrile gradient (15%-28%) using a detector operating at 214 nm. This procedure yielded a series of partially purified peptide fractions which were screened for activity in the rectal gland by determining their effect on oxygen consumption in slices of the gland of Scyliorhinus. One of these fractions ("Fraction 13") was found to be a potent stimulator of ouabain-sensitive oxygen consumption and ouabain binding in the slices from both Scyliorhinus and Raja