The study has also revealed that the lymphatic system of the skin is regionalized so that lymph from one particular area enters the popliteal node in one specific lobe while that from an adjacent area of skin enters a different lobe.

3. The lymph draining the muscle of the lower limb collects in vessels which join the main femoral lymphatic post-nodally.

It was therefore possible to collect pure muscle lymph by cannulating the main femoral lymphatic and ligating the post-nodal lymph vessel close to the node.

The mean control lymph flow from muscle was 21 ($\mu$l/100 g)/min whilst that from skin was 240 ($\mu$l/100 g)/min. The protein concentration of muscle lymph was 25·5± S.E. of mean 1·9 mg/ml (n=10) while that of skin lymph in the same animals was 23·2±1·9 mg/ml.

After thermal injury there was about a two-fold increase in the protein concentration (37·8±4·7 mg/ml) and a 3–5 fold increase in the flow of skin lymph. On the other hand there was no change in either protein or flow of muscle lymph. This finding indicated that the injury caused an increase in vascular permeability in the skin but not in the muscle.

On the other hand there was a pronounced increase in the lactic dehydrogenase (LDH) activity in muscle lymph (from 0·79±0·2 to 11·18±4 u/ml) indicating that the injury had caused significant damage to the muscle fibres. This cellular damage was probably produced directly and not through reflex nerve activity since maximal stimulation of the sciatic nerve did not produce such a leakage of enzyme into the lymph.

It therefore appears that a different relationship exists between blood vessels and lymph vessels in skin and muscle.

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## Potentiation of the biphasic bradykinin response of the guinea-pig ileum

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When the isolated guinea-pig ileum with resting tone is challenged by bradykinin only contractile responses are observed. If, however, the ileum is first contracted by acetylcholine (ACh) or other agonists, and without washing out, bradykinin is added, then a relaxation, immediately followed by a contraction, is seen (Hall & Bonta, 1972). The magnitude of the relaxation, but not of the contraction was found to be dependent on the concentration of the ACh or the percentage of maximum contraction of the ileum (Hall & Bonta, 1973a). The involvement of catecholamines or an action on the adrenergic receptors has been ruled out (Hall & Bonta, 1973b).

It is well known that contraction of some intestinal smooth muscles by bradykinin can be potentiated by a variety of compounds (Walaszek, 1970). These include certain thiols, such as cysteine, 2,3–dimercaptopropanol (BAL) and $\alpha$-thiol glycerol; and also the mixture of Bradykinin Potentiating Factors (BPF) isolated from the venom of *Bothrops jararaca* (Ferreira, Bastelt & Greene, 1970). There appears to be limited experimental work on the potentiation of the relaxation (Camargo & Ferreira, 1971). We have examined the above potentiating compounds on the biphasic response to bradykinin of the ACh contracted guinea-pig isolated ileum.

Cysteine, BAL, α-thiol-glycerol or $BPP_{5a}$ (a synthetic pentapeptide similar to the pentapeptide isolated from BPF) potentiate both the bradykinin relaxation and contraction. Cysteine and BAL were up to 10 times more potent at potentiating the bradykinin relaxation than the contraction. There was no potency difference for α-thiol-glycerol or $BPP_{5a}$. High concentrations of cysteine and BAL produced inconsistent effects, at some concentrations potentiating and others reducing the bradykinin responses. Cysteine at high concentrations potentiated, while BAL reduced the ACh contraction. α-Thiol-glycerol and $BPP_{5a}$ had no effect at any concentration examined.

In similar experiments using phentolamine, we have shown that, although the bradykinin relaxation was reduced, the contraction was either unaffected or potentiated by phentolamine. These results suggested the possibility of separate receptors for the bradykinin-induced relaxation and contraction of the acetylcholine contracted guinea-pig isolated ileum.

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## Potentiation of dibutyryl cyclic 3'5'-AMP-induced gastric acid secretion in rats by non-steroidal anti-inflammatory drugs

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Indomethacin, a potent inhibitor of prostaglandin (PG) synthesis (Vane, 1971), can increase pentagastrin-stimulated acid secretion in the rat (Main & Whittle, 1973). We have now investigated the effects of non-steroidal anti-inflammatory drugs on the secretory response evoked by dibutyryl cyclic 3'5'-AMP (dbcAMP) injected intravenously (Whittle, 1972).

Gastric acid output and gastric mucosal blood flow (MBF) were measured in the urethane-anaesthetized rat (Main & Whittle, 1972). Intravenous injection of indomethacin, in doses which had no effect on basal acid secretion but which lowered resting MBF, caused a dose-dependant potentiation of secretion induced by dbcAMP (10–20 mg/kg I.V.) accompanied by an increase in MBF. Sodium meclofenamate had a similar effect (Table 1). Equilibrium dialysis experiments indicated that these effects

TABLE 1. *Effect of pretreatment with anti-inflammatory drugs on the secretory response to dbcAMP (20 mg/kg) injected intravenously during basal secretion in the rat. Acid output (μ-equiv) is the increase from basal during the 80 min. following injection of dbcAMP. All results, expressed as mean ±S.E.M. where (n) is the number of values, differ significantly from the control ($P < 0.001$).*

| Drug | (mg/kg) | | | Acid output, μ-equiv. | |
|---|---|---|---|---|---|
| Control | — | | | 8±1 | (16) |
| Indomethacin | (10) | I.V. | 1 h | 29±3 | (3) |
| Indomethacin | (20) | I.V. | 1 h | 34± 6 | (3) |
| Indomethacin | (30) | I.V. | 1 h | 90±20 | (4) |
| Indomethacin | (15) | S.C. | 24 h | 55± 3 | (3) |
| Indomethacin | (15) | S.C. | 6 h | 57± 5 | (3) |
| Indomethacin + Theophylline | (15) S.C. 6 h; (20) I.V. 1 h | | | 123±11 | (3) |
| Phenylbutazone | (100) | S.C. | 6 h | 52± 4 | (2) |
| Meclofenamate | (30) | I.V. | 1 h | 52±19 | (3) |