Propranolol lowers and alprenolol has no significant effect on cardiac output (Åblad *et al.*, 1967); bunolol had an effect similar to that of propranolol.

Propranolol may increase femoral perfusion pressure by reflex activation of the sympatho-adrenal system (Nakano & Kusakari, 1965; Kalaalp & Kiran, 1966), the initiating stimulus being a reduced pulse pressure or rate of change of pressure (Heymans & Neil, 1958). The β-sympathomimetic activity of alprenolol, possibly by supporting cardiac function above the depressed level usually following β-adrenoceptor antagonism and by causing diastolic hypotension, may maintain pulse pressure and thereby attenuate one stimulus for initiating cardiovascular reflexes.

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The kinin-forming system in rabbit hind limb lymph after thermal injury

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It was shown that after injury to dog hind limbs, the kinin-forming potential of the lymph draining the limb increased (Edery & Lewis, 1963). Pseudoglobulin was used to provide excess substrate. Later Jacobsen & Waaler (1966) suggested that the increase was due to an enzyme impurity in the pseudoglobulin acting on an increased amount of kininogen entering the lymph from the plasma. In the present experiments in rabbits, it was found that excess kininogen was always present in plasma and lymph. It was therefore unnecessary to use pseudoglobulin.

However, it was necessary to activate the kinin-forming enzyme. This was done in two ways—first, by 5 min contact with glass ballotini (100 mg/0·6 ml) in the presence of the kininase inhibitor *o*-phenanthroline HCl (0·1 ml of 1% solution) and second by acidification to pH 2·0 with N HCl and 0·2 N HCl/KCl. Kinin formation was measured by assay on the rat uterus in the presence of bromolysergic acid diethylamide (0·6 mg/l.). After glass activation the kinin was assayed immediately, but after acidification the sample was neutralized with 0·33 N NaOH and phosphate buffer to pH 6·4, *o*-phenanthroline (0·1 ml. of 1% solution) was added; the sample was then assayed after 20 min.

After thermal injury there was an increase of up to 70 times in the activity produced by acid activation, but no increase in that following glass contact. The increase generally occurred in two peaks—within 2 h and 4–6 h after injury. These two peaks of activity appeared to correspond to changes in vascular permeability as indicated by increases in lymph protein. However, it is not clear whether the changes in permeability were the cause or the effect of changes in the kinin system.

There are three reasons why the increase in acid activatable kinin-forming enzyme was not simply the result of passage of the enzyme or substrate from the plasma into the lymph. First the kinin-forming activity increased up to 70-fold whereas the overall lymph protein increased less than twice. Second, although in some experiments there was an increase in the acid activatable kinin-forming enzyme in the plasma, in others the increase was observed only in the lymph. Third, the increase in the activity of the plasma was sometimes less than, and sometimes occurred at a different time from, that in lymph.

A possible explanation of some of these findings is as follows: prekallikrein leaks into the injured tissue where it is activated by tissue activators (Lewis, 1959). The active enzyme is, however, rapidly neutralized by kallikrein inhibitor to form a complex which is dissociated by acid (Kraut, Frey & Werle, 1930). The acid activatable enzyme measured in the present experiments was therefore probably a measure of the kallikrein which had been activated and subsequently neutralized.

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Possible existence of different types of angiotensin II receptors

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The actions of five structure analogues of Valyl-5-angiotensinamide II on the contractility of three different smooth muscle preparations were studied. For this purpose, isolated colon and uterus from the rat and strips of rabbit aorta were suspended in a temperature regulated, oxygenated Krebs solution.

Dilutions of analogues and of Valyl-5-angiotensinamide II were compared by finding the concentration of each that was required in the tissue bath to cause an equal and moderate response of the muscle (at around the ED50 of Valyl-5-angiotensinamide II). The ratio of activity was often substantially different for each one of the organs tested (Table 1). Theoretically, if the receptors in the three different organs are the same, a similar ratio of activity of the analogues compared with Valyl-5-angiotensinamide II should be expected.

TABLE 1. *Ratio of activity of analogues of Valyl-5-angiotensinamide II*

	Rat colon	Rat uterus	Rat aorta
Valyl-5-angiotensinamide II	100	100	100
Ornithine-2-angiotensinamide II	5·00±0·57*	4·18±0·19	0·38±0·08
Phenylalanine-4-angiotensinamide II	5·16±0·04	0·66±0·04	0·24±0·01
Phenylalanine-4-angiotensin II	5·65±0·68	3·87±0·46	2·00±0·20
Tyrosine-5-angiotensin II	0·25±0·04	0·5±0·05	0·03±0·00
Proline-9-phenylalanine-10-angiotensinamide I	0·41±0·03	0·52±0·03	0·62±0·01

* Mean±S.E.M., effect of the analogue in per cent of Valyl-5-angiotensinamide II activity, considered as 100%. All the analogues were obtained by courtesy of Dr. B. Riniker (CIBA Research Laboratories, Basle).