The specificity of the antagonism for angiotensin has been assessed by measuring the effect of the 8 substituted angiotensins against AII, AI, and noradrenaline (NA) on the rat blood pressure, AII, AI, acetylcholine (ACh) and 5-hydroxytryptamine (5-HT) on the rat isolated colon. The 8 substituted analogues of AII antagonize the pressor effects of AII and AI and slightly that of NA, but do not influence the myotropic effect of ACh and 5-HT on the rat isolated colon.

It is proposed that: (a) 6-His is essential for binding angiotensin to the receptor and an aromatic ring in position 8 is necessary for pressor and myotropic activities, (b) AI acts on the same receptor as AII, (c) 8 substituted analogues of AII may fulfil the criteria for competitive inhibitors, because inhibition is reversible and the extent of the inhibition depends on the relative concentration of agonist and antagonist.

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Inhibition of prostaglandin synthesis augments the effects of sympathetic nerve stimulation on the cat spleen

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Indomethacin blocks the synthesis of prostaglandins E_2 and $F_{2\alpha}$ from arachidonic acid by cell-free homogenates of guinea-pig lungs (Vane, 1971) and the release of prostaglandins from dog spleens when they are contracted by adrenaline (Ferreira, Moncada & Vane, 1971). Hedqvist (1970) proposed that prostaglandin release by the spleen is a feed-back mechanism controlling the output of noradrenaline from sympathetic nerves. The following results support this hypothesis.

Nine cats were anaesthetized with pentobarbitone sodium (30 mg/kg i.m.). The splenic pedicle was dissected to separate artery, vein and nerves. The spleen was removed and perfused with Krebs solution containing dextran (2–3% w/v) at 8–15 ml/minute. Part of the splenic outflow superfused assay tissues which detected prostaglandins (Ferreira, Moncada & Vane, 1971). Perfusion pressure and spleen weight were measured.

The resting spleen perfusion pressure and weight remained stable for several hours. Stimulation of the splenic nerve (1–3 ms pulse, 5–30 V, 1–10 pulses/s, trains of 20–120 s) gave reproducible rises in perfusion pressure and falls in spleen weight. There was also an output of prostaglandin into the perfusate which, when measured as E_2, represented an increase of 1–20 ng/ml.

When indomethacin (0·3–5 μg/ml) was infused into the spleen there was no change in spleen weight but the perfusion pressure increased, sometimes by as much as 250%. At the same time, there was a decrease in the basal secretion of prostaglandins, as shown by relaxation of the assay tissues. When nerve stimulation was repeated, the contraction of the spleen was greater than before. The rise in perfusion pressure

was also augmented, sometimes in height and always in duration. No prostaglandin release was detected during indomethacin infusion.

In three experiments when the change in spleen weight and perfusion pressure induced by splenic nerve stimulation had been increased by indomethacin, infusions of prostaglandin E_2 (1·5–5 ng/ml) into the spleen decreased the effects of nerve stimulation.

After cessation of indomethacin infusion, changes in weight, perfusion pressure and prostaglandin release induced by nerve stimulation gradually returned towards pretreatment levels.There was also a reduction in basal perfusion pressure which was associated with an increase in the continuous output of prostaglandins.

These experiments support Hedqvist's hypothesis that in the spleen, prostaglandin release is a feed-back mechanism which limits the effects of nerve stimulation. This is especially true for the duration of the effect. In addition our results show that there is a continuous basal release of prostaglandins which affect the perfusion pressure by actively causing vasodilatation.

We wish to thank the Wellcome Trust for a grant.

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Rabbit-aorta contracting substance (RCS) may be a prostaglandin precursor

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Rabbit-aorta contracting substance (RCS) is an unstable principle released from guinea-pig isolated lungs during anaphylaxis, and by infusions of arachidonic acid (Piper & Vane, 1969, 1971; Vargaftig & Dao, 1971). The release of RCS and prostaglandins is inhibited by aspirin and indomethacin (Piper & Vane, 1969, 1971; Vane, 1971). Vane (1971) equated prostaglandin release with biosynthesis and demonstrated that aspirin and indomethacin inhibit enzymic synthesis from arachidonic acid of prostaglandin E_2 and prostaglandin $F_{2\alpha}$. Because these results suggest that RCS may be related to prostaglandins, we have looked for RCS formation by a prostaglandin synthetase system.

The enzyme preparation was a washed particulate fraction (10,000–100,000 g) of homogenate of dog spleen. It was incubated for 20 min at 37°C with arachidonic acid (10 μg/ml) in a medium (Änggård & Samuelsson, 1965) containing glutathione (50 μg/ml) and hydroquinone (0·5 μg/ml); the generation of prostaglandins was 100–400 ng (assayed as prostaglandin E_2) per mg protein.

Samples of incubation mixture did not contract strips of rabbit aorta but RCS is very unstable. To test more immediately for RCS generation, two banks of assay tissues, each containing a strip of rat stomach (RSS) and rabbit aorta (RbA) were superfused at 5 ml/min with Krebs solution containing arachidonic acid (5 μg/ml). The Krebs solution passed through a coil (volume 10 ml) of silicone tubing at 37°C