previously constricted vein. These blocking effects of both practolol and ICI-66082 were overcome by increasing the rate of infusion of isoprenaline.

This study has demonstrated that propranolol is effective in blocking both heart rate and peripheral vascular responses to infused isoprenaline, but practolol and ICI-66082 are less effective in blocking peripheral vascular responses.

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Central hypotensive effect of propranolol in the rabbit

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The action of propranolol in the treatment of hypertension is not well understood. The effective dose in chronic oral treatment may be very high (Prichard & Gillam, 1969) and although propranolol induces a rapid fall in cardiac output, the fall in arterial pressure is usually a gradual one. Several antihypertensive drugs exert actions on noradrenergic pathways in the central nervous system (CNS) and this is a possible site of action for propranolol, which achieves high CNS concentrations.

Intracerebroventricular (ICV) injection of (±)-propranolol (500 μg) produced a rapid rise in mean arterial pressure (MAP) in the conscious rabbit, 27·5±6·0 mmHg at 5 min, followed by a prolonged fall, 8·8±3·3 mm Hg at 4 h. A similar early rise in MAP was produced by (+)-propranolol 500 μg ICV, 42·2±4·5 mmHg, but there was no late fall. Procaine (1 mg) ICV produced a similar rise, 51·0±10 mm Hg at 5 min. The pressor effect of both (+)-propranolol and procaine were both abolished by pentobarbitone anaesthesia. This early rise in MAP may be related to the membrane stabilizing action shared by procaine and both isomers of propranolol.

(−)-Propranolol 500 μg ICV raised MAP 20·8±4·1 mm Hg at 5 min, but the subsequent fall was greater than that produced by the racemate (14·6±4·5 mmHg at 4 h). The central hypotensive effect of (−)-propranolol was abolished by pretreatment of rabbits one week previously with intracisternal 6-hydroxydopamine (500 μg/kg), which destroys CNS noradrenergic neurones.

Isoprenaline (50 μg ICV) caused a transient fall in MAP, 10·0±0·4 mmHg at 5 min. In rabbits pretreated with 500 μg (−)-propranolol ICV 2 h previously, this response to central isoprenaline was abolished.

It appears therefore that propranolol can lower arterial pressure in the rabbit by an action on the CNS. This action is dependent on the integrity of noradrenergic neurones and the effect is related to β-adrenoceptor blocking activity and not to local anaesthetic activity.

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Rabbit monoarticular arthritis and synovial prostaglandins

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An immune arthiritis is produced in the rabbit using a modification of the method of Dumonde & Glynn (1962). Essentially, this consists of sensitizing the animals intra-

dermally with 10 mg ovalbumin (O.A.) in Freund's complete adjuvant, and three weeks later challenging the animals intra-articularly with O.A. We have found the optimal challenge dose to be 5 mg O.A., 10 mg O.A. caused widespread deaths due to systemic anaphylaxis, while 100 μg O.A. was insufficient to produce a marked response. With this method of sensitization we have produced chronic, progressive arthritis which is characterized by synovial effusion, synovial hyperplasia, pannus formation, plasma cell infiltration, follicular lymphocyte aggregation and bone and cartilage erosions.

Monoarticular arthritis in rabbits is strain and age dependent. Old English rabbits (O.E.) gave a better response than New Zealand White (NZW) rabbits, which in turn were superior to Dutch rabbits. In addition, thirteen week-old rabbits gave a better response than nine week-old rabbits.

Cell-free synovial fluid from arthritic rabbits has been examined for the presence of prostaglandins (PG). The fluid was superfused in Krebs solution over isolated rat fundic strip and rat colon preparations. The tissues were blocked by a combination of atropine, phentolamine, methysergide and mepyramine (all 10^{-7} g/ml) and propranolol (2×10^{-6} g/ml). Prostaglandin-like activity was assayed as PGE_1 or PGE_2. In preliminary experiments in two NZW rabbits, 60–80 ng PG-like substance was found in the synovial sac of one rabbit killed 18 h post challenge and 15–18 ng PG-like substance was found in one rabbit killed 7 days post challenge. However, PG-like activity could not be detected in 8 out of 9 O.E. rabbits killed 8 weeks after challenge. The remaining rabbit from this group contained 30 ng PG-like substance. This animal also showed the highest polymorph infiltration of the group.

Similar levels of PG to those found at 18 h in monoarticular arthritis have been found by Eakins, Whitelocke, Perkins, Bennett & Unger (1972) in their study of acute immunogenic uveitis in the rabbit. Results of further investigations into the presence and importance of PG in rabbit monoarticular arthritis will be presented at the meeting.

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Effect of intraperitoneal administration of (+)-INPEA on oxytocin and prostaglandin evoked responses of the isolated rat uterus

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The effect of optical isomers of INPEA (N-isopropyl-p-nitrophenyl ethanolamine hydrochloride) on oxytocin-evoked (Saini & Sharma, 1971) and on prostaglandin-evoked (Rao & Sharma, 1972) responses of isolated rat uterus has been reported (−)-INPEA exhibited a weak antioxytocin activity but had no effect on prostaglandin-evoked responses. In contrast, (+)-INPEA potentiated the action of oxytocin and prostaglandins when added to the bath fluid at a concentration of 1×10^{-5} g/ml. In the present investigation, the effect of intraperitoneal administration of (+)-INPEA on prostaglandin (PGE_1, PGE_2, $PGF_2\alpha$) and oxytocin-evoked responses was studied on the same preparation.

Uterine strips from (+)-INPEA treated rats (10 mg/kg body weight I.P., one hour before the start of experiment) were suspended in an organ bath (10 ml) containing aerated de Jalon's solution at 29° C and equilibrated for a period of 30 min. Responses were recorded to the graded doses of each of the agonists (oxytocin, PGE_1, PGE_2 and $PGF_2\alpha$) on a potentiometric recorder. Seven experiments were performed with each drug. In all the experiments there was marked increase in the amplitude of oxytocin and prostaglandin (PGE_1, PGE_2 and $PGF_2\alpha$) evoked responses when compared to controls.