to ovariectomized rats on the first and third day of dioestrous in doses ranging from 4 to 100 mg/kg. Intact animals received fixed doses of progesterone (50 mg/kg). Both groups of animals received a single dose of stilboestrol (100 μg/kg), on the fourth day of dioestrous 18 hr before killing.

Vaginal smears were taken and the sensitivity to oxytocic drugs—namely acetylcholine, oxytocin and 5-hydroxytryptamine—was studied after suspending the isolated uterine horns in a 5 ml. bath containing De-Jalon solution at 30° C. A 3 point assay method was used comparing oxytocin and 5-hydroxytryptamine to acetylcholine; the results were expressed as equipotent molar ratios.

Vaginal smears of all rats treated with progesterone (50 mg/kg) showed abundant leucocytes indicating absence of stilboestrol effect. Progesterone therapy in ovariectomized animals increased the sensitivity of the uterus to oxytocic drugs. The maximum increase in sensitivity was observed with progesterone (50 mg/kg) where the sensitivity to acetylcholine, oxytocin and 5-hydroxytryptamine was increased by 4, 11 and 3 times respectively as compared with the control rats in induced oestrous. In intact animals, on the other hand, progesterone (50 mg/kg) therapy decreased the sensitivity to acetylcholine, oxytocin and 5-hydroxytryptamine by 2, 1.4 and 17.7 times respectively. In these experiments progesterone therefore desensitizes the uterus to the effect of stilboestrol only in normal rats. This shows that the ovary is essential for the desensitizing effect of progesterone similar to reserpine. The probable mechanism of release of yet another chemical substance from the ovary is put forward.

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Pharmacological activity in polyvinyl chloride (PVC) tubing

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In searching for pharmacological activity in lymph and plasma after injury it was discovered that when stored in "Portex" polyvinyl chloride (PVC) tubing these fluids contained activity which they did not possess when freshly collected. Plasma stored in the tubing contracted the guinea-pig isolated ileum slowly and usually increased the spontaneous activity of the tissue. In addition, the plasma inhibited non-specifically the contractions of the rat uterus to many stimulating substances.

The amount of both activities leaching out of the tubing depended on the time during which the fluid remained in the tubing. After 3 min contact, only traces of activity appeared in the plasma, after 10 min a considerable amount had leached out, while in 60 min the concentration reached a maximum. But when the plasma was removed and replaced by fresh plasma the leaching process occurred again as before, and this procedure could be repeated many times with a similar result. The leaching still occurred after washing the tubing either with water or organic solvent.

The amount of activity leached out was also dependent on the concentration of the protein in the fluid. Lymph, which contains about a third of the plasma protein concen-

tration, caused the leaching out of a smaller amount of activity than plasma itself but even protein-free Tyrode solution contained some activity after being in contact with the PVC tubing for an hour. The activity leached into a solution of purified bovine albumin was proportional to the concentration of the albumin.

The PVC tubing used in the present experiments was made up of the following constituents kindly supplied by Portex Limited: polyvinylchloride polymer, 50–60%; plasticizers (mainly acetyl tri-*n*-butyl citrate), 35%; additives, 5–15% (including soya bean oil containing triglycerides of unsaturated fatty acids; Ca/Zn stearate; stearic acid). The additives all caused contraction of the guinea-pig ileum and collectively account for the smooth muscle stimulating activity in the tubing. The inhibitory activity leaching out of the tubing was associated with only one constituent—acetyl tri-*n*-butyl citrate—but this plasticizer made up about 35% of the total weight of the tubing. It appears not to be acetyl tri-*n*-butyl citrate itself which possessed the activity, however, because addition of this oily immiscible fluid does not inhibit the uterus. But if the substance is shaken for a few minutes with water, inhibitory activity develops in the aqueous layer.

As PVC tubing is commonly used as part of the apparatus in many pharmacological experiments, these active substances contained in it might well interfere with either the efficiency of the preparation or in particular with the pharmacological analysis of perfusates or extracts.

The actions of morphine, pethidine and nalorphine on some blood vessel preparations

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In humans, morphine occasionally produces a hypotensive effect which is mainly due to peripheral vasodilation. Pethidine, nalorphine and levallorphan can have similar effects. While nalorphine or levallorphan antagonizes an already existing hypotension due to morphine or pethidine, it does not necessarily prevent the cardiovascular effects of subsequent injections (see Eckenhoff & Oech, 1960).

In anaesthetized laboratory animals peripheral vasodilation is again the dominating factor but analysis is complicated, in the case of morphine, by the rapid development of a prolonged tachyphylaxis (Schmidt & Livingston, 1933; Evans, Nasmyth & Stewart, 1952). This period of insensitivity is of appreciably shorter duration in isolated preparations, four of which were accordingly used in the present study (perfused rabbit ear and spiral strips of rabbit anterior mesenteric (portal) vein, descending thoracic aorta and pulmonary artery).

The predominant responses to morphine, pethidine and nalorphine were vasodilation in the rabbit ear and relaxation in the strip preparations. The effects were relatively weak, however, in that large doses of the drugs were required (rabbit ear: morphine, 200–2,000 μg; nalorphine, 60–1,000 μg; pethidine, 60–200 μg; strip preparations—final bath concentrations, as free bases: morphine, $4–12\times10^{-4}$ g/ml.; nalorphine, $1–12\times10^{-4}$ g/ml.; pethidine, 2×10^{-5} g/ml.), and even these only manifested effects if the preparations had first been stimulated by noradrenaline, phenylephrine or 5-hydroxytryptamine. The actions of morphine or pethidine were unaffected by equal doses of nalorphine applied within the preceding 1–20 min.

The non-specific nature of the vasodilation or relaxation caused by morphine or pethidine was further indicated by the ineffectiveness of atropine, pentolinium, phentolamine,