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,

propranolol and mepyramine as antagonists. As previous workers (Feldberg & Paton, 1951; Evans *et al.*, 1952) have reported partial antagonism of the cardiovascular effects of morphine by mepyramine, however, experiments were carried out to resolve this question for the isolated strip preparations. The results showed that morphine did not produce its relaxant action on the strips by the liberation of histamine. The further possibility that morphine might act by antagonizing tone due to endogenous 5-hydroxytryptamine (Gyermek, 1961) was also examined.

In the isolated preparations used, the vasodilator and relaxant actions of morphine, and possibly those of pethidine and nalorphine, do not seem to be mediated either by the liberation of known biogenic amines or by interaction with their specific receptors.

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The effect of phenylbutazone and indomethacin on stress-induced cortisol release in guinea-pigs

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During investigations on the effect of anti-rheumatic drugs on cortisol metabolism, we injected ^{14}C-cortisol into guinea-pigs (white, males) to determine the space of distribution and the decomposition rate for the hormone.

Forty, 80 and 160 min after injecting ^{14}C-cortisol into an exposed leg vein the animals were decapitated and bled. The concentration of ^{14}C-cortisol in plasma was determined by paper chromatography and radiochromatogram scanning and the total concentration of plasma cortisol (bound+free) by spectophotofluorometry.

In control animals the total plasma concentration of cortisol increased from a control level of 243 ± 42 (S.E. of mean) ng/ml. ($n=12$) up to 370 ± 54 ng/ml. ($n=7$) at 80 min after the injection. At 160 min after injection the control level was reached again. After pretreatment with phenylbutazone (150 mg/kg I.P. twice daily for 3 days) or indomethacin (100 mg/kg I.P. twice daily for 3 days), the stress-induced increase in plasma cortisol was lower (in the case of phenylbutazone-treatment the reduction was statistically significant) and the maximum concentration was found after 40 min (333 ± 55 and 333 ± 60 ng/ml., respectively). Eighty and 160 min after the injections the values did not differ from the control level for the two anti-rheumatics (195 ± 49 and 224 ± 69 ng/ml. respectively).

These figures show that experimentally induced stress affects the endogenous liberation of cortisol. Measurements of ^{14}C-cortisol, however, showed that the rate of cortisol disappearance was unaffected by the various pretreatments.