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 $243 \pm 42$ (S.E. of mean) ng/ml. ($n=12$) up to $370 \pm 54$ 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 ($333 \pm 55$ and $333 \pm 60$ ng/ml., respectively). Eighty and 160 min after the injections the values did not differ from the control level for the two anti-rheumatics ($195 \pm 49$ and $224 \pm 69$ 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.