Lines per frame	125
Elements per line	250
Frames per s	4
Thermal resolution	0·1°–0·2° C at 30·0 °C

Display unit

Oscilloscope with 35 mm or " Polaroid " camera attachment.

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Trial of etorphine hydrochloride (M99 Reckitt) in carcinoma pain: preliminary report

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The thebaine derivative etorphine (M99, Reckitt) has a potency in laboratory animals approximately 1,000 times that of morphine (Blane, Boura, Fitzgerald & Lister, 1967). Like morphine it is addictive in monkeys (Deneau & Seevers, 1964), and can cause respiratory depression. Nevertheless, ultra-rapid upt ke without untoward side-effect after intramuscular or sublingual administration to rats (Blane, 1967) and dogs (Dobbs, Blane & Boura, 1969), combined with extensive experience of safety in a vast variety of species where etorphine in high dose is used as an immobilizing agent, indicated the desirability of a clinical trial to assess possible therapeutic utility.

In a pilot study of safety and efficacy, etorphine was given by intramuscular injection to twenty-seven patients for relief of pain in terminal malignant disease. Three patients received more than one dose of the drug and two were more satisfactorily stabilized during their last weeks on etorphine plus heroin than they had been on heroin alone.

The drug was found to be a clinically efficacious analgesic at doses of 1 μg/kg, having rapid onset (less than 10 min after intramuscular injection) and moderately short duration of action (about 2 h). There was a high incidence of sedation at effective analgesic dose-levels and a significant incidence of undesirable light-headedness at the top dose levels. Bradypnoea caused clinical anxiety on one of the 185 occasions etorphine was injected. Nalorphine proved to be effective in restoring the respiratory rate to normal within a few seconds of injection. The dose rate in this subject was close to 2 μg/kg.

Sublingual etorphine (tablets) were prescribed for thirty-two cancer patients. In more than 5,000 treatments the dose was most commonly 100 μg (per man) but varied between 50 and 400 μg. The only side-effect was occasional slight sedation. Etorphine was found to be an effective analgesic and was preferred to alternative

drugs in eighteen out of the thirty-two cases, often in combination with other analgesics.

Since etorphine did not cause vomiting it was especially useful in patients suffering from nausea or vomiting with their regular, oral analgesic. Use of etorphine made it possible for these patients to be maintained on oral medication, often to the end.

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The mechanism of the reversal of the effect of guanethidine by amphetamines in cat and man

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The reversal of the effects of guanethidine by amphetamines is well known (Day & Rand, 1962), but the mechanism of the antagonism is unclear. The effects of amphetamines on the release of guanethidine in cat and man have therefore been examined.

The isolated cat spleen perfused with oxygenated Krebs was labelled with a solution containing ^{3}H-guanethidine (10^{-6} g/ml) for 20 min and then washed out with drug-free Krebs solution. Collections (2 min) of the effluent perfusate were assayed for noradrenaline and ^{3}H-guanethidine before and during splenic nerve stimulation at 30 Hz for 10 s at 30 min intervals. This dose of guanethidine caused just-complete block of the splenic response to nerve stimulation during the first stimulation period after wash-out.

In four experiments an intra-arterial injection of dexamphetamine (20 μg) reversed the blocking effects of guanethidine. The times of the injection varied, being before the second, third, fifth and sixth stimulation periods after washing out guanethidine, at which times the response of the spleen was reduced by 50–90%. The injection of dexamphetamine did not cause splenic contraction but produced a striking increase in the resting output of guanethidine without releasing noradrenaline. The lack of splenic response despite the release of large amounts of guanethidine indicates that under these conditions guanethidine has no post-synaptic agonist properties. When the spleen was subsequently stimulated, the release of both noradrenaline and guanethidine was enhanced. The noradrenaline/guanethidine ratio of samples obtained during stimulation was greater after (1·7) than before (0·7) dexamphetamine reversal. This is probably a result of blocking the reuptake of noradrenaline to a greater extent than that of guanethidine. Both reduction of the extravesicular