The respiratory pattern was recorded on a Mingograf 81 recorder from a pneumotachograph. The e.c.g. and BP record were similarly recorded. The BP was measured directly from a polyethylene catheter inserted percutaneously in the radial artery, from which blood samples were obtained for the determination of pO_2 pCO_2 and halothane concentrations. A fourth channel was used to record the e.e.g. from two frontal electrodes. In addition, the e.e.g. signal was transmitted over a telephone data link to an Elliott 903 computer for on-line frequency analysis.

Althesin produced rapid anaesthesia in all patients. Apnoea followed induction in every patient given the larger dose (mean duration 146 s) and in five patients given the smaller dose (mean duration 36 s). This difference in duration of apnoea was significant ($P<0.05$). In group one the arterial pCO_2 rose from 38 mmHg before induction to 50·5 mmHg at the end of apnoea, and in group two from 34 mmHg to 43·5 mmHg. Both these rises were significant ($P<0.001$).

The heart rate increased in every patient from a mean of 62 beats/min to a mean maximum of 88/min in the first group and from 68/min to a mean maximum of 88/min in the second group. This maximum rate was always reached within 1–2 min of induction, and no dysrhythmias were observed. Simultaneously, the mean BP fell in five patients in group one (73 mmHg to 54 mmHg) and in all patients in group two (81 mmHg to 68 mmHg).

The e.e.g. records of patients in group one showed periods of suppression of activity after induction, which were not seen in patients in group two. Frequency analysis of the e.e.g. in all patients produced consistent spectra before and after induction. The pre-induction spectra were all fairly flat over the range 5–30 Hz with a large but variable amount of lower frequency activity, probably caused by movement artefacts. After induction, a distinct change developed in the shape of the spectra ; the amplitude of the e.e.g. decreased linearly with increase of frequency. This pattern has also been observed following thiopentone induction and during deep halothane anaesthesia.

The equipotent dose ratio of diamorphine and morphine administered by mouth

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Terminal cancer patients prescribed a diamorphine and cocaine elixir were randomly divided into diamorphine and morphine receiving groups. The traditional diamorphine:morphine dose potency ratio of 1:2 was initially accepted as correct. Thus, patients in the morphine group prescribed, say, diamorphine 10 mg were supplied with a mixture containing morphine 20 mg/dose. The study was 'double-blind' and increases in 'diamorphine equivalents', though not cocaine, were made as needed. Maximum doses supplied were diamorphine 40 mg and morphine 80 mg/dose.

On account of the limited shelf life of diamorphine solutions (Rizzotti, 1935), any still unused after two weeks was discarded. After death a record was made of the maximum dose of diamorphine or morphine received orally by patients who

had received one of the mixtures for at least five days. This was found to reflect the effective analgesic dose on which the patient had been stabilized.

Of the 116 patients, 61 received diamorphine and 55 morphine. Other drugs, prescribed by the ward physician when necessary, were distributed equally between both groups. A comparison of the maximum doses revealed unequal distribution, the morphine group being 'weighted' in favour of the smaller doses. By dividing the diamorphine group into high (>20 mg) and low ($\leqslant 20$ mg) subgroups, it is possible to compare the diamorphine with the morphine doses at three different ratios. A balanced distribution occurs at a ratio of 1:1·5.

As a more exact test the total daily dose of diamorphine or morphine was compared after three weeks in the 41 surviving patients. The totals were compared in the same way as the maximum individual doses. A ratio slightly in excess of 1:1·5 was obtained.

The fact that the equipotent oral dose ratio is other than unity demonstrates that diamorphine can survive, at least in part, in a form other than morphine until it has been absorbed by the alimentary tract.

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REFERENCE

RIZZOTTI, G. (1935). Contributo allo studio delle alterazioni delle soluzioni acquose di eroina. *Arch. int. Pharmacodyn. Thér.*, **52**, 87–96.

Effects of chlorpromazine on thermoregulatory reflexes in man

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Although chlorpromazine is used primarily as a major tranquillizer, it also produces a fall in body temperature when administered systemically to man and animals in relatively large doses (Dobkin, Gillent & Lamoureaux, 1954; Kopera & Armitage, 1954). Use is made of this property of the drug in the production and maintenance of hypothermia in clinical medicine (Gray & Graham, 1971). However, the mechanism by which chlorpromazine produces its effect on temperature is unclear. It could act within the central nervous system by reducing the sensitivity of thermoregulatory processes, or peripherally by interfering with thermoregulatory vasomotor control by producing vasodilatation (Ginsburg & Duff, 1956).

It has been shown in man (Cooper, Cranston & Snell, 1964) that a linear relationship exists between an applied thermal load (cal kg^{-1}) and the integral of the induced oral or ear temperature change (°C min). The slope of the line relating these two variables provides an index of thermal sensitivity (S_t) with dimensions of cal kg^{-1} °C min^{-1}. Control estimations of S_t were made in six healthy male volunteers. Each subject then received oral chlorpromazine (30 mg/day in divided doses) for 3 days; S_t was determined at the end of this period and again one week later. Mean pre-treatment and post-treatment (1 week) values for S_t were