Quantities as small as 300 pg/ml can be measured by this method.

Twenty patients received diamorphine hydrochloride and twenty-four morphine sulphate, administered orally every 4 h in an elixir. The dose of diamorphine hydrochloride ranged from 5-60 mg (median 10 mg) and the dose of morphine sulphate from 3.75-90 mg (median 19 mg). The two groups were comparable in terms of sex, age, primary site and survival. Although most blood samples were obtained before or shortly after the 9 a.m. drug round, five specimens were obtained more than 40 min later. At the time of venepuncture all the patients had received an opiate regularly for more than a week.

The serum concentrations showed a significant correlation with the dose administered. Linear correlation coefficients for the two groups were: oral diamorphine, $r = +0.91$ ($p < 0.001$), oral morphine, $r = +0.73$ ($p < 0.001$) and for both groups, $r = +0.79$ ($p < 0.001$). There was no apparent difference between the two groups in the serum concentrations measured at comparable dose levels.

Our results demonstrate that it is possible to measure unconjugated morphine in serum from patients who have been receiving either diamorphine or morphine by mouth regularly for a number of days. It is detectable both at the beginning and the end of the 4 h interval between administrations. The positive correlation between dose and serum concentration supports recently published data showing a similar association between the dose administered and urinary recovery (Twycross, Fry & Wills, 1974). Further experiments to determine rates of absorption and elimination for the two drugs are planned in both volunteers and patients.

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A microsomal oxidase system in rat intestinal mucosa

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Orally administered drugs may be metabolized before reaching the general circulation. For example, L-dopa is decarboxylated in the human gastric tissue (Rivera-Calimlin, Dujovne, Morgan, Bianchine & Lasagna, 1971); clorazepate is converted to N-desmethyldiazepam, also in the human stomach (Boehringer Ingelheim Ltd., personal communication); orally administered isoprenaline is conjugated in the gut wall during absorption (Dollery, Davies & Connolly, 1971) and propranolol has been suggested to be extensively metabolized during the first passage through the liver (Shand, Nuckolls & Oates, 1970).

In an earlier report we showed that chlorpromazine is destroyed in rat intestinal tissue *in vitro* and *in vivo* (Curry, D'Mello & Mould, 1971); this reaction is believed to occur in man (Sakalis, Curry, Mould & Lader, 1972). It is possible that a mixed-function oxidase system similar to that in liver may exist in the rat intestine, as Takesue & Sato (1968) have already demonstrated the existence of enzymes associated with such a system in the microsomal fraction isolated from the mucosa of another species, rabbit. In contrast to this, Chhabra, Pohl & Fouts (1974) were unable to detect one of the enzymes concerned, cytochrome P-450, in the mucosa of rat small intestine. We would like now to report on the separation and partial evaluation of a microsomal fraction from the mucosal cells of rat small intestine, containing cytochrome P-450.

The mucosa was scraped off 10 cm lengths of proximal rat small intestine and homogenized in 0.05 M phosphate buffer pH 7.4 containing 1.15%

KCl. The homogenate was centrifuged at 10,000 g for 20 min, followed by a further centrifugation of the supernatant at 140,000 g for 90 min, to obtain the microsomal pellet. The pellet was then resuspended in buffer and, following a further centrifugation at 140,000 g for 45 min, it was finally suspended in 0.1 M phosphate buffer pH 7.6. Cytochromes P-450 and b_5 were determined by the method of Omura & Sato (1964) and NADPH-cytochrome c reductase by the method of Phillips & Langdon (1962). The metabolism of foreign compounds was measured over 30 min at 37°C using the incubation conditions described by Mazel (1971).

The concentration of cytochrome P-450 was 9 times lower than that found in liver (intestine 0.046 ± 0.004 nmol.mg protein^{-1}; liver 0.43 ± 0.05), of cytochrome b_5 was 5 times lower (intestine 0.080 ± 0.014 nmol.mg protein^{-1}; liver 0.42 ± 0.08) and of NADPH-cytochrome c reductase was $2\frac{1}{2}$ times lower (intestine 57.4 ± 5.1 nmol.mg protein^{-1} min^{-1}; liver 142 ± 3.10). Pretreatment with phenobarbitone (75 mg/kg daily, i.p.) over a period of 3 days lowered slightly the mean concentrations of cytochrome P-450 (0.031 ± 0.006 nmol.mg protein^{-1}) and NADPH-cytochrome c reductase (44.3 ± 4.1 nmol.mg protein^{-1} min^{-1}) but appeared to increase the concentration of cytochrome b_5 (0.108 ± 0.013 nmol.mg protein^{-1}). The 10,000 g supernatant was shown to be N-demethylate, ethylmorphine and aminopyrine.

This evidence suggests the presence of a mixed-function system in rat intestinal tissue similar to that found in liver.

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The acetylation of HC-3 by choline acetyltransferase

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The main action of HC-3 on cholinergic transmission is presumed to be an inhibition of the uptake of choline into the presynaptic nerve terminal (MacIntosh, Birks & Sastry, 1956). It has also been suggested that HC-3 might itself be incorporated into the nerve terminal where it may be acetylated by choline acetyltransferase (ChAc) and subsequently released as a false neurotransmitter (Rodriguez de Lores Arnaiz, Zieher & de Robertis, 1970; Hemsworth, 1971).

The acetylation of HC-3 by ChAc *in vitro* has been studied in a number of laboratories with conflicting results (Diamond & Milfay, 1972). The present experiments were therefore performed to investigate these differences in the acetylation of HC-3. Several different established methods for determination of ChAc activity were utilized to detect any acetylated product that might be formed by enzymatic acetylation.

The observed acetylation of 10^{-3}M HC-3 by soluble rat brain ChAc, compared with the acetylation of choline at the same concentration, varied between 0 and 27% depending on the procedure used for the isolation of the acetylated product.