an important role in the release of beta-lipoprotein in fatty liver induced by a low-protein diet.

Thus, the present work demonstrates that phospholipid has a curative effect on experimental fatty liver and that the effect is due to the release of lipoprotein from the liver.

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URINARY EXCRETION PATTERNS OF MORPHINE IN HUMANS FOLLOWED BY AN RADIOIMMUNOASSAY METHOD

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Recently, morphine was added to the list of compounds which can be detected in biological fluid by radioimmunoassay methods (1-4). Production and the specificity test of the antibodies directed to three morphine derivatives have led to development of radioimmunoassay of morphine by the use of morphine 3-glucuronide (M-3-G) directed antibody (5). In the present experiment, applicability of the method for clinical use was tested.

Morphine HCl was injected i.v. into five humans as the basal anesthetic in doses of 10 to 50 mg/patient and thereafter 24 hr urine samples were collected for one week. During the experimental period, other drugs known to interfere the binding of morphine to the antibody were not ingested. The sample was stored below -20°C before analysis and the radioimmunoassay of morphine was carried out as previously described (5). Before analysis, the urine sample was warmed to room temperature and the supernatant analyzed. The quantity of the drug in an aliquot (100 μ l) of the sample or of its dilution up to 50 fold, was read off by a standard curve run for M-3-G in the presence of the corresponding amount of normal urine, as the urine contained the interfering factor(s).

Results are shown in Table I. On the average, more than half of the drug was recovered in the first sample. For the next 4 days, the excretion of the drug was detectable in all cases and in two for an additional two days. The results parallel those found in

TABLE I. Analyses of urine samples from humans on morphine

Urine collection (hr)	dose, i.v.				
	A 10 mg	B 20 mg	C 30 mg	D 40 mg	E 50 mg
0-24	*5.334 (53.3) ** 3810	12.407 (62.0) 2385	8.775 (29.3) 975	26.100 (65.3) 1450	35.100 (70.2) 1190
24-48	0.525 (5.3) 2500	0.500 (2.5) 2500	2.880 (9.6) 2400	2.220 (5.6) 1900	1.720 (3.4) 2000
48-72	0.870 (8.7) 1350	0.189 (0.9) 700	1.163 (3.9) 2300	2.090 (5.2) 2020	0.250 (0.5) 500
72-96	0.350 (3.5) 1100	0.902 (4.5) 1100	0.920 (3.1) 1550	1.130 (2.8) 1580	0.151 (0.3) 1080
96-120	0.260 (2.6) 1200	0.243 (1.2) 900	0.549 (1.8) 1100	0.702 (1.8) 1130	0.077 (0.2) 1100
120-144	0.084 (0.8) 1200	0.000 (0.0) 1400	0.051 (0.2) 1500	0.426 (1.1) 1350	0.000 (0.0) 1800
144-168	0.000 (0.0) 1750	0.000 (0.0) 1450	0.045 (0.2) 900	0.124 (0.3) 1850	0.000 (0.0) 2600
0-168	7.423 (74.2)	14.241 (71.2)	14.383 (47.9)	32.792 (82.0)	37.298 (74.6)

* indicates the amounts of morphine 3-glucuronide and free morphine (mg). Figures in parentheses indicate the amount of the drugs as a percent of the dose.

** Urine volume (ml).

Patients: A—Myoma of uterus, B—Gallstones, C—Pancreatic cancer. The bile was conducted outside for surgical purpose. D—Uterine cancer and E—Aortic insufficiency.

rats in which 10 mg/kg of morphine or codeine was given and the drug was detectable for at least five days after the administration even without manipulation of the sample (5). The drug excreted in urine from humans was in a more diluted concentration than that in the rat. However, peculiar excretion patterns were seen in urine from patients A, B. There was a second peak in the pattern, which never had appeared after administration of either dihydrocodeine to healthy adults or morphine to rats (5). The rigid specificity of the M-3-G antibody excludes the possibility that the other agents ingested by the patients could produce a false pattern by interfering with the morphine-antibody binding. In fact, the urine of the volunteers to whom an anti-inflammatory drug with high binding affinity to serum protein had been given, exhibited no inhibitory influence on the morphine-antibody binding (unpublished data). Therefore, such a peculiar excretion pattern may be attributed to abnormal conditions such as depressed function of the internal organs, venous hyperemia following surgery, etc.

The radioimmunoassay method can indeed be applied to determine the excretion levels of a drug, and our results herein suggest that development of methods for other therapeutics would lead not only to a re-evaluation of the drugs themselves but could be utilized as a diagnostic indicator of the physiological conditions involved.

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