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Enteral absorption of hyoscine *N*-butylbromide

SIR,—In a recent paper, Herxheimer & Haefeli (1966) investigated the oral absorption of hyoscine *N*-butylbromide (Buscopan) in man using the appearance of atropine-like effects as a criterion of oral efficacy. Oral doses of the drug up to 600 mg (approximately 10 mg/kg) failed to produce the effects seen after parenteral injection and it was concluded that the drug was not absorbed from the gastrointestinal tract. However, the results of experiments comparing the toxicity of hyoscine *N*-butylbromide administered by different routes provides evidence for the enteral absorption of the compound.

Three similar groups of Sprague-Dawley rats (females), which had been fasted for the preceeding 12 hr, underwent laparatomy under ether anaesthesia, after which the drug or physiological saline was injected through a fine needle into the lumen of the stomach and duodenum. The operation wound was then sutured, and each animal injected subcutaneously with physiological saline or drug. One group of rats was given the drug subcutaneously, saline being injected into the stomach and duodenum. A second group was given the drug into the stomach, saline being injected subcutaneously and into the duodenum. In the third group of animals, the drug was given into the duodenum and saline was injected subcutaneously and into the stomach. By this experimental design, operative stress and number of injections per animal were evenly distributed throughout the groups. The animals were observed for the following 24 hr and the LD 50 obtained for each route of administration was calculated using the method of Litchfield & Wilcoxon (1949). The values were as follows: LD50 of hyoscine *N*-butylbromide (1) subcutaneously = 510 (386–673) mg/kg, S = 1·365; (2) instilled into the stomach = 1040 (897–1206) mg/kg, S = 1·130; (3) instilled into the duodenum = 180 (154–211) mg/kg, S = 1·195.

In the group of animals given the drug into the duodenum, convulsions started 1 to 2 min after injection and death occurred within 4 to 10 min. When the drug was given subcutaneously or injected into the stomach, the animals did not die for several hr. The drug given into the duodenum was 2·8 times more toxic than when given subcutaneously, which, together with the quick onset of effects, indicates its rapid and good absorption. The possibility that the lower toxicity of hyoscine *N*-butylbromide given into the stomach is caused by decreased gastric peristalsis and slowed passage of the drug to the site of absorption in the small intestine is now being investigated.

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