determined colorimetrically using pure hematin as a standard. No other toxic symptoms than transient nausea and vomiting were noted. The results show a marked increase in blood volume in all cases, and indicate that several days are required for complete elimination of the acacia. The results of the spectroscopic method, herewith described, and of the Hartmann method are in good agreement as a whole, as shown in Table I. But it is to be noted that the Hartmann method is much more laborious, time-consuming, and requires a larger blood sample.

7796 C

Action of Dilaudid on the Gut.*

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David[1] has reported a comparative study of metabolic and other effects of dihydromorphinone hydrochloride ("Dilaudid" N.N.R.) and its parent substance, morphine. This new keto-derivative has a narcotic potency 5 to 10 times that of morphine, but apparently its use is not attended by freedom from the undesirable side-effects of morphine to quite the extent suggested by Alvarez.[2] Study of the relative addiction tendencies of the 2 drugs in human subjects is of great importance but will require competent clinical observation over an extended period because of the intrinsic difficulties in such a comparison. Meanwhile it is of interest to investigate the more easily measurable physiological side-actions of the new agent, as has been done for certain subjective and objective effects by David.

In regard to the effect of dilaudid on the gastro-enteric tract, David found no marked difference from morphine in the occurrence of nausea, vomiting, diarrhea, and constipation in student volunteers to whom there was administered subcutaneously a dose equivalent in narcotic efficacy to a therapeutic dose of morphine. Of 74 subjects receiving 0.01 to 0.04 mg. per kg. of dilaudid, 58% were nauseated, 20% vomited, 8% showed diarrhea and 30% con-

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[1] David, N. A., *J. Am. Med. Assn.*, 1934, **103**, 474.

[2] Alvarez, W. C., *Proc. Staff Meet., Mayo Clinic*, 1932, **7**, 480.

stipation in comparison with 63% nausea, 27% vomiting, 3% diarrhea and 37% constiption respectively in 41 subjects receiving 0.14 to 0.22 mg./kg. of morphine sulphate.

Vomiting and nausea, which occur after the 2 drugs, are of central origin and it seems in humans that dilaudid does not vary much from morphine in the ratio of emetic dose to therapeutic dose. Leake[3] found that 10 mg./kg. of morphine sulphate causes emesis in dogs within 12 minutes, while we caused vomiting in only one of 4 dogs injected with 2 mg./kg. of dilaudid, although marked salivation and licking of chops were present in all. With subcutaneous dilaudid in dogs, the vomiting center may be too rapidly depressed, as with intravenous morphine, for emesis to occur regularly. That dilaudid definitely depresses the vomiting center after a slight initial stimulation, as demonstrated for morphine by Leake,[3] is shown by the fact that 1 mg./kg. of apomorphine HCl subcutaneously one hour after the administration of dilaudid failed to elicit any symptoms of vomiting whatsoever.

In order to ascertain whether or not further evidence might support David's observations on humans that dilaudid has essentially the same qualitative action on the gut as morphine, a series of experiments on animals were undertaken. As previously,[4] 3 pharmacological techniques were used. Macht's method indicated but little depression of peristalsis in the small intestine during the second hour following a subcutaneous injection of 0.1 mg./kg. of dilaudid, since the test meal traversed 53%±9% of the tract between pylorus and anus in 50 minutes as compared with 56%±6% in untreated animals. In rabbits, Eddy's technique demonstrated a depression of 75-100% in the number of rabbits of 10 defecating per hour, starting almost immediately after subcutaneous administration of 0.1 mg./kg. of dilaudid. Only one of 20 rabbits treated showed diarrhea, occurring after the fourth hour of observation. Results of these 2 tests indicate that the delay is chiefly in the colon and rectum, as is the case with morphine in man.[5] On strips of duodenum isolated from 6 different rabbits and suspended in oxygenated Locke's solution at 37°C., dilaudid was found to have slightly greater action than morphine in comparable therapeutic concentrations, particularly as shown by spastic contraction after washing out the drug. This suggests greater relative intensity of withdrawal symptoms, should dilaudid addiction occur. On this basis, also, dilaudid should be

[3] Leake, C. D., *J. Pharmacol. Exp. Therap.*, 1923, **20**, 359.

[4] Emerson, G. A., PROC. SOC. EXP. BIOL. AND MED., 1933, **31**, 278.

[5] Zehbe, M., *Ther. Mon.*, 1913, **27**, 406.

more helpful than morphine in preventing post-operative intestinal stasis.[6] The isolated gut shows no qualitative differences in reaction to morphine and dilaudid, and a morphinized gut shows no further depression with dilaudid and vice versa. In general, the findings of Uhlmann and Abelin[7] were confirmed in regard to the relative effects of various concentrations of morphine. While these observations are merely indicative of possible effects in patients, it may be expected that dilaudid will have much the same qualitative action on the gut as morphine but probably with less intensity in equivalent therapeutic dosage.

7797 C

Transformation of Hemolytic Streptococci.*

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Two methods of typing hemolytic streptococci have been suggested by recent investigators: (a) the Lancefield method[1] based on the existence of at least 5 antigenically distinct type-specific "carbohydrates" in different human, veterinary and environmental strains, and (b) the Tillett-Garner-Madison technic,[2] based on the presence of at least 3 different type-specific fibrinolysins. Both methods assume that the selected diagnostic character is genetically stable.

To test this assumed stability an attempt was made to transform a typical antihuman fibrinolytic strain of *S. hemolyticus* into a non-fibrinolytic strain of apparent veterinary origin. The strain selected for this attempt was originally isolated by Lancefield from a case of scarlet fever. The strain (C203) is specifically lytic for human fibrin and contains only one type-specific carbohydrate.

To make the proposed transformation, 4 rabbits were injected intraperitoneally with doses varying from 2 to 20 cc. of a 24-hour

[6] Orr, T. G., *Ann. Surg.*, 1933, **98**, 835.

[7] Uhlmann, F., and Abelin, R., *Z. exp. Path. Therap.*, 1920, **21**, 58.

*Supported in part by the Rockefeller Fluid Research Fund of Stanford University School of Medicine.

[1] Lancefield, R. C., *J. Exp. Med.*, 1933, **57**, 571.

[2] Tillett, W. S., and Garner, R. L., *J. Exp. Med.*, 1933, **58**, 485. Madison, R. R., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 641.