TABLE II.
Summary of Aspartic Acid Deaminase Experiments.

Exp. No.	Ammonia nitrogen formed			
	No supplement, γ	Biotin, γ	Oxybiotin, γ	Desthiobiotin, γ
1	11.8	18.0 (.001 γ)	17.3 (.001 γ)	—
2	11.5	58.5 (.001 γ)	25.0 (.001 γ)	—
3	10.0	51.5 (.001 γ)	16.0 (.001 γ)	—
4	3.5	30.0 (.001 γ)	41.5 (1.0 γ)	—
5	13.0	57.5 (.001 γ)	—	15.0 (.001 γ)

Figures in parentheses indicate the quantity of supplement tested per 2 ml reaction mixture.

acid at pH 7 then was determined according to the protocol given in Table I. A strain of *Proteus vulgaris* was the organism employed. The oxybiotin* (O-heterobiotin)* and the desthiobiotin used were racemic mixtures. The quantities used in this paper are in terms of active D– component employed.

Results and discussion. The results that have been obtained are summarized in Table II. It is apparent from experiments 1-3, where biotin and oxybiotin were tested at equivalent levels, that oxybiotin is active in stimulating the aspartic acid deaminase system, although it is somewhat less active than is biotin. As demonstrated by experiment 4, when tested at a high level (1.0 γ/tube) oxybiotin can replace completely the functions of biotin in the bacterial deamination of aspartic acid. Desthiobiotin, as the results of experiment 5 indicate, is essentially inactive. Thus it appears that ring closure is essential for activity in the present system as it is in other systems involving biotin that have been studied previously.

Summary. Oxybiotin is less active than biotin in stimulating the aspartic acid deaminase system of bacterial cells that have been inactivated by exposure to M phosphate buffer of pH 4. In sufficient amount, however, oxybiotin duplicates completely the stimulation produced with biotin.

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Effect of Hepatectomy upon the Analgetic Action of 1 Methadone.* (17983)

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While it may be considered that the liver is probably the chief site of detoxification of 1 Methadone, it was of interest to test this hypothesis. It was proposed to determine this by examining the effect of partial hepatectomy upon the duration of analgesia following a standard dose of the drug administered to rats.

* Assisted in part by a grant from Hoffmann-La Roche, Inc., Nutley, New Jersey.

Methods. Male albino rats (Red Bank) weighing 250 to 350 g were used. Analgesia was measured using a modification of the D'Amour Smith method(1,2) in which radiant heat is applied to the terminal portion of the rat's tail. One of the chief features

1. D'Amour, F. E., and Smith, D. L., *J. Pharmacol.*, 1941, v72, 74.

2. Bonnycastle, D. D., and Molland, J., *Fed. Proc.*, 1948.

of this modification is that the rats determine by their original reaction times, the maximal allowable stimulation at any one time. This restriction permits the repeated application of the stimulus without any great hazard of producing tissue injury.

After preliminary experiments, it was decided that a standard intraperitoneal dose of 1.5 mg/kg 1 Methadone was suitable, because this dose was sufficient to abolish a reaction to the stimulus within the period of stimulation in all cases, and yet the animals had returned to normal within two hours. The experimental group of animals, 18 in number, was treated with this standard dose of 1.5 mg/kg of 1 Methadone, and the effect of the drug observed for 3 hours.

The next day, partial hepatectomy was carried out upon 9 of these rats, following the method of Higgins and Anderson(3). It was calculated that for this group of animals, 72 to 81% of the total liver had been removed. A mock operation, consisting of laparotomy alone, was performed on the remaining 9 rats of the group. Five days postoperatively the animals were tested with 1.5 mg/kg intraperitoneally of 1 Methadone and subsequently on the 15th postoperative day. The differences in duration of analgesia were compared statistically by standard methods.

Results. In the control series the animals all exhibited a failure to react to the stimulus following the administration of the 1 Methadone but all had returned to their previous levels of reaction within 2 hours.

It is seen in Fig. 1 that in response to the standard dose there is a difference in the incidence and duration of analgesia between the unoperated normal control values and the post-laparotomy values. This difference in the duration is significant. The effect of the standard 1.5 mg/kg dose of 1 Methadone upon the partial hepatectomized group and the control laparotomy group is shown in Fig. 2. Here the difference in duration of analgesia is highly significant, as also is the difference between the normal control and partially hepatectomized group.

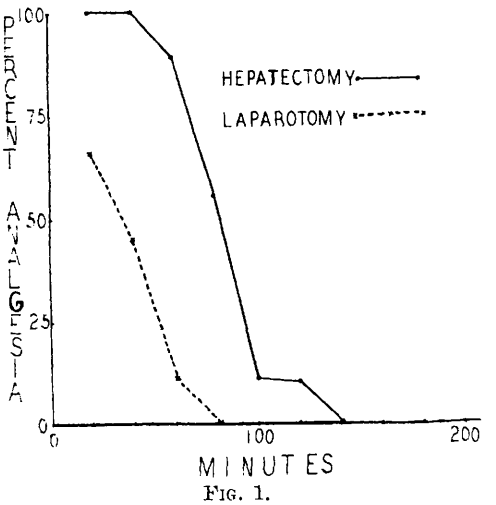

FIG. 1.

Fig. 3 presents the values obtained 15 days postoperatively, and shows that the two groups, *i.e.*, the laparotomy and partially hepatectomized groups, react to the drug in essentially the same manner as before the operations.

Discussion. The effect of partial hepatectomy in increasing the duration of the action of 1 Methadone as tested in this manner is of interest. It does suggest that the liver is of great importance in the metabolism of the drug. At the time these experiments were completed, a report by Chen-Yü Sung *et al.*(4) appeared in which essentially the same findings were obtained for d,l Methadone. These investigators also stated that *in vitro* studies led to the conclusion that the liver was the chief site of metabolism of the drug.

It is of interest that there was a significant degree of difference between the effect of the drug in the laparotomy-control group and the effect on the same animals before operation. This again emphasizes the fact that in such experiments control animals should be used upon which sham operations have been carried out.

While at 15 days postoperatively the livers of the partially hepatectomized group had apparently regenerated sufficiently so that the response was similar to that obtained in

3. Higgins, G. M., and Anderson, R. M., *Arch. Path.*, 1931, v12, 186.

4. Sung-Chen Yu, and Way, E. L., *J. Pharmacol.*, 1950, v98, 172.

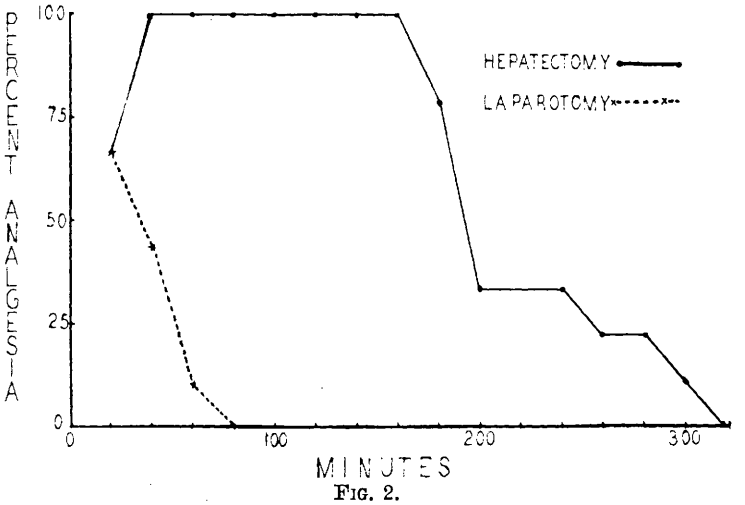

FIG. 2.

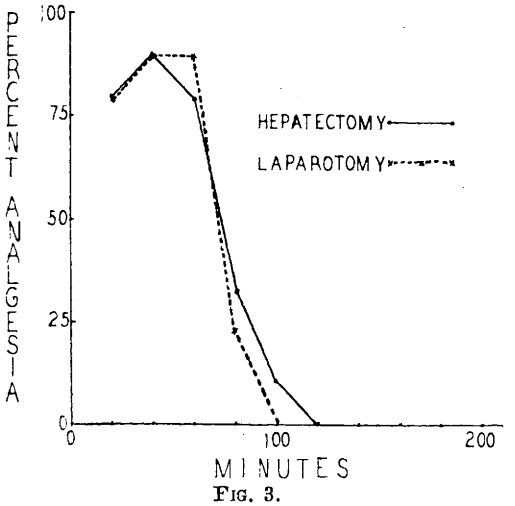

FIG. 3.

the control period, it cannot be taken to indicate that complete regeneration has taken place. In fact it has been stated that this takes 28 to 30 days(3) or possibly longer.

Summary and conclusions. A comparison of the analgetic response of 1.5 mg/kg intraperitoneally of 1 Methadone in normal, sham-operated and partially hepatectomized rats was carried out 5 days postoperatively, and 15 days postoperatively.

These experiments suggest that the liver is the chief site for the destruction of 1 Methadone.

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Persistence of Brunhilde Poliomyelitis Virus in Rodent Brain without Evidence of Adaptation.* (17984)

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Although all evidence indicated that non-Lansing types of human poliomyelitis virus would be difficult to adapt to nonprimate hosts, it seemed worthwhile to reinvestigate the problem using a virus of high titer and a reasonably large number of animals. The method of alternating passage between rhesus monkeys and other animals was employed in addition to passage from rodent to rodent.

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