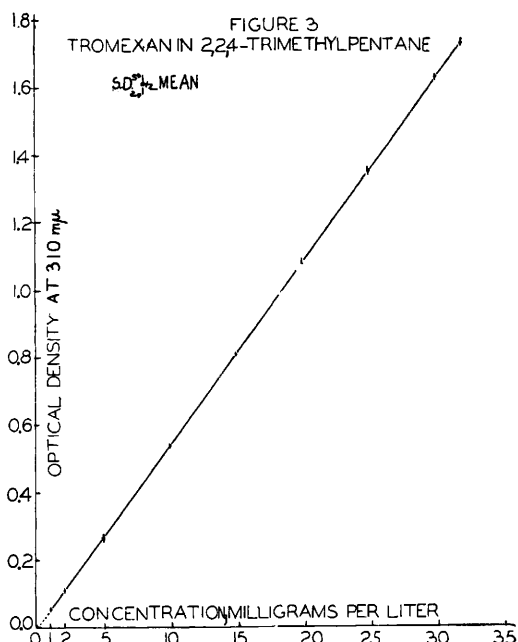
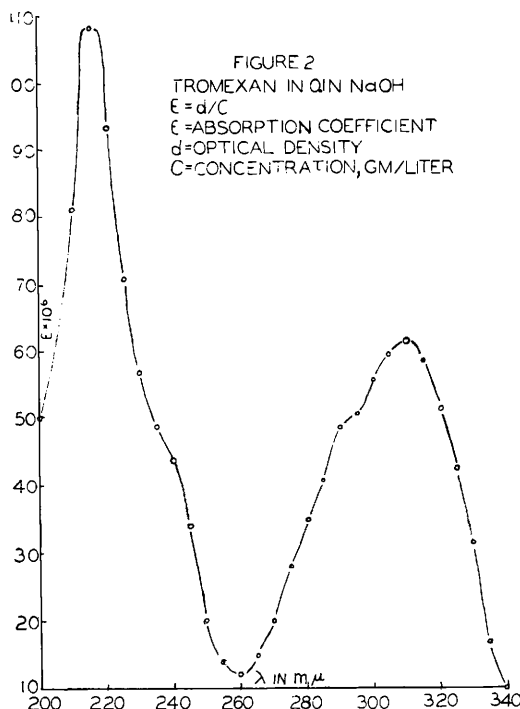


3.2% sodium citrate solution to every 9 cc of whole blood. Tromexan content determinations may be made with equal accuracy on plasma or serum using the test described above.

**Conclusions.** (1) Tromexan in amounts of .005 to .2 mg partitions from 1 ml of acidified



plasma into 5 ml of 2,2,4-trimethylpentane to the extent of  $97.2 \pm 3.5\%$ . (2) The optical density of such solutions varies in accordance with Beer's law. (3) On this basis a procedure for estimating plasma and serum concentrations of Tromexan by ultraviolet spectrophotometry was evolved.

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### Effect of Lactate on Renal Tubular Transfer of p-Aminohippurate in Man. (18893)

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The presence of sufficient quantities of acetate, pyruvate, or lactate in the ambient fluid of the renal tubule is associated with an increased uptake of p-aminohippurate by the tubular cells *in vitro* and an increased  $Tm_{PAH}$  in dogs(1,2). The present study was undertaken to determine the effect of parenterally

administered lactate on  $Tm_{PAH}$  in human subjects.

**Method.** The effect of intravenous administration of lactate on  $Tm_{PAH}$  was determined for 8 male subjects free of demonstrable renal

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TABLE I. Effect of Intravenous Infusion of Na Lactate or Na Bicarbonate on Glomerular Filtration Rates and  $T_{PAH}$  in Humans.

| Subject                       |     | Cl <sub>IN</sub> , cc/min |       | Tm <sub>PAH</sub> , mg/min |       | pH <sub>s</sub> at 38° |       | (BHC <sub>3</sub> ) <sub>s</sub> , meq/l |       | Plasma lactate, meq/l |       |
|-------------------------------|-----|---------------------------|-------|----------------------------|-------|------------------------|-------|------------------------------------------|-------|-----------------------|-------|
| Age                           | Exp | Control*                  | Exp†  | Control*                   | Exp†  | Control*               | Exp†  | Control*                                 | Exp†  | Control*              | Exp†  |
| Na-lactate administration     |     |                           |       |                            |       |                        |       |                                          |       |                       |       |
| 40                            | A   | 96.5                      | 115.8 | 76.8                       | 97.4  | 7.43                   | 7.47  | 24.5                                     | 29.2  | .49                   | 5.95  |
|                               | B   | 99.8                      | 111.3 | 76.2                       | 95.4  | 7.43                   | 7.49  | 25.2                                     | 28.5  | .38                   | 4.50  |
| 62                            | A   | 63.5                      | 78.8  | 84                         | 99.6  | 7.44                   | 7.48  | 25.6                                     | 29.7  | .63                   | 4.92  |
|                               | B   | 67.5                      | 85.6  | 84.1                       | 112.1 | 7.48                   | 7.50  | 24.6                                     | 30    | .53                   | 5.80  |
| 59                            | A   | 91.3                      | 112.4 | 55.8                       | 104.9 | 7.48                   | 7.52  | 27.8                                     | 29.8  | .50                   | 5.36  |
|                               | B   | 74.6                      | 87.6  | 72.1                       | 89.1  | 7.47                   | 7.51  | 27.1                                     | 31.1  | .45                   | 5.34  |
| 51                            | A   | 82.7                      | 93.1  | 52.4                       | 71.2  | 7.40                   | 7.48  | 26.7                                     | 30.8  | .42                   | 5.86  |
|                               | B   | 81.3                      | 90.9  | 55.9                       | 76.4  | 7.44                   | 7.51  | 26.8                                     | 31.8  | .38                   | 5.21  |
| 65                            | A   | 73.2                      | 99.5  | 69.6                       | 81.2  | —                      | —     | —                                        | —     | .45                   | 8.91  |
|                               | B   | 75.7                      | 92.5  | 72.4                       | 79.1  | 7.45                   | 7.49  | 24.8                                     | 29.2  | .50                   | 5.58  |
| 63                            | A   | 66.1                      | 79.2  | 72.3                       | 88.2  | 7.42                   | 7.47  | 24.1                                     | 27.7  | .57                   | 5.87  |
|                               | B   | 65.2                      | 74.3  | 72.4                       | 90    | 7.40                   | 7.45  | 25.5                                     | 28.3  | .38                   | 3.44  |
| 57                            | A   | 76.9                      | 87.1  | 63.9                       | 85.4  | 7.42                   | 7.50  | 26.7                                     | 30.3  | .62                   | 5.98  |
|                               | B   | 79                        | 93.9  | 70.6                       | 81.2  | 7.44                   | 7.50  | 26.7                                     | 29.4  | .49                   | 3.67  |
| 70                            | A   | 68.2                      | 79.7  | 71.5                       | 88.9  | 7.41                   | 7.46  | 24.8                                     | 27.7  | .74                   | 3.18  |
|                               | B   | 79                        | 81.2  | 66.1                       | 81.7  | 7.42                   | 7.47  | 22.4                                     | 24.8  | .62                   | 3.21  |
| Mn                            |     | 77.53                     | 91.43 | 69.76                      | 88.86 | 7.434                  | 7.486 | 25.55                                    | 29.22 | .509                  | 5.174 |
| Na-bicarbonate administration |     |                           |       |                            |       |                        |       |                                          |       |                       |       |
| 51                            |     | 82.7                      | 88.7  | 48.5                       | 51.8  | 7.38                   | 7.46  | 27.7                                     | 34.2  | .61                   | .46   |
| 62                            |     | 66.1                      | 72.6  | 78.5                       | 83.7  | 7.44                   | 7.46  | 26.2                                     | 29.6  | .65                   | .54   |

\* Mean of three 12-min urine collection periods before administration of Na lactate or Na bicarbonate.

† Mean of last four 12-min urine collection periods during administration of Na lactate or Na bicarbonate.

disease. Each subject was studied on 2 different occasions at intervals of a week or more. The experimental design was the same for all subjects except as noted. Using the saturation method outlined by Goldring and Chasis(3), 3 control urine collection periods, each of 12 minutes duration, were obtained for the estimation of  $T_{PAH}$ . During the first 5 minutes of the fourth collection period 100 cc of M r-lactate (100 mM) was injected intravenously. Immediately after this priming dose of M lactate, an intravenous infusion of 200 cc of 0.5 M lactate at a rate of approximately 4.0 cc/min. (2.0 mM/min.) was instituted. Following this fourth period which was 15 minutes in length, 4 more 12-minute collection periods were obtained. In one subject, age 70, only the lactate priming dose was given for the 2 tests. Arterial blood samples for determination of lactate, plasma inulin and PAH concentrations and serum pH ( $pH_s$ ) and  $BHCO_3$  concentrations,  $(BHCO_3)_s$ , were ob-

tained for every urine collection period except the second control period. To evaluate the relationship of changes in the  $pH_s$  and  $(BHCO_3)_s$  to the observed increase in  $T_{PAH}$  2 subjects were studied during the infusion of 200 cc of 0.45 M sodium bicarbonate following a primer dose of 100 cc of 0.9 M sodium bicarbonate. In 3 subjects the effect of the administration of the hypertonic solution of lactate on the renal blood flow was determined under the same condition of lactate administration that existed for the  $T_{PAH}$  determinations. Inulin was determined by the method of Harrison(4). PAH determinations, using diluted urine and cadmium sulfate filtrates of plasma, were made by the method of Bratton and Marshall(5). Lactate was determined according to the method of Barker and Summerson(6). The glass electrode method of

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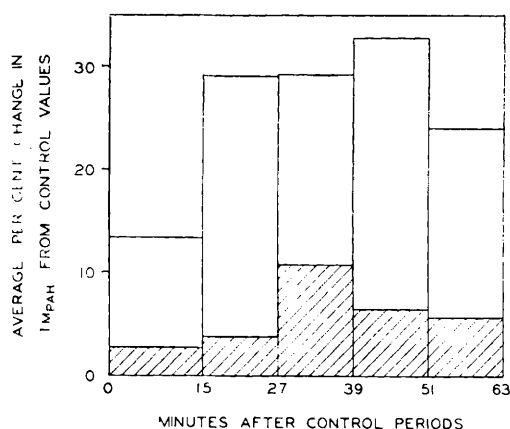


FIG. 1. Height of the clear columns represents the mean % change in  $Tm_{PAH}$  of 8 subjects receiving 200 mM of lactate intravenously for 5 consecutive urine collection periods. Height of the hatched columns represents the mean % change in  $Tm_{PAH}$  of 2 of 8 subjects receiving 180 mM of bicarbonate intravenously.

Dill, Daly, and Forbes(7) was used for the measurements of  $pH_s$ , and total  $CO_2$  content of the blood was determined by the micro-method of Shock and Hastings(8).  $(BHCO_3)_s$  values were computed by use of a nomogram(9).

**Results.** Following the injection of the lactate primer and during the lactate infusion there occurred a significant increase in  $C_{IN}$ ,  $Tm_{PAH}$ ,  $pH_s$ ,  $(BHCO_3)_s$ , and blood lactate concentration (Table I). Increases were observed in all 16 experiments on the 8 subjects. The average inulin clearance increased from 77.53 to 91.43 cc/min. ( $t = 84$ ,  $P < .01$ ) and the average  $Tm_{PAH}$  increased from 69.76 mg per min. to 88.86 mg/mm ( $t = 8.0$ ,  $P < .01$ ). Comparable  $t$  values for  $pH_s$ ,  $(BHCO_3)_s$ , and blood lactate concentration changes were 8.4, 13.2, and 11.2, respectively, all of which yield  $P < .01$ . The maximum mean per cent increase in  $Tm_{PAH}$  for the entire group of subjects following the injection of lactate was 33% and occurred during the urine collection period 39 to 51 minutes following the begin-

ning of lactate administration (Fig. 1).

The  $pH_s$  and  $(BHCO_3)_s$  displacements produced by the intravenous administration of sodium bicarbonate in 2 subjects (ages 51 and 62) were the same as those induced by lactate, but the administration of bicarbonate effected average increases in  $Tm_{PAH}$  of only 6.6 and 6.7%, respectively (Table I, Fig. 1). The intravenous administration of sodium bicarbonate in amounts of 10 and 14 g did not cause an elevation in the blood lactate levels contrary to what might be expected from other reports (Table I)(10,11,12).

In the 3 subjects studied, the average increase in renal blood flow was 11.2% of control values, and there was no appreciable change in the filtration fraction (Table II).

**Discussion.** The increase in  $Tm_{PAH}$  resulting from the lactate administration is considered to be predominantly a result of an increased rate of tubular cell excretion of PAH. The possibility of the observed changes in PAH excretion being due to an increased  $pH_s$  and/or  $(BHCO_3)_s$  is remote in view of the failure to produce changes in  $Tm_{PAH}$  with increased  $pH_s$  and  $(BHCO_3)_s$  by the administration of sodium bicarbonate comparable to those produced by lactate administration.

The possibility that the observed increases in  $Tm_{PAH}$  resulted from a perfusion of an increased number of nephrons is unlikely. The

TABLE II. Effect of Intravenous Infusion of Na Lactate on  $C_{IN}$  and  $C_{PAH}$ .

| Subject Age* | Inulin clearance, cc/min |       | PAH clearance, cc/min |        | Lactate, meq/l |       |
|--------------|--------------------------|-------|-----------------------|--------|----------------|-------|
|              | Control†                 | Exp‡  | Control†              | Exp‡   | Control†       | Exp‡  |
| 51           | 86.4                     | 100   | 478.9                 | 537.7  | .57            | 4.97  |
| 59           | 82                       | 91    | 436.5                 | 466.8  | .90            | 5.81  |
| 62           | 75.9                     | 84    | 369.4                 | 424.1  | .99            | 4.96  |
| Mean         | 81.43                    | 91.67 | 428.27                | 476.20 | .820           | 5.247 |

\* Same subjects as shown in Table I. Identified by age.

† Mean of three 12-min urine collection periods before administration of Na lactate.

‡ Mean of last four 12-min urine collection periods during the administration of Na lactate.

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*in vitro* studies of Cross and Taggart(1) have demonstrated that the rate of PAH accumulation by thin slices of rabbit kidney cortex is accelerated by the presence of acetate, pyruvate or lactate in the suspending medium. Under conditions of greatly decreased renal vascular resistance associated with increases in renal blood flow of 75 to 100 percent there is a small and variable change in  $Tm_{PAH}$  (3,13). The increases in renal blood flow observed under the present experimental conditions were between 10 and 15%. Even if this increase were indicative of a perfusion of previously ischemic nephrons, it would not

account for the increases in  $Tm_{PAH}$  observed.

**Summary.** The intravenous administration of sodium lactate causes a statistically significant increase in  $Tm_{PAH}$  in man. The average maximum increase amounted to 30% of the preinjection levels, and the effect was observed in each of 8 subjects tested twice. Neither the observed increases in  $pH_a$  and  $(BHCO_3)$  nor the changes in renal blood flow appear to bear a causal relationship to the increases in  $Tm_{PAH}$  produced.

The technical assistance of Mrs. Elsie Beard, Miss Margaret McCollum, Mr. Arthur Dinan, and Mr. W. Irving Jones is gratefully acknowledged.

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## Evaluation of Segmental Gastric Resection for Peptic Ulcer.\* (18894)

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For many years surgeons have done a three-quarter gastric resection for peptic ulcer in which the entire gastrin-containing area of the stomach along with a large segment of the acid-secreting area is excised utilizing the Billroth I or Billroth II technics. In order to overcome some of the limitations of these methods, it was proposed(1) to reverse the usual procedure of gastric resection by leaving the antrum intact, excising a larger fragment of the acid-secreting area, and leaving not more than 10% nor less than 5% of the total gastric area in the fundic segment. Diminution of acid secretion is then assured, and optimal conditions afforded for neutralization and digestion by bile and pancreatic juice. Moreover, it was hoped that segmental gastric resection might obviate some of the problems

of the "dumping syndrome" observed rather commonly following the conventional types of gastric resection.

Berger(2) has mapped out the parietal cell distribution on 8 normal stomachs. He pointed out that there are virtually none of these cells in the antral area, and that there are 50% as many parietal cells in the fundic and cardiac portions of the stomach as in the corpus. Ferguson(3) showed in a dog with the stomach divided into 4 distinct pouches that the upper pouch, representing 19% of the stomach by weight, secreted half as much acid per g of stomach on histamine stimulation as the middle area of the stomach representing 60% of the stomach by weight. This finding correlates well with Berger's parietal cell counts. The present study was undertaken to ascertain how much of the acid-secreting area of the stomach needs to be removed to protect against ulcer formation when the gastric antrum is allowed to remain intact.

**Present study.** Six series of dogs were studied.

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