the blood. If anything, the stilbesterol-treated ducks showed a lower rate of acetone body accumulation than did the control ducks.

It is now recognized by many that the acetone bodies are the products of normal fat oxidation in the liver.[6,7] It has been demonstrated also that an infiltration of fat in the liver is associated with the lipemia produced by stilbesterol injections,[2,3] presumably in consequence of an extensive mobilization of fat from the depots to the blood stream. Accordingly, if the availability of lipid substrate were a factor in the oxidation of fat in the liver, an increase in the rate of acetone body production would ensue in consequence of stilbesterol administration. Our data indicate that the latter does not occur. Hence, they support the hypothesis that the availability of fats and their oxidation in the liver are two independent phenomena and that an increase in the former does not influence the latter.

Summary. The administration of stilbesterol produces a marked lipemia but does not influence the rate of acetone body production.

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Changes in Blood and Urine after Intravenous Amino Acid Mixture in Patients with Liver Disease.*

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Recent reports of studies on patients show that mixtures of the essential amino acids, as obtained by enzymatic digestion of casein, can be used to maintain nitrogen balance when given intravenously.[1-6] The statement has been made, however, that in patients with liver disease the method is contraindicated. Our clinical experience does not support this conclusion and, although the question requires further study, the data acquired in the present experiments seem to have some relevancy.

Experimental Method. The solution of amino acids used ("Amigen") was supplied by Dr. Warren M. Cox, Jr. of Mead Johnson and Company, and consisted of a sterilized aqueous nonpyrogenic 10% solution of an enzymatic hydrolysate of purified casein and pork pancreas. The nitrogen of the solution is present chiefly as nitrogen of amino acids and polypeptides, and the material is not allergenic. The solution contains the amino acids essential for maintenance and growth as shown by animal experiments. The hydrogen ion concentration of the solution was adjusted to a pH value of 6.5.

Amino acid concentration in whole blood and plasma was determined by the ninhydrin-CO_2 method recently developed by Van Slyke, MacFadyen and Hamilton.[7] Amino acid concentration in urine was likewise determined by the ninhydrin-CO_2 technic devised by the same investigators but as yet unpublished.[8] Standard methods were

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TABLE I.

Plasma and Urine Changes During Amino Acid Infusion.

Between samples 1 and 2, 1000 cc 10% amino acids solution (Amigen) was given intravenously in 5 to 6 hours. Sample 3 was taken 24 hours after sample 1. The patients were fasting but took water as desired.

Case	Sample	Plasma			Urine		
		HCO_3, vol/100 cc	Amino N, mg/100 cc	NPN, mg/100 cc	Vol., cc	Amino N, mg	Total N, mg
1. ♀ Toxic hepatitis, liver failure	1	58.7	7.2	22.6	168	9	910
	2	49.4	9.0	32.8	403	69	3,295
	3				1,030	102	9,600
2. ♀ Obstructive jaundice, stone	1	58.1	8.0	13.9	220	17	482
	2	50.3	13.5	35.5	430	128	1,660
	3	57.3	5.7	23.1	870	86	6,870
3. ♀ Same	1	60.5	7.3	34.0	103	9	427
	2	54.7	10.7	45.9	665	70	3,030
	3	51.0	9.5	36.8	865	62	5,280
4. ♀ Cirrhosis, liver failure	1	75.5	6.3	25.3	30	11	322
	2	70.0	14.3	49.3	285	236	2,840
	3	69.2	6.1	36.1	345	158	5,450
5. ♂ Obstructive jaundice, liver failure	1	85.5	5.1	47.0	*		
	2	73.8	13.7	74.7	330	96	6,130
	3	71.3	3.1	73.7	675	95	12,530
6 ♀ Toxic hepatitis, melena, anemia	1	62.0	5.0	16.2	*		
	2	54.7	10.5	42.0	860	104	3,370
	3	55.2	4.3	23.9	1,230	28	5,920
7. ♂ Herniorraphy, convalescent	1	71.3	7.6	24.6	*		
	2	63.6	12.4	46.8	545	66	4,380
	3	69.0	4.9	34.0	1,445	92	11,345
8. ♂ Echinococcus cyst of liver, not jaundiced	1	65.3	5.2	21.4	*		
	2	59.8	8.7	61.5	645	132	3,795
	3	50.7	3.8	34.7	1,510	65	6,820

*Discarded.

used in the other analyses.

The patients were kept under observation constantly during the study and in no case was it necessary to discontinue the infusion on account of untoward symptoms. The infusions were given through arm veins by steady drip, the rate being kept as nearly as possible the same in comparable experiments. Urine was collected without loss by means of an indwelling urethral catheter in the experiments of Table II, while in the other cases the patients were able to void at stated intervals. The patients had fasted overnight only. Water was drunk as desired during the experiments but no food or drugs were taken.

Presentation of data. Table I is based on studies of patients who received 1000 cc 10% amino acid solution intravenously at a fairly constant rate, between 5 and 6 hr being required for the infusion. Sample No. 1 was taken at the beginning of the infusion, sample No. 2 at the end. Sample No. 3 was obtained 24 hr after the first sample, while the patient was still fasting. Patients 1, 2, 3, 4, 5 and 6 had severe liver disease, while patients 7 and 8 had no demonstrable disturbance in liver or kidney function and hence served for control observations.

In Table II are shown changes in plasma and urine resulting from giving amino acids at a rapidly increasing rate intravenously without increasing, however, the volume of fluid infused. Blood samples were taken at the beginning and at the end of the infusion. In the final period urine was collected but

[8] Personal communication from Dr. D. D. Van Slyke.

TABLE II.
Effects of Amino Acids Infusion in Patient Z, Female, Toxic Hepatitis and Liver Failure (Case 1) and in Patient C, Female, Possible Biliary Dyskinesia (Case 2).

		Infusion			Urine			Plasma	
Case	Period	Sol., quantity	Duration, min.	Tot. N, mg	Vol., cc	Tot. N, mg	Amino N, mg	Amino N, ——— Tot. N	Amino N, mg/100 cc	NPN, mg/100 cc
1	1	300 cc 5% glucose	85	0	54	340	9	2.6%	3.8	14.6
	2	" { 2.5% amigen + 7.5% glucose	110	900	95	880	19	2.1		
	3	" { 5% amigen + 5% glucose	110	1,800	115	1,130	30	2.6		
	4	" 10% amigen	125	3,600	173	1,595	52	3.3	7.6	19.3
	5		135	0	100	991	23	2.3		
	Total		565	6,300	537	4,936	133			
2	1	300 cc 5% glucose	90	0	240	547	5	0.9%	5.8	21.9
	2	" { 2.5% amigen + 5% glucose	110	900	137	415	4	1.1		
	3	" { 5% amigen + 5% glucose	110	1,800	217	653	17	2.6		
	4	" 10% amigen	110	3,600	145	547	19	3.5	11.2	29.8
	5		150	0	650	1,832	28	1.5		
	Total		570	6,300	1,389	3,994	73			

The rate of intravenous administration of amino acids was progressively increased, but the volume of fluid infused was not increased. There was no interval between the different infusions. The patients were fasting but were allowed to drink small amounts of water as desired. Urine was collected without loss by means of an indwelling catheter.

no fluid was administered intravenously. Except during the first period the fluid given was hypertonic as compared with plasma, and slightly acid in reaction. In Case 1 severe liver disease was present. In Case 2 liver and kidney function tests were normal.

Comments. In these experiments the urinary nitrogen data have little significance with respect to nitrogen balance, for the patients had fasted only overnight beforehand. The experimental plan was not designed to show the extent of utilization of amino acids injected in this manner. It is of interest, however, that only trivial amounts of amino acids were excreted in the urine, even during and after excessively rapid administration. The urinary total nitrogen in every case was large, from which it appears that the severely damaged liver still possesses the power to deaminize amino acids at a rapid rate. This conclusion depends on the validity of the method used for determining amino acid nitrogen in the urine. The urea nitrogen was not determined in the urine as such, but presumably this formed the chief component of the total nitrogen excreted. In only one of the 8 patients of Table I was the non-protein nitrogen of the plasma elevated beyond the normal range 18 hr after the amino acid infusion. Evidently the power of the kidneys to excrete nitrogen was adequate, even in patients showing signs of liver failure, such as jaundice, ascites and anasarca.

The rapid infusion of 100 gm of amino acids resulted in a doubling of the plasma amino acid concentration, but the increase was transitory and 18 hr later the value was usually less than the original. This may be interpreted as indicating that amino acids are freely and rapidly diffusible into the tissue fluids, and a large volume of fluid, presumably including intracellular fluid, would be required for the even dilution of the quantities injected in these experiments. The fasting plasma amino acid concentration in 7 observations in the patients with liver disease were similar to the values in 3 patients who showed no evidence of impairment of hepatic function, and the increase following infusion of amino acids was of comparable extent. The amino acid concentration

was as a rule somewhat higher in whole blood than in plasma, both before and after the amino acid infusions. Reduction in plasma bicarbonate concentration occurred invariably as an immediate result of the amino acid infusion, both in the patients with liver disease and those not having hepatic impairment.

When the rate of infusion of amino acids was progressively increased, as shown in Table II, the changes in urine and plasma amino acid concentration are found to be similar in the patient with toxic hepatitis and in the patient without liver disease. The amount of amino acid excreted in the urine in the 2 cases increases somewhat, but remains a small percentage of the total nitrogen excreted. At the end of the period of observation, which lasted 9 hr, there was still a large retention of nitrogen in both cases.

Conclusion. The changes in plasma and urine following infusion of an amino acid mixture were found to be comparable in 2 groups of patients, one group having advanced liver disease and the other showing no evidence of hepatic disability. In neither were untoward clinical effects noted.

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A Study of Gastric Secretion as Influenced by Changes in Duodenal Acidity.

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In spite of numerous investigations there remains considerable difference of opinion regarding the effect of injecting HCl into the intestine on the volume output of gastric juice. Some investigators[2,3] have reported that acid in the intestine may stimulate the flow of gastric juice, others have reported inhibition[1,4,5,7] whereas still others[6] have found that injecting acid into the duodenum appeared to have no significant effect on the volume or acidity of gastric juice secreted in response to a standard meal. Similarly discordant results were obtained in experiments carried out in this laboratory some years ago and the results obtained early in this investigation were likewise inconstant.

This communication is a preliminary report of the results obtained up to the present in our efforts to determine why, on one occasion, the addition of a given volume of HCl to the intestinal contents may profoundly inhibit gastric secretion and may, on another occasion, apparently under the same conditions, have little or no effect.

Two dogs were used each of which was provided with a Pavlov pouch and with a gastric and a duodenal fistula as previously described by one of us.[8,9] The volume of the secretion collected from the Pavlov pouch was measured at 15-min intervals for one hr before and for from 4 to 7 hr after a standard meal consisting of 300 g of beef heart free from visible fat. Thirty-two experiments were performed of which 21 were normal

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