

been stated that it is the first duty of a physician to keep a patient alive so that he may be given a chance of being cured later. However, until such chances are increased beyond what they appear to be at present, in the case of our standardized hemorrhagic shock, the practical value of maintaining a somewhat lower body temperature appears vanishingly small. However, it must be kept in mind that the shock induced in our animals is of a severe form and the possibility exists that hypothermia may be of greater benefit in other types of shock.

Summary. Observations on 44 dogs submitted to standardized bleeding and reinfusion procedures which induce irreversible hemorrhagic shock showed that the survival period following reinfusion of heparinized blood is definitely extended by a hypothermic state, but with one exception all dogs succumbed.

² Blalock, A., and Mason, M. F., *Arch. Surg.*, 1941, **42**, 1054; Elman, R., *et al.*, *Proc. Soc. Exp. Biol. and Med.*, 1942, **51**, 350; Rosenthal, S. M., *Pub. Health Rep.*, 1942, **57**, 1923; Wakim, K. G., and Gateh, W. D., *J. Am. Med. Assn.*, 1943, **121**, 903; Allen, F. M., *Am. J. Surg.*, 1943, **60**, 335.

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Metabolic Studies in Patients with Cancer of the Gastro-Intestinal Tract. XX. Lipotropic Properties of Protein.*

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Recent studies from these laboratories have demonstrated the value of protein-rich diets in the treatment of the hepatic dysfunction of patients with gastro-intestinal cancer. This conclusion has been based chiefly upon the increased functional capacity of the liver as determined by multiple function tests. The livers of these patients, when untreated, almost uniformly contain at laparotomy abnormally high concentrations of lipid and probably low concentrations of glycogen,¹ and there is reason to believe that this unusual chemical constitution, in turn, may account for a part of the reduced functional state of the organ.^{2,3} In an earlier investigation it was demonstrated that the livers of patients with gastro-intestinal cancer readily could be depleted of their excess fat. One method by which this could

be accomplished was by the oral administration of inositol or lipocaic merely during the night preceding operation.⁴ For these reasons, it appeared desirable to learn if the return towards normal hepatic function induced by the feeding of high protein diets to the patients studied was associated with the restoration of a normal chemical composition of their livers.

Methods. The methods used in the present study have been described in previous communications.^{1,4}

Results. In a previous investigation¹ the concentrations of lipid in the livers of 28 patients with gastro-intestinal cancer who came to laparotomy after the usual 10-hour pre-operative fast ranged from 5.3 to 35.0 g and averaged 16.40 g %. The glycogen content of these livers, in turn, varied from 0.5 to 8.3 g and averaged 2.56 g %.

In contrast, the concentrations of fat in the livers of 7 patients with gastro-intestinal cancer who ingested 2.5 g of complete protein per kg per day for from 10 to 21 days, were all

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¹ Ariel, I. M., Abels, J. C., Murphy, H. T., Pack, G. T., and Rhoads, C. P., *Ann. Int. Med.*

² Conner, C. L., *Am. J. Path.*, 1938, **14**, 347.

³ Soskin, S., and Hyman, M., *Arch. Int. Med.*, 1939, **64**, 1265.

⁴ Abels, J. C., Ariel, I. M., Murphy, H. T., Pack, G. T., and Rhoads, C. P., *Ann. Int. Med.*

TABLE I.
Effects of Ingested Protein and Amino Acids on Chemical Composition of Livers of Patients with Gastro-Intestinal Cancer.

Dietary supplement	No. of patients	Hepatic conc. of lipid		Hepatic conc. of glycogen	
		Range, g %	Avg, g %	Range, g %	Avg, g %
None	28	5.3-35.0	16.40	0.5-8.3	2.56
High protein (2.5 g/kg/day)	7	4.6-7.55	5.59	0.8-3.8	2.23
Amino acids (75 g)	9	9.05-26.2	15.45	1.3-3.3	2.39

within normal limits.⁵ These values ranged from 4.6 to 7.55 g and averaged 5.59 g %, or 0.34 that of the fasted patients. The concentrations of glycogen in these livers, however, varied from 0.8 to 3.8 g and the average value was only 2.23 g % or even less than that of the fasted control group.

On the other hand, the chemical composition of the livers of 9 patients with gastro-intestinal cancer who received 75 g of amino acids[†] during the 10-hour period before operation were not significantly different from those of fasted patients. This amount of amino acids was chosen because it was the largest that could be given orally in a 10-hour period without inducing untoward reactions. The livers of this group were found to contain from 9.05 to 26.2 g % of lipid (average 15.45 g %) and from 1.3 to 3.3 g % of glycogen (average 2.39 g %).

Comment. It has become widely recognized that the administration of protein-rich diets to patients with hepatic insufficiency frequently results in considerable clinical benefit.⁶ This, likewise, appears to be true in patients with gastro-intestinal cancer who have fatty infiltration of the liver. There is

some reason to believe that the hepatic dysfunction of this group of patients may be due to the very presence of the excess fat of the liver cells. Lipid is deposited apparently without water⁷ (in contrast to the deposition of glycogen⁸) so that the available hepatic water necessarily becomes distributed through a greater tissue volume, and the solution of essential water-soluble constituents thus is decreased. Moreover, an increased hepatic content of lipid probably favors the solution and retention of many lipid-soluble substances deleterious to the liver,⁹ compresses the sinusoids, and induces ischemia.² It is possible, therefore, that it is the lipotropic effects of the protein which may account in part for the functional improvement of the organ.

Conclusions. 1. Patients with gastro-intestinal cancer fed protein-rich diets pre-operatively do not have fatty infiltration of the liver at laparotomy. 2. Patients with gastro-intestinal cancer who ingested 75 g of amino acid mixture during the 10 hours before operation were found at laparotomy to have concentrations of fat as abnormally high as those of fasted patients.

⁵ Ralli, E. P., Rubin, S. H., and Rinzler, S., *J. Clin. Invest.*, 1941, **20**, 93.

[†] Acid hydrolysate of casein procured through the courtesy of Frederick Stearns & Co., Detroit, Mich.

⁶ Patek, A. J., Jr., and Post, J., *J. Clin. Invest.*, 1941, **20**, 481.

⁷ McLachlan, P. L., Hodge, H. C., Bloor, W. R., Welch, E. A., Truax, F. L., and Taylor, J. D., *J. Biol. Chem.*, 1942, **143**, 473.

⁸ McBride, J. J., Guest, M. M., and Scott, E. L., *J. Biol. Chem.*, 1941, **139**, 943.

⁹ Goldschmidt, S., Vass, H. M., and Ravidin, I. S., *J. Clin. Invest.*, 1939, **18**, 277.