Plasma and Urinary Amino Acids in Laennec's Cirrhosis

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Plasma amino acid concentrations and urinary excretion of free amino acids were measured in 7 patients with severe hepatic decompensation (precoma) in Laennec's cirrhosis. Upon maximal improvement these patients served as their own controls. Contrary to earlier reports, the changes were found to be unspectacular. Plasma concentrations of amino acids proved to be remarkably stable. Decreased plasma concentrations of valine, leucine, and isoleucine pointed to a component of steatonecrosis, which was found in liver biopsy specimens and laboratory parameters. The urinary excretion of threonine, serine, asparagine/glutamine, alanine, ethanolamine, and histidine was increased significantly during hepatic decompensation when compared to the excretion values of the same patients at maximal compensation; but even here the changes were within the normal range. General aminoaciduria was observed in 3 cirrhotic patients who had undergone surgical portacaval shunts. It is possible that these changes are a sequence of the surgical procedure.

PROTEIN METABOLISM represents one of the major metabolic activities of the liver. Among the best appreciated of these functions are the deamination of amino acids, production of urea, and synthesis of some of the plasma proteins. It is not surprising that the influence of liver disease—e.g., Laennec's cirrhosis—on amino acid metabolism has been the subject of numerous investigations. Early information concerned complete and fatal liver failure. Rokitansky[1] described leucine and tyrosine crystals on the cut surface of livers from patients who had succumbed to "acute yellow atrophy." Frerichs[2] found the same types of crystals in the urinary sediment of patients with "acute yellow atrophy." Mann[3] pointed out that the liver possesses remarkable functional reserve power, and that the amino acid metabolism is affected only by profound hepatocellular failure. The removal of less than 85% of the liver of a dog did not result in a significant disturbance of the amino acid metabolism.

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Nevertheless, there have been reports of derangement of amount and proportions of amino acids in the plasma of patients with severe Laennec's cirrhosis.[4–12] Abnormally high plasma concentrations of methionine, cystine, and the aromatic amino acids were reported by several investigators.[4, 6, 8, 9, 11–14] Aminoaciduria, either generalized or confined to certain amino acids, was reported in other studies.[5, 13–19]

Others have been able to find only limited, inconstant, or uncharacteristic changes of amino acids in serum and urine,[20–22] although Knauff *et al.* found evidence of decreased amino acid tolerance in patients with Laennec's cirrhosis.[7] Most investigators did not find general changes of amino acids in plasma or urine, but rather shifts in the concentrations of some individual amino acids, which were confusing in their variety. Some experimental evidence seemed to suggest that the shifts in plasma amino acids may be characteristic for specific hepatocellular damage. Rats poisoned with thioacetamide suffered a disturbance of the urea cycle, but methionine and the aromatic amino acids remained within normal range. When carbon tetrachloride was given in the diet, the urea cycle was not disturbed, but plasma methionine, threonine, tyrosine, and phenylalanine were increased, similarly to these acids in some of the cirrhotic patients of Knauff *et al.*[22]

In view of the diversity of findings concerning plasma and urinary amino acids in Laennec's cirrhosis, it seemed desirable to measure them with a more quantitative method than had been used in all but one of the cited studies. The measurements were taken in patients with severe hepatic decompensation, who served as their own controls upon improvement.

MATERIALS AND METHODS

Seven patients, who survived severe decompensation of alcoholic hepatic cirrhosis, were selected for study. All were considered precomatose, with severe jaundice, ascites, and grossly abnormal liver function tests. The serum potassium concentrations were normal in 4 patients; 3 had hypokalemia (3.5, 3.8, and 3.9 mEq./L.). All serum potassium concentrations were normal at the time of maximal improvement. Follow-up studies on each patient were undertaken at a time when it was considered that maximal improvement had been reached. At that point neither the clinical appearance of the patients nor most laboratory findings had returned to normal. The clinical diagnosis of Laennec's cirrhosis was confirmed by liver biopsy in all but 2 cases.

There was moderate evidence of steatonecrosis in 4, and a greater amount in 1, patient. At the time of maximal hepatic decompensation of the 7 patients, the serum concentrations of SGOT were 14, 52, 83, 87, 118, 234, and 234 Babson units. In the precomatose state the nutritional intake and medication of these patients consisted of intravenous infusions of fluids, B-complex vitamins, electrolyte replacement, and aldactone therapy. Later, after the danger of hepatic coma had subsided, they received normal diets. Three additional pa-

tients, who had hepatic cirrhosis with surgical portacaval shunts, received a 40-gm. protein diet.

Blood plasma specimens were obtained at 8 A.M. and 9 P.M. for amino acid analysis determinations. All samples were collected in heparinized polyethylene centrifuge tubes, the plasma was separated immediately, and the portion to be used for amino acid analysis was precipitated by picric acid, according to the method by Tallan *et al.*[23] Toluene (6 ml.) and chloroform (6 ml.) were used as bactericidal preservatives for each 24-hr. urine specimen. After volume and specific gravity had been measured and the individual's body weight had been recorded, an aliquot of the urine was stored at −20° C. until analysis.

Free amino acids of plasma and urine were determined by ion-exchange chromatography, using an automatic amino acid analyzer (Spinco, Model 120B,* adapted to 8% cross-linked sulfonated styrene copolymer resins, PA-28 and PA-35), as described by Spackman *et al.*[24] The free plasma amino acids are reported as micromoles per 100 ml. of plasma, the free urinary amino acids as micromoles per kilogram of body weight per 24 hr. Asparagine and glutamine were eluted as a single peak and are so reported.

Measurements of 17-OHCS were done by the Peterson *et al.* modification[25] of the method of Silber and Porter. Determinations of plasma nonprotein-bound 17-OHCS were performed as described by Lohrenz *et al.*[26] Measurements of corticosteroid-binding globulin (CBG) were made according to the method of Doe *et al.*[27]

RESULTS

During the period of observation, from precoma to maximal recovery, the mean total serum bilirubin of these 7 patients had decreased from 9.44 to 2.35 mg./100 ml., the mean bromsulphthalein (BSP) retention from 37.9 to 20.26% in 45 min., and the SGOT from a mean of 126.3 units to 36. Table 1 shows the plasma concentration of free amino acids in these patients during precoma and compares these values to those of the same individuals after maximal improvement. In addition, the plasma amino acid concentration is given for 24 normal males, 3 cirrhotic patients with surgical portacaval shunts, and 1 individual with advanced hepatolenticular degeneration. Plasma tyrosine concentration was above normal during precoma as well as at maximal compensation. The differences between precoma and maximal improvement are not striking, although in the state of severe hepatic decompensation and in 3 patients with portacaval shunts the plasma concentrations of methionine tended to be elevated, whereas asparagine/glutamine, valine, leucine, and isoleucine were decreased in comparison to normal males. Proline was the only plasma amino acid which was materially increased in the patient with hepatolenticular degeneration. Comparing the precomatose state with maximal improvement, we can discern statistically significant changes in only three

*Beckman Instruments, Inc., Fullerton, Calif.

TABLE 1. FREE PLASMA AMINO ACIDS (AS μMOLES PER 100 ML. OF PLASMA)

	7 patients with Laennec's cirrhosis				*24 normal males*		*Porta-caval shunts (Mean of 3)*	*Wilson's dis. (1 pt.)*
Amino acid	*D**	*C†*	*t*	*p*	*Mean*	*S.D.*		
Taurine	2.8	5.1	5.8	0.01	6.3	2.4	3.5	5.1
Aspartic acid	—	—	—	—	0.8	0.5	2.7	0.3
Threonine	19.3	12.6	1.0	0.4	13.7	2.2	11.0	15.9
Serine	12.2	9.9	1.8	0.1	11.2	2.3	12.7	11.3
Citrulline	2.6	3.2	3.0	0.01	3.6	0.9	1.9	4.6
Asparagine/ glutamine	15.1	20.5	1.4	0.2	32.0	17.1	20.1	24.1
Proline	19.9	20.8	0.6	0.6	20.3	5.3	18.0	34.2
Glutamic acid	16.0	17.1	0.2	0.8	16.0	9.3	11.5	7.9
Glycine	26.8	23.2	1.2	0.3	22.9	3.1	20.5	24.3
Alanine	26.8	28.4	0.5	0.6	36.6	9.9	25.8	39.6
α-NH_3-n-butyric acid	2.4	1.7	7.0	0.01	2.7	1.0	3.2	1.2
Valine	15.6	14.6	0.4	0.7	26.2	5.6	21.8	23.9
Cystine/2	8.6	11.6	1.4	0.2	7.2	2.1	10.2	4.7
Methionine	4.0	2.5	0.6	0.6	2.4	0.8	3.4	3.5
Isoleucine	5.4	5.4	0.2	0.8	7.6	1.9	8.0	9.4
Leucine	8.6	7.4	1.3	0.2	13.2	3.1	11.1	13.8
Tyrosine	10.0	10.9	0.6	0.6	6.3	0.9	12.6	7.9
Phenylalanine	6.7	6.0	1.6	0.2	6.0	1.1	7.8	6.7
Ornithine	7.4	8.9	1.5	0.2	5.6	1.6	6.3	8.3
Lysine	21.2	14.0	2.3	0.1	17.6	2.8	16.5	15.6
Histidine	5.3	5.5	0.5	0.7	6.8	1.2	5.9	5.0
Arginine	5.2	6.7	2.1	0.1	7.4	2.7	6.8	4.5

* During hepatic precoma (decompensation).
† At maximal improvement (compensation).

amino acids: taurine, citrulline, and α-amino-n-butyric acid. It should be noted that these were changes within the normal range of plasma amino acid concentrations. The plasma concentrations of these patients failed to show the diurnal variations which were described for tyrosine, phenylalanine, and tryptophan in normal individuals.[28]

Table 2 shows the urinary excretion of free amino acids in these patients. There was no general aminoaciduria, whether during precoma or the stage of maximal compensation, when we consider the entire group by comparison with normal males. Significantly greater amounts of serine, asparagine/ glutamine, alanine, ethanolamine, lysine, 1-methyl histidine, and histidine were excreted in the precomatose state. Considering that all but 2 patients had ascites and edema at that stage, which increased the average weight by 11%, we must add threonine to this group of amino acids which were excreted in significantly greater amounts during precoma. Glycine excretion did not follow the general trend of diminution upon compensation. It increased in 4 of the 7 patients. This increase is noteworthy, particularly since it exceeded the normal range in 1 patient. The significance of this finding is obscure at the present time.

TABLE 2. FREE URINARY AMINO ACIDS
(AS μMOLES PER KG. OF BODY WEIGHT PER 24 HR.)

	7 patients with Laennec's cirrhosis				*24 normal males*		*Porta-caval shunts (Mean of 3)*	*Wilson's dis. (1 pt.)*
Amino acid	*D**	*C†*	*t*	*p*	*Mean*	*S.D.*		
Taurine	4.4	11.1	1.9	0.1	14.2	8.9	6.2	24.0
Threonine	4.0	1.4	1.5	0.2	3.4	1.4	6.1	14.7
Serine	5.3	2.3	3.3	0.01	6.2	2.3	13.2	18.7
Asparagine/ glutamine	7.1	3.6	2.5	0.05	10.7	4.4	18.7	31.6
Glutamic acid	0.8	1.0	0.5	0.7	0.6	0.2	1.9	0.7
Glycine	9.8	15.4	1.2	0.3	22.3	12.2	32.3	87.7
Alanine	4.1	3.1	2.5	0.05	5.2	2.2	17.7	10.2
α-NH_3-n-butyric acid	2.5	1.8	2.0	0.9	1.1	0.5	0.8	1.2
Valine	0.5	0.5	0.5	0.7	0.8	0.8	4.1	0.8
Cystine/2	1.8	1.8	1.3	0.3	1.6	1.1	5.4	46.7
Cystathionine	1.0	0.8	0.3	0.8	0.8	0.2	1.5	1.6
Methionine	1.3	0.9	5.0	0.1	1.0	0.3	1.3	1.0
Isoleucine	0.5	0.5	0	1.0	0.8	0.3	1.1	0.8
Leucine	0.6	0.6	1.6	0.2	1.2	0.3	2.5	2.0
Tyrosine	1.6	1.4	1.0	0.4	1.9	0.7	7.8	4.3
Phenylalanine	0.8	0.8	0	1.0	1.1	0.5	4.1	1.6
α-NH_3-isobutyric acid	1.3	2.3	0.8	0.5	2.1	1.8	2.7	—
Ornithine	0.4	0.6	1.0	0.4	0.5	0.3	1.1	2.4
Ethanolamine	5.8	3.3	4.2	0.01	5.0	1.4	13.6	6.6
Lysine	2.0	1.2	4.0	0.01	4.2	2.6	10.2	12.4
1-CH_3-histidine	2.9	5.4	2.4	0.05	6.7	4.4	16.9	13.0
Histidine	8.4	4.3	3.6	0.01	14.2	6.0	25.6	32.8
3-CH_3-histidine	3.0	3.4	1.0	0.4	4.7	1.1	4.1	5.0
Arginine	0.3	0.2	0.3	0.1	tr.‡	—	1.1	tr.‡

* During hepatic precoma (decompensation).
† At maximal improvement (compensation).
‡ Traces

The patients with cirrhosis and surgical portacaval shunt and the patient with hepatolenticular degeneration showed an aminoaciduria, which appeared to exist quite independently of the plasma concentration of amino acids. The aminoaciduria involved most but not all amino acids: glutamic acid, α-NH_3-n-butyric acid, methionine, isoleucine, and 3-methyl histidine were not involved in either group.

COMMENTS

The seven patients under study served as their own controls after they had reached maximal improvement from their hepatic decompensation. The loss of ascites and edema reduced their average weight by 11%. None of the patients reached a state of normal liver function. Although their protein intake was low during the precomatose state, but high at the time of recovery, there was little change in the concentrations of free plasma amino acids. Mean values for threonine and tyrosine exceeded the normal means, and those of

valine, isoleucine, and leucine were decreased. Statistical comparison of the plasma changes from precoma to maximal recovery found significant decreases only in the plasma levels of taurine, citrulline and α-amino-n-butyric acid, but even these changes occurred within the normal values for plasma concentration of these amino acids. This remarkable constancy of plasma amino acids had also been encountered when urinary excretion of amino acids was increased under the influence of cortisol[29] or pregnancy.[30] A short-lived general decrease of all amino acids can be induced by exogenous[31] or endogenous[32] insulin. May Ning and associates[33] have described an increase of the plasma concentrations of glutamic acid and decreases of valine, leucine, and isoleucine in patients with alcoholic hepatitis. The histologic lesions of the patients in this study were those of alcoholic cirrhosis, but each one had a component of steatonecrosis. The concentrations of the branched amino acids—valine, isoleucine, and leucine—were indeed below the normal range, but glutamic acid was found in normal plasma concentrations.

Changes in the urinary excretion of amino acids upon maximal recovery were not spectacular. Significant changes involved only threonine, serine, asparagine/glutamine, alanine, ethanolamine, lysine, 1-methyl histidine, and histidine, but here again these changes were within the normal range for males.

General aminoaciduria was not seen in any one of 7 patients with decompensated cirrhosis. The compensation state of these patients still fits into the category of extensive alcoholic cirrhosis. Neither general aminoaciduria nor the increase of individual amino acids could be found at that time. As a matter of fact, several of the urinary amino acids were excreted to a lesser degree than was the case in the normal controls. The findings in patients with portacaval shunt and Wilson's disease were different: The free plasma amino acids of 3 cirrhotic patients with surgical portacaval shunts were within the normal range, but there was a striking general aminoaciduria. These patients were not in a state of precoma or hepatic decompensation. Their aminoaciduria was not of the pattern which we have observed as an effect of increased free plasma cortisol,[29, 30] since it involved almost all of the amino acids which were measured. The patient with hepatolenticular degeneration had an even more striking and extensive aminoaciduria, while his free plasma amino acids remained normal with the exception of proline. Both conditions, portacaval shunt and Wilson's disease, appear to be associated with an aminoaciduria of renal origin. In the case of Wilson's disease this is readily explained as a result of copper toxicity involving the proximal renal tubular epithelium and impairment of reabsorption of amino acids from the glomerular filtrate.[34–36] There is no facile explanation for the renal mechanism of aminoaciduria in the patients with portacaval shunt. The speculation can be ventured that we are dealing with an effect of the portacaval shunt on the renal blood flow. Other metabolic abnormalities have been noted following portavacal anastomoses. The appearance of clinical diabetes mellitus in the wake of a surgical portacaval shunt was noted by Larcan *et al.*[37] Cotes and associates[38] studied 3

patients who developed progressive dyspnea on exertion following an operation of portacaval anastomosis. Pulmonary function studies pointed to a low ventilation perfusion ratio, which was most likely to be due to changes in the pulmonary circulation. In the dependent parts of the lung, dilation of alveolar vessels would increase the perfusion relative to ventilation and thus cause hypoxemia. The perfusion of the remaining pulmonary alveoli would be reduced and the effective surface available for the exchange of gas decreased.

The failure of this study to detect significant general aminoaciduria in severe Laennec's cirrhosis is in contradiction to some of the previous reports. In one instance extensive aminoaciduria had been mistakenly attributed to Laennec's cirrhosis, whereas the condition in question was Wilson's hepatolenticular degeneration.[39] It is possible that previous reports contained similar but unrecognized cases. The bulk of discrepancies between the findings of this study and some of the previous reports, however, may be attributed to several reasons: All of the reports with which this study is in disagreement employed semiquantitative methods for the determination of amino acids, either paper chromatography,[4, 5, 17] thin-layer chromatography,[19] microbiological assays,[13–15, 18] or chromatography on columns of Dowex-50.[8] Moreover, several of those studies measured amino acid concentrations of a morning urine specimen[4, 5] or during a clearance determination[15] (this selection of urine specimen would necessarily yield erroneously high concentrations of solutes). Oliguria is common in Laennec's cirrhosis. Four of the 7 patients in this study had urine volumes of 400–800 ml. within a 24-hr. period. The solutes, among them amino acids, were highly concentrated, but when related to the urinary output per kilogram of body weight in a 24-hr. period, the aminoaciduria was found to be within the normal range. A more recent study[22] is in agreement with the findings of this paper; that study also employed quantitative determinations of amino acids by means of chromatography on Amberlite columns of an automatic amino acid analyzer.

REFERENCES

1. ROKITANSKY, C. *A Manual of Pathological Anatomy* (Vol. 2), Transl. by E. Sieveking. New Sydenham Soc., London, 1849.
2. FRERICHS, F. T. *A Clinical Treatease on Diseases of the Liver* (Vol. 1), transl. by C. Murchison. New Sydenham Soc., London, 1860.
3. MANN, F. C. The effects of complete and of partial removal of the liver. *Medicine 6*:419, 1927.
4. WALSHE, J. M. Disturbances of amino acid metabolism following liver injury. *Quart J Med 22*:483, 1953.
5. KNAUFF, H. G., SELMAIR, H., and REITLINGER, A. Untersuchungen über die Freien Aminosäuren in Harn und Blutplasma von Gesunden und von Leberkranken. *Klin Wschr 38*:812, 1960.
6. EARLE, D. P., and VICTOR, J. The effect of various diets on the liver damage caused by excess cystine. *J Exp Med 75*:179, 1942.
7. KNAUFF, H. G., SEYBOLD, D., and KANTERS, A. Freie Plasmaaminosäuren und Blutammoniak nach oraler Proteinzufuhr. Untersuchungen bei Gesunden und bei Patienten mit Lebercirrhose. *Klin Wschr 43*:382, 1965.

8. IBER, F. L., ROSEN, H., LEVENSON, S. M., and CHALMERS, T. C. The plasma amino acids in patients with liver failure. *J Lab Clin Med 50*:417, 1957.
9. WU, C., BOLLMAN, J. L., and BUTT, H. R. Changes in free amino acids in the plasma during hepatic coma. *J Clin Invest 34*:845, 1955.
10. WATSON, C. J. The prognosis and treatment of hepatic insufficiency. *Ann Intern Med 31*: 405, 1949.
11. GUACCI, L., RONCHI, R., DE PASQUALE, C., and DI MASSIMO-SIMONETTI, S. Gli Aminoacidi liberi del sangue nella cirrosi epatica. *Med Clin Sper 13*:583, 1963.
12. PAYET, M., CÉSAIRE, O. G., and CAMAIN-GIABICANI, R. Renseignements donnés par l'exploration chromatographique des acides aminés libres du sérum dans les cirrhoses et le cancer primitif du foie. *Strasbourg Méd 9*:295, 1958.
13. GABUZDA, G. J., ECKHARDT, R. D., and DAVIDSON, C. S. Urinary excretion of amino acids in patients with cirrhosis of the liver and in normal adults. *J Clin Invest 31*:1015, 1952.
14. DUNN, M. S., AKAWAIE, S., YEH, H. L., and MARTIN, H. E. Urinary excretion of amino acids in liver disease. *J Clin Invest 29*:302, 1950.
15. KINSELL, L. W., HARPER, H. A., BARTON, H. D., HUTCHIN, M. E., and HESS, J. R. Studies in methionine and sulfur metabolism: I. The fate of intravenously administered methionine in normal individuals and in patients with liver damage. *J Clin Invest 27*:677, 1948.
16. MARTIN, E., and MILHAUD, G. Studies in amino acid metabolism with paper chromatography. *Chem Abstr 47*:3453, 1953.
17. MEHTA, S., WALIA, B. N. S., GHAI, O. P., and TANEJA, P. N. A qualitative study of plasma and urinary amino acids in Indian childhood cirrhosis. *Indian J Pediat 31*:187, 1964.
18. PAIN, S. K. Studies on the nitrogenous constituents of urine in normal subjects and in patients suffering from cirrhosis of liver, subacute nephritis and hypertension. *Indian J Med Res 45*:35, 1957.
19. AMBERT, J. P., PÉCHARY, C., LOMONIER, A., HOUSSET, E., and HARTMAN, L. Dosage et différentiation des acides aminés urinaires chez le cirrhotique avant et après anastomose porto-cave. *Ann Biol Clin (Paris) 24*:41, 1966.
20. WHEELER, J. E., and GYORGY, P. Studies of urinary excretion of methionine by normals and by patients having liver diseases. *Amer J Med Sci 215*:267, 1948.
21. DENT, C. E., and WALSHE, J. M. "Amino Acid Metabolism in Liver Disease." In *Ciba Foundation Symposium on Liver Disease,* Wolstenholme, C. E. W., and Sherlock, S., Eds. Blakiston, Philadelphia, 1951.
22. KNAUFF, H. G., SEYBOLD, D., and MILLER, B. Die Freien Plasmaaminosäuren bei Lebercirrhose und Hepatitis. *Klin Wschr 42*:326, 1964.
23. TALLAN, H. H., MOORE, S., and STEIN, W. H. Studies on the free amino acids and related compounds in the tissues of the cat. *J Biol Chem 211*:927, 1954.
24. SPACKMAN, D. H., STEIN, W. H., and MOORE, S. Automatic recording apparatus for use in the chromatography of amino acids. *Anal Chem 30*:1190, 1958.
25. PETERSON, R. E., KARBER, A., and GUERRA, S. L. Evaluation of the Silber-Porter procedure for the determination of plasma hydrocortisone. *Anal Chem 29*:144, 1957.
26. LOHRENZ, F. N., SEAL, U. S., and DOE, R. P. Adrenal function and serum protein concentrations in a kindred with decreased corticosteroid-binding globulin (CBG) concentration. *J Clin Endocr 27*:966, 1967.
27. DOE, R. P., FERNANDEZ, R., and SEAL, U. S. Measurement of corticosteroid-binding globulin in man. *J Clin Endocr 24*:1029, 1964.
28. WURTMAN, R. J., ROSE, C. M., CHOU, C., and LARIN, F. L. Daily rhythms in the concentrations of various amino acids in human plasma. *New Eng J Med 279*:171, 1968.
29. ZINNEMAN, H. H., JOHNSON, J. J., and SEAL, U. S. Effect of short-term therapy with cortisol on the urinary excretion of free amino acids. *J Clin Endocr 23*:996, 1963.
30. ZINNEMAN, H. H., SEAL, U. S., and DOE, R. P. Urinary amino acids in pregnancy, following progesterone and estrogen-progesterone. *J Clin Endocr 27*:397, 1967.
31. LOTSPEICH, W. D. The role of insulin in the metabolism of amino acids. *J Biol Chem 179*:175, 1949.
32. ZINNEMAN, H. H. NUTTALL, F. Q., and GOETZ, F. C. Effect of endogenous insulin on human amino acid metabolism. *Diabetes 15*:5, 1966.

33. Ning, M., Lowenstein, L. M., and Davidson, C. S. Serum amino acid concentrations in alcoholic hepatitis. *J Lab Clin Med 70*:554, 1967.
34. Dent, C. E. The renal aminoacidurias. *Exp Med Surg 12*:229, 1954.
35. Dent, C. E., and Walshe, J. M. Amino acid metabolism. *Brit Med Bull 10*:247, 1954.
36. Bickel, H. Die Wilsonsche Krankheit als Stoffwechselproblem. *Deutsch Med Wschr 83*: 766, 1958.
37. Larcan, A., Grosdidier, J., Huriet, C., and Kiffer, B. Diabète sucré après anastomose porto-cave: À propos d'une observation. *Le Diabète* 235, 1965.
38. Cotes, J. E., Field, G. B., Brown, G. J. A., and Read, A. E. Impairment of lung function after portacaval anastomosis. *Lancet 1*:952, 1968.
39. Dent, C. E., and Stowers, J. M. Adult Fanconi syndrome and cirrhosis. *Brit Med J 1*:520, 1965.

Lecture on Gastrointestinal Hormones

The nineteenth annual lecture for the Gastrointestinal Section of the American Physiological Society will be held on Thursday, Apr. 17, 1969, during the spring meeting of the Federation of American Societies for Experimental Biology in Atlantic City, N. J. Morton I. Grossman, M.D., Veterans Administration Center, Los Angeles, Calif., will speak on gastrointestinal hormones.