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Free Amino Acid Patterns of Serum of the Patients with Gastric Cancer, Especially on their Control by Infusions of Amino Acid Solution

Effect of Infusion of Amino Acid Mixture on Plasma Free Amino Acids Following Gastrectomy

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Introduction

The importance of nutrition especially protein nutrition in the field of surgery has been especially emphasized due to the profound effect on the operative result and wound healing. A specific post-operative metabolic change especially in protein metabolism due to the operative insult has been repeatedly pointed out by many investigators. Recent progress in the method of determination of amino acid has gradually led to the study of individual amino acid due to operative insult. Since amino acid preparations became readily available, the importance of studying the relationship between the administration of such preparation and amino acid fluctuations became evident. No definite findings have yet been obtained.

Concerning the amino acid preparations, Elman[1~4] in 1939 for the first time administered a mixed solution with addition of tryptophane, methionine, and cystine in living body and observed the equilibium of nitrogen balance, decrease in albumin concentration, and a diminution in the degree of body weight decrease, as the first application of amino acid in the field of clinical surgery. Using the regeneration of blood protein of dogs as the index, Madden[5~10] and Whipple studied the effect of administration of solutions of amino acid crystals with various composition and prepared the Vuj mixture, which proved to be clinically effective. Werner[11] used this Vuj mixture following gastrectomy and found a positive effect on improving the nitrogen balance. Howe[12] subsequently improved it to prepare Vuj-N mixture. As the standard amino acid composition, the composition of FAO published in 1957 are available. Both of these formulas are in widespread clinical use at present.

In the field of peroral nutrition, daily requirement of each essential amino acids has been established. According to Rose's[13] study, the whole egg has the composition of amino acids most close to that of the ideal crystalline amino acid mixture to maintain nitrogen metabolism. However, a standard composition of amino acids in the fluid for intravenous administration to be used in patients in whom oral administration is impossible has no been established. Only studies by Everson[14], Matsushita[15], Cryssel[16], and Oishi[17] are available since Howe. For the purpose of classifying the amino acid metabolism in gastrectomized subjects, the effect of administration of these amino acid preparations on the postoperative amino acid metabolism was studied. Some new informations

were obtained in the ratio of mixture of amino acids.

Materials and Methods

Experimental Subjects

Twenty-one cases of gastric cancer and 11 cases of gastric ulcer, total of 32 cases of gastrectomy hospitalized at the First Department of Surgery, Sapporo Medical College Hospital were studied. Cases in which only exploratory laparotomy or gastroenterostomy was carried out were excluded. Only those with normal values in preoperative liver function and adrencortical function tests were selected.

As an additional study, vitamin B_1 concentration was determined for the purpose of studying the relationship between amino acid fractions and vitamin B_1 concentration in 20 patients hospitalized at the First Department of Surgery.

Fluctuations in amino acid fractions in postoperative patients were studied in 3 groups. As shown in Table 1, group 1, 2 and 3 in which amino acid was added in patients with group 2 as seen in the Table were used.

Table 1 *Transfused Amino Acid Constitution* (mg/dℓ)

	Group 1	Group 2	Group 3 (added group 2)								
			G. T	T. S	T. T	K. F	Y. S	S. O	S. T	S. Y	K. D
Lys	1,920	1,440		750	750		750	750	500		500
Thr	700	640	175	105	105	140	105		70		70
Mct	680	960		60		60		60		40	
Try	300	320			15						
Leu	1,000	1,090						30			
Meu	660	960									
Phe	960	640									
Val	640	960									
Arg	1,090	1,000	500								
His	470	500									
Gly	600	1,490									
Sorbitol	5,000	5,000									
Total amino acid	9,400	10,000									
Total Volume of Amino Acid	200	600									

In group 1, 200 mℓ of fluid was given parenterally once daily, while 600 mℓ was given daily for 7 days in groups 2 and 3. In order to make the experimental condition as constant as possible, 50 mg of vitamin B_1, 50 mg of vitamin B_2, 500 mg of vitamin C, 50 mg of vitamin B_6, 1 mg of vitamin B_{12}, 30 mg of vitamin K_1, 300 mℓ of Glyco-Algin, 200 mℓ of electrolyte mixture, and 200 mℓ of 5% glucose solution were given intravenously. In groups 2 and 3, 100–200 mg of vitamin B_1, 100–150 mg of vitamin B_2, 500–700 mg of vitamin C, 120 mg of vitamin B_6, 2 mg of vitamin B_{12}, 100 mg of vitamin K_1 12.5 mg of Durabolin, 300 mℓ of glucose solution, and 300 mℓ of Glyco-Algin were given intravenously by dripping.

In addition the fractions of additional amino acid was determined in group 5 and the proportion to the normal value of amino acid concentration was calculated in % for each amino acid, and 2 or 3 acids showing the minimum concentration were selected.

Total protein was measured by Hitachi proteinometer. Protein fractions were determined with Tiselius electrophoresis and A/G ratio was calculated from these results.

Results

1. *Amino Acid Fractions during Operative Insult*

In order to observe the changes in the amino acid fractions due to operative insult, 5 patients subjected to gastrectomy with normal preoperative liver function and A/G ratio were selected for study.

GOF anesthesia was always used to keep the operative stress to the minimum. Blood samples were obtained 30 minutes after the end of the operation. The operation lasted 60–130 minutes. The method was according to Billroth I in 4 and Billroth II in 1. (Table 2 Fig. 1)

Total amino acid content decreased in all cases. The rate of decrease was 77.2 to 88.5% with the average of 84.8 %. Upon reviewing individual amino acids, most of the amino acid showed a decrease. Alanine was increased in 3, valine in 3, phenylalanine in 2, arginine in 2, and cysteic acid, aspartic acid, cystine, and tryptophane in 1 case each. All other amino acids showed a decrease in all 5 cases.

The rate of decrease in essential amino acids was proportional to the rate of decrease in total amino acids. The rate of decrease in total amino acids and the time required for operation were unrelated each other.

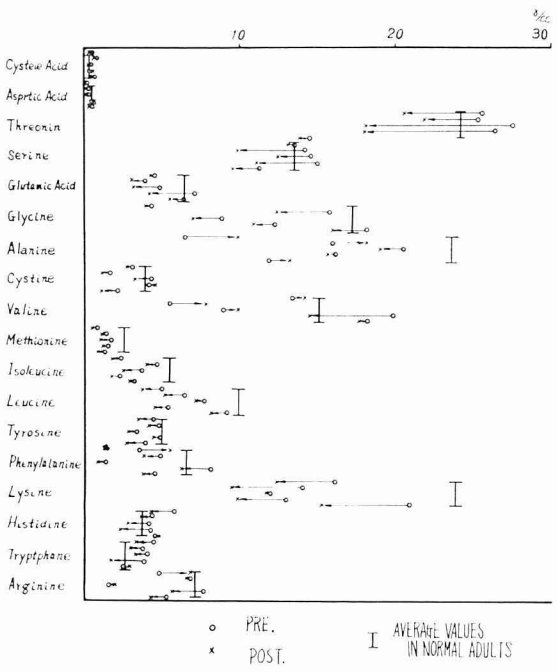


Fig. 1 Changes in amino acid fractions due to operative attack.

Concerning the rate of decrease of individual amino acid, lysine, cystine, serine, leucine and aspartic acid showed high rates of decrease, while alanine, valine, tryptophane and aspartic acid show low rates.

The time required for operation was not particularly related with the method of operation or A/G. In 4° with far advanced cancer, the rate of decrease of lysine, cystine, serine, leucine, and aspartic acid in response to surgery was high, indicating the presence of some relationship.

Table 2 *Amino Acid Fractions upon Operative Insult* (r/mℓ)

Name	T. M			T. T			K. M			S. Y			T. H		
	Pre. ope	Post. o.	CV%	Pre. ope	Post. o.	CV%	Pre. ope	Post. o.	CV%	Pre. ope	Post. o.	CV%	Pre. ope	Post. o.	CV%
Cys・NH_2	0.50	0.48	96.00	0.80	0.70	87.50	0.38	0.32	84.21	0.33	0.51	154.54	0.58	0.53	91.37
Asp	0.14	0.121	85.71	0.25	0.14	56.00	0.14	0.10	71.42	0.51	0.52	101.96	0.33	0.30	90.90
Thr	25.51	20.50	80.36	25.30	21.80	86.16	27.50	18.10	65.81	26.34	18.01	68.37	14.54	13.89	95.52
Ser	13.50	13.10	97.04	14.15	9.85	69.61	14.60	12.30	84.24	15.08	11.10	73.60	11.32	9.50	83.92
Glu	4.50	4.48	99.56	3.90	3.01	77.17	4.85	3.20	65.97	7.12	4.27	59.97	6.40	5.50	85.93
Gly	4.30	4.00	93.02	15.80	12.40	78.48	8.70	7.00	80.45	12.32	10.93	88.71	18.19	16.00	87.96
Ala	6.50	8.90	136.92	16.00	18.10	113.12	20.60	19.00	92.23	16.19	15.75	97.28	11.85	13.20	111.39
Cys	3.05	2.85	93.44	1.70	1.10	64.71	4.45	3.30	74.15	4.23	4.31	101.89	2.22	1.05	47.29
Val	13.42	14.20	105.81	5.05	7.80	154.45	9.00	9.90	10.00	19.97	14.49	72.55	18.26	17.89	97.97
Met	0.80	0.68	85.00	1.40	1.30	82.85	1.75	1.00	57.14	1.50	1.35	90.00	1.31	0.90	68.70
Ileu	2.35	1.98	84.25	4.65	4.00	86.02	3.75	2.50	66.67	2.32	1.80	77.58	3.16	3.00	94.93
Leu	5.00	4.70	94.00	6.52	5.20	79.75	7.70	7.20	93.50	5.40	4.25	78.70	9.22	8.10	87.85
Tyr	4.56	3.50	76.75	4.80	4.20	87.50	3.49	2.84	81.37	4.90	4.50	91.83	3.95	2.77	70.12
Phe	3.54	5.50	155.36	4.94	3.90	126.66	1.42	0.95	66.90	8.20	6.28	76.58	4.65	3.87	83.22
Lys	16.14	12.45	77.13	14.05	9.50	67.62	12.06	11.85	98.25	13.06	9.85	75.42	20.92	15.22	72.75
His	5.85	4.34	74.18	4.20	3.70	88.09	4.25	2.80	65.88	4.30	2.34	54.42	4.59	0.50	88.03
Try	4.50	3.42	76.00	3.85	3.00	77.92	4.10	3.40	82.92	2.96	1.75	59.12	2.50	2.92	116.80
Arg	4.80	6.05	126.04	6.85	6.65	97.08	1.60	1.90	18.75	7.69	5.68	73.86	5.35	4.20	78.50
Total amino acid	118.96	105.77	88.91	134.21	116.35	86.69	130.34	107.66	82.59	152.42	117.69	77.21	139.34	123.34	88.52
Essential amino acid	71.26	63.43	89.01	65.76	56.50	85.91	67.28	54.90	81.59	79.75	57·78	72.45	74.56	65.79	88.23
Ope. time (m)	90			90			70			80			60		
Ope. Method	BI			BII			BI			BI			BI		

2. *Changes in Postoperative Amino Acid Fractions due to Administration of a Small Amount of Amino Acid* (Fig. 2 Table 3)

Serum total amino acids decreased on the 1st and 3rd postoperative day, followed by a gradual increase on the 5th and 7th day. In 2 cases the level on the 7th day was higher than the preoperative level while the recovery did not reach the preoperative level in 6 others.

Changes in Individual Amino Acids will be Described Next.

Blood concentration of leucine increased on the 1st and 3rd post-operative day followed by a gradual decrease on the 5th and 7th day, but the return to the normal value did not take place. In 2 cases, a gradual increase was noted on the 5th and 7th day. Valine increased on the 1st day, followed by a decrease in 2 cases, increase by the 3rd day and then decrease in 2 cases, increase by the 5th day and decrease in 2 cases, persistent decrease until the 7th day in 1 case, and persistent increase until the 7th day in 1 case. Return to the normal value did not take place in any of them.

Isoleucine decreased after an increase on the 1st day in 4 cases, after an increase until the 3rd day in 1 case, after an increase until the 5th day in 3 cases, and continued to increase until the 7th day in 1 case. In each case, the variation was rather wide with a marked difference from the normal level.

Tryptophan increased until the 3rd postoperative day in 5 cases, and until the 5th day in 3 cases. Among these cases, a gradual decrease followed the increase in 7 and a rapid increase in 1, so that the values became close to the normal value by the 7th day.

Lysine was already much lower than the normal value already at the time of admission in almost all cases. On the first postoperative day, these values decreased further, and started to rise again slowly from the 3rd to 5th day but failed to reach the preoperative value.

Methionine showed a tendency to decrease in almost all cases from the first to the third postoperative day in almost all cases. Slow and gradual decrease persisted thereafter until the 7th day in 4 cases, an increase was seen in 4 but normal values were not reached.

Threonine showed a rapid decrease from the day of operation to the third day in almost every case in which the preoperative level was close to the lower limit of normal. Further decrease until the 7th day was seen in 4, and a gradual increase was seen in 4. The values only reached the range close to the lower limit of normal.

Phenylalanine decreased on the 1st day in 4 cases, and increased in 4 cases. Subsequent increase from the 3rd to the 7th day was seen in 5, and a gradual decrease was seen in, but scarcely any of them reached the normal level.

Alanine increased on the 1st day and decreased on the third day, followed by a gradual return by the 7th day but none of the values reached the normal range. However, in 2 cases a gradual increase during the 7 postoperative days was seen in 2 cases.

Serine decreased on the 1st and 3rd day and subsequently continued to increase by the 7th day. The values did not return to the preoperative value or normal level.

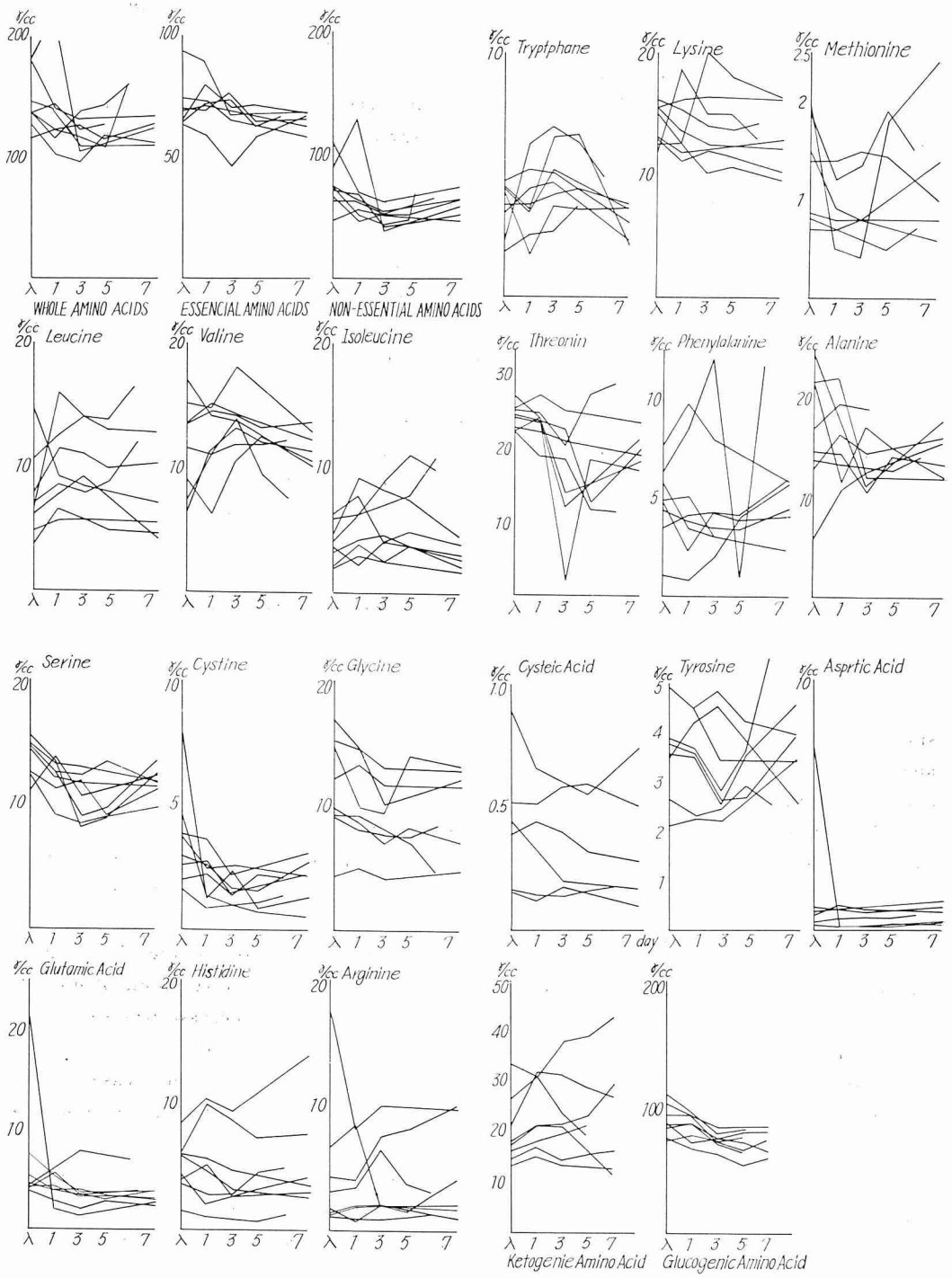

WHOLE AMINO ACIDS
ESSENCIAL AMINO ACIDS
NON-ESSENTIAL AMINO ACIDS
Tryptphane
Lysine
Methionine
Leucine
Valine
Isoleucine
Threonin
Phenylalanine
Alanine
Serine
Cystine
Glycine
Cysteic Acid
Tyrosine
Asprtic Acid
Glutamic Acid
Histidine
Arginine
Ketogenic Amino Acid
Glucogenic Amino Acid
day

Fig. 2

Cystine decreased on the 1st day followed by a gradual increase in 4 cases, gradually increased following a decrease until the 3rd day in 5 cases, and gradually increased following a decrease by the 5th day in 1 case. Values did not return to the normal range.

Glycine showed a gradual decrease from the 1st to the 7th day in almost all cases in which the value at admission was less than normal. In only one case a gradual elevation was noted.

Glutamine showed a tendency of decrease by the third day in most cases. The value was sustained until the 7th day with no tendency of recovery.

Histidine decreased until the 1st day in 1, until the 3rd day in 2, and until the 5th day in 1, followed in each case by a gradual recovery. In 2 cases a gradual and persistent decrease was found from the day of operation until the 7th day. In 2 cases in which values higher than normal was obtained at the time of admission, temporary decrease was found on the 3rd and 5th day followed by an elevation.

Arginine kept increasing until the third day and showed a tendency of decrease until the 7th day. Fluctuations under the normal level were seen in many cases. In 2 cases a gradual increase was seen by the 7th day.

Cysteic acid showed an elevation on the first postoperative day rather than the time of admission in 1 case and showed a decrease by the third day in 1 case. Decrease followed in each case giving a value lower than at the time of admission. However, in 2 cases a decrease was seen until the 3rd and 5th day followed by an increase.

Tyrosine decreased until the third day followed by an increase until the 7th day in 4 cases, while an increase was seen until the third and fifth day followed by a decrease in 3 cases.

Aspartic acid showed a decrease or an increase on the 3rd day, showing a considerable elevation over the level at admission on the 7th day.

3. *Postoperative Fluctuations of Amino Acid Fractions Following an Administration of a Large Amount of Amino Acid.* (Fig. 3 Table 4)

Serum total amino acid values decreased on the 1st and 3rd post-operative day, followed by an increase on the 5th and 7th day. As compared with group 1, the rate of decrease on the 3rd day was smaller and the rate of increase on the 7th day was greater.

Total essential amino acid showed a smaller rate of decrease on the first and the third day as compared with group 1, slight decrease being seen on the 3rd day in 2 cases and on the 5th day in 2 cases. A decrease was noted on the 7th day in 2 cases but all other cases showed a recovery to or above the preoperative value.

Total non-essential amino acid decreased on the 1st and 3rd day followed by a tendency of increase on the 5th and 7th day, returning approximately to the preoperative value.

Changes of Each Amino Acid will be Discussed.

Leucine increased until the 1st and 3rd postoperative day followed by a decrease until the 7th day in 5 cases. A decrease continued until the 3rd day in 1, and a wide variation was seen in 1.

Valine showed an elevation on the 1st day followed by a decrease in 3 cases,

Table 3-a *Changes in Post Operative Amino Acid Fraction Due to Administration of a Small Amount of Amino Acid Group 1* (r/mℓ)

Name	K. M					T. T					T. M					S. S		
Day	A	1	3	5	7	A	1	3	5	7	A	1	3	5	7	A	1	3
Cys・NH_2	0.39	0.44	0.40	0.32	0.28	0.89	0.65	0.60	0.55	0.73	0.52	0.51	0.58	0.59	0.50	0.16	0.14	0.14
Asp	0.15	0.12	0.10	0.12	0.15	7.20	0.15	0.12	0.21	0.31	0.12	0.11	0.15	0.18	0.19	0.31	0.45	0.50
Thr	22.50	24.00	2.00	18.50	17.00	24.23	23.51	14.20	15.20	18.34	24.77	23.97	22.40	12.70	19.46	25.17	24.80	20.20
Ser	14.60	12.60	12.40	13.50	11.70	12.37	11.30	11.90	9.10	11.30	14.60	12.59	9.00	9.80	13.54	15.40	13.40	8.20
Glu	5.40	4.10	4.00	3.50	3.00	3.85	2.90	2.20	2.80	2.40	4.45	5.70	3.50	3.02	3.85	4.50	6.20	7.80
Gly	9.70	8.60	7.00	8.20	7.00	14.79	9.91	9.41	14.00	13.20	4.31	4.90	4.20	4.42	4.80	9.20	9.10	8.00
Ala	21.60	11.50	17.20	15.00	12.00	17.21	19.50	19.00	20.50	22.90	6.45	10.90	12.50	13.50	15.40	13.72	13.40	12.85
Cys	4.60	1.30	2.40	9.90	1.40	1.67	0.90	1.00	0.80	0.60	2.94	2.62	1.70	1.65	2.75	2.01	2.25	1.45
Val	9.10	6.20	10.50	12.50	10.50	6.56	11.40	13.20	14.00	11.40	13.51	14.45	14.10	13.20	13.61	11.51	11.10	11.82
Met	1.90	0.50	0.42	1.80	2.40	1.38	1.48	1.48	1.42	1.00	0.69	0.68	0.79	0.98	1.38	1.91	1.20	1.35
Ileu	3.60	2.20	4.10	4.80	4.00	4.52	9.03	8.25	7.50	4.50	2.08	3.96	2.45	3.75	2.81	5.90	6.20	8.90
Leu	7.70	11.40	11.00	9.80	10.20	6.41	16.00	14.00	13.00	12.80	4.89	5.66	5.75	4.90	4.63	10.60	12.50	14.00
Tyr	3.79	3.59	2.60	2.65	3.87	4.94	4.50	4.80	4.20	3.90	3.56	3.54	2.58	3.50	4.48	3.90	3.70	2.80
Phe	1.12	0.98	2.05	4.10	5.63	4.89	2.34	4.25	4.10	5.89	4.34	3.80	3.50	3.42	4.32	6.30	8.50	12.00
																6.98		
Lys	13.06	11.80	12.10	12.35	12.80	12.50	12.50	10.00	10.50	9.40	15.02	12.50	20.00	18.00	16.20	11.63	18.50	15.00
His	4.30	2.02	2.60	3.20	4.42	4.04	5.19	2.70	2.85	2.89	6.14	9.98	8.70	7.25	7.59	3.69	2.80	2.85
Try	4.36	1.70	3.75	3.60	3.63	3.79	3.79	4.20	4.41	3.79	4.51	3.58	6.60	6.70	2.06	1.98	2.50	2.70
Arg	1.70	0.80	2.00	2.00	2.04	6.65	8.30	2.00	1.50	4.16	4.30	4.05	7.50	8.05	9.98	3.16	3.46	6.45
Total amino acid	129.57	103.85	96.62	116.84	112.02	137.89	13.25	123.31	126.64	129.51	117.20	123.50	126.00	115.77	127.55	137.80	116.08	138.29
Essential amino acid	63.34	58.78	45.92	67.45	66.61	64.28	79.95	69.58	70.13	67.12	69.81	68.60	75.59	63.65	64.47	75.21	85.30	85.97
Non essential amino acid	66.23	45.07	50.70	49.39	45.86	73.61	63.30	53.73	56.51	62.39	47.39	54.90	50.41	52.12	63.08	62.59	30.78	52.30

Table 3-b

Name	S. S		N. I					S. T				S. Y				I. A			
Day	5	7	A	1	3	5	7	A	1	3	7	A	1	3	7	A	1	3	7
Cys・NH_2	0.16	0.18						0.15	0.12	0.18	0.10	0.44	0.32	0.20	0.17				
Asp	0.47	0.57						0.74	0.82	0.91	1.14	0.90	0.80	0.76	0.90	0.62	0.94	0.82	0.73
Thr	27.30	28.83	22.20	19.00	18.50	11.85	11.60	25.55	27.25	25.12	23.49	26.90	24.20	12.00	21.30	22.89	22.35	20.86	19.28
Ser	9.00	9.90	12.30	9.20	8.50	9.10	12.40	14.80	13.20	13.00	11.90	14.40	12.10	11.80	11.50	11.05	13.85	10.75	12.40
Glu	7.50	7.00	7.60	5.40	4.00	3.60	3.90	4.31	4.40	3.38	3.03	4.60	3.90	3.50	3.70	22.20	2.11	1.40	2.70
Gly	7.00	4.60	9.00	8.00	7.60	7.50	8.41	16.70	14.30	10.10	12.20	15.20	14.50	13.00	12.80	12.03	13.23	11.70	11.50
Ala	12.70	13.96	14.67	14.50	10.50	14.10	13.28	24.60	18.00	11.11	17.60	21.80	22.10	12.00	11.90	13.21	16.39	14.40	16.02
Cys	2.30	2.17	7.80	1.40	1.00	1.20	1.50	3.84	3.65	2.23	3.17	3.75	2.50	2.61	2.25	2.67	2.77	1.512	2.25
Val	11.80	12.10	7.25	11.25	13.82	9.50	7.74	17.10	14.10	13.80	10.00	15.20	14.80	18.10	13.00	13.64	15.19	14.25	12.32
Met	1.90	1.52	0.80	0.70	0.60	0.50	0.70	2.31	2.31	2.42	2.62	1.50	0.90	0.80	0.80	0.86	0.78	0.80	0.58
Ileu	11.10	9.90	4.10	6.20	7.00	7.80	10.80	6.30	7.80	4.10	3.20	3.20	4.10	4.60	2.30	1.85	2.94	2.42	1.72
Leu	13.80	16.30	7.06	8.50	7.85	8.70	11.70	14.40	9.20	8.40	7.10	6.10	7.80	9.20	4.20	3.72	6.58	5.70	5.50
Tyr	3.60	5.40	2.67	2.34	2.48	2.90	2.50	4.99	4.51	3.45	3.35	3.50	4.20	4.50	2.50	2.16	2.27	2.21	3.44
Phe	1.05	11.60	3.49	4.10	4.25	3.82	4.05	7.70	9.80	7.90	5.80	4.90	5.10	3.10	2.70	5.70	3.38	3.11	2.32
		11.72	17.02				18.55												
Lys	15.00	12.80	16.13	15.38	14.00	13.78	14.16	15.50	13.50	12.50	12.03	12.80	11.00	12.00	10.60	15.57	16.13	16.40	16.08
His	6.55	4.91	1.53	1.02	0.84	0.72	1.13	5.83	4.80	3.20	2.54	6.00	5.70	4.80	3.52	8.48	10.43	9.40	13.79
Try	3.78	3.79	2.31	6.30	7.00	6.40	4.90	4.82	5.21	5.10	3.03	3.41	4.50	4.70	2.27	4.49	3.42	5.20	3.60
Arg	3.80	3.08	1.19	0.95	0.99	1.01	1.38	1.21	1.91	2.01	1.75	1.41	1.85	2.10	1.16	17.32	8.20	10.01	9.68
Total amino acid	142.50	160.33	137.12	123.42	116.49	109.04	214.57	183.13	218.96	105.24	124.05	145.91	140.37	108.91	109.10	180.02	140.96	130.94	133.91
Essential amino acid	85.73	96.84	63.34	71.43	73.02	62.35	65.65	93.68	89.17	66.92	67.27	74.01	72.40	64.50	57.17	68.72	70.77	68.74	61.40
Non essential amino acid	56.77	63.49	73.78	51.99	43.47	46.69	148.92	89.45	129.79	38.32	56.78	71.90	67.97	44.41	51.93	111.30	70.19	62.20	72.51

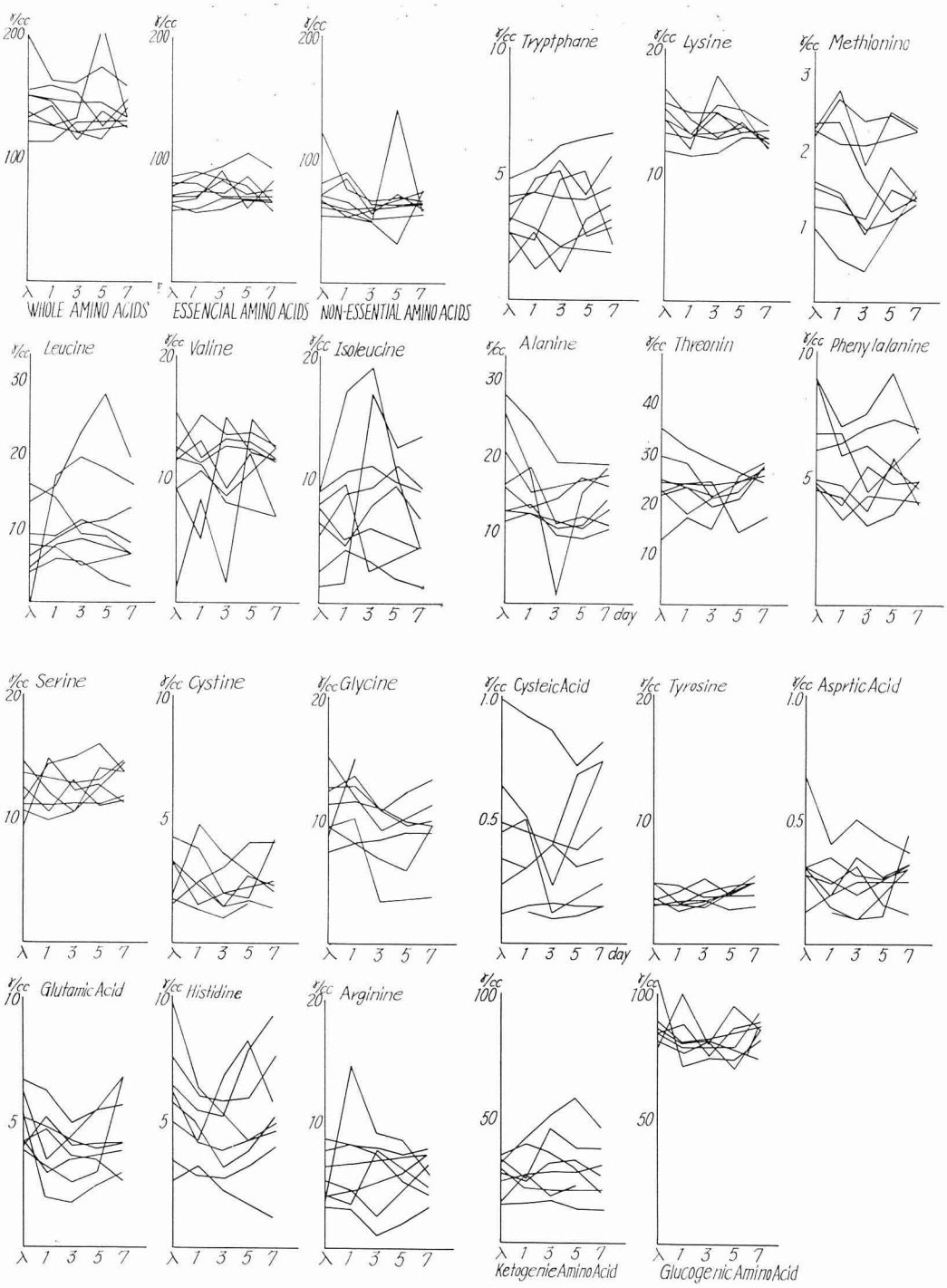

γ/cc
WHOLE AMINO ACIDS
ESSENCIAL AMINO ACIDS
NON-ESSENTIAL AMINO ACIDS
Tryptphane
Lysine
Methionine
Leucine
Valine
Isoleucine
Alanine
Threonin
Phenylalanine
day
Serine
Cystine
Glycine
CysteicAcid
Tyrosine
AsprticAcid
Glutamic Acid
Histidine
Arginine
KetogenicAminoAcid
GlucogenicAminoAcid

Fig. 3

elevation on the 3rd day followed by a decrease in 3 cases, and kept increasing until the 5th day followed by a decrease in 2 cases. As compared with group 1, the value was far lower than the controls.

Isoleucine showed an increase on the 1st day in 2 cases, kept increasing until the 3rd day in 4 cases, and kept increasing until the 5th day in 2 cases, followed by a decrease. In both of the 2 cases in which a decrease was seen on the 1st day, subsequent increase was noted. The width of fluctuation was larger than in group 1.

Tryptophane increased until the 3rd day followed by a decrease in 3, and continued to increase slowly until the 7th day in 4. The difference from normal values was greater than in group 1.

Lysine decreased on the 1st postoperative day in all cases, followed by an increase on the 3rd and 5th day and a slow decrease by the 7th day, showing subnormal values in all except one. The range of variation was, however, smaller than that in group 1.

Methionine decreased until the 3rd day in each case and increased on the 5th day. Increase was continued until the 7th day in 4 cases, while a decrease was again seen in 4 cases. Values were closer to normal range in all cases.

Threonine decreased on the 1st postoperative day in all cases, followed by a gradual increase around the 7th day, reaching the preoperative value and approaching the normal value.

Phenylalanine decreased on the 1st and 3rd day in most cases, followed by a gradual increase by the 7th day. The fluctuation was smaller than in group 1, approaching the normal range.

Alanine decreased on the 1st and the 3rd day and gradually increased on the 5th and 7th day, but did not reach the normal value. The difference from the normal value was greater than in group 1.

Serine decreased on the 1st day in 6 cases, and increased in 2 cases. In 3 cases further decrease was noted on the 3rd day. Increase was again seen on the 5th and 7th day approaching the normal value. As compared with group 1, a tendency of increase was noted from the 3rd day, approaching the normal value.

Cystine decreased until the 3rd day in 3 cases, and until the 5th day in 2 cases, followed by an increase in each instance. Subsequent fluctuation was larger than in group 1.

Glycine decreased until the 3rd day and then gradually increased until the 7th day in 4 cases, while a persistent and slow decrease from the 1st to the 7th day was seen in 3. No great difference from the preoperative value was noted. Fluctuations were smaller than in group 1.

Glutamic Acid decreased until the 3rd day in most of the cases, followed by some increase by the 7th day. As compared with group 1, recovery towards the preoperative value was better, approaching the normal value.

Histidine decreased on the 1st and 3rd day followed by a gradual increase until the 7th day. As compared with group 1, the fluctuation was smaller. In many instances values higher than normal were seen on the 7th day.

Arginine increased on the 1st postoperative day in 3 cases, and increased until the

Table 4-a *Changes in Postoperative Amino Acid Fraction Due to Administration of a Large Amount of Amino Acid Group 2* (r/mℓ)

Name	T.Y					Y.S					T.H					H.Y			
Day	A	1	3	5	7	A	1	3	5	7	A	1	3	5	7	A	1	3	5
Cys・NH_2	0.12	0.15	0.16	0.15	0.15	0.34	0.30	0.40	0.68	0.73	0.49	0.45	0.41	0.83	0.47		0.13	0.10	0.11
Asp	0.68	0.40	0.50	0.42	0.37	0.13	0.20	0.25	0.27	0.31	0.31	0.35	0.28	0.26	0.30		0.13	0.10	0.11
Thr	12.80	17.20	14.80	25.20	27.90	29.40	18.00	21.00	22.00	16.90	22.80	18.00	21.00	22.00	17.00	21.68	23.36	19.32	20.89
Ser	11.19	11.10	11.25	12.10	12.85	11.30	14.50	15.00	16.00	13.80	12.50	10.50	13.10	11.00	11.50	9.40	14.84	12.24	12.76
Glu	6.70	6.25	5.00	5.50	6.88	6.50	3.50	4.50	5.50	5.70	5.70	2.00	1.80	2.50	3.00	4.18	4.77	3.63	3.56
Gly	12.52	13.65	10.82	9.65	9.97	11.20	11.50	11.00	9.80	9.60	9.00	15.00	14.80	17.80	19.20	12.58	12.78	10.89	12.02
Ala	16.20	18.50	11.00	12.00	10.82	25.40	18.00	1.50	15.00	18.30	16.20	13.20	14.20	17.00	16.00	11.57	12.50	10.39	10.72
Cys	1.81	1.321	1.00	1.61	11.44	1.65	2.50	1.45	1.71	1.42	4.20	3.80	2.00	1.80	4.20	3.21	2.34	1.44	2.77
Val	15.28	11.50	13.15	12.80	11.15	12.30	11.05	12.50	12.10	11.37	11.40	13.00	9.00	12.00	9.80	12.07	15.10	13.47	13.65
Met	1.65	1.45	0.90	1.50	1.33	1.25	1.20	1.10	1.80	1.38	2.38	2.40	1.65	1.21	1.38	2.18	2.68	2.41	2.84
Ileu	2.49	4.25	3.28	2.01	1.39	1.25	1.50	17.00	12.60	13.60	9.00	17.20	19.00	10.50	4.50	5.44	8.08	9.26	11.18
Leu	4.34	5.78	5.50	3.33	2.16	1.30	17.00	19.50	18.00	16.00	16.00	14.20	9.20	9.00	6.40	13.67	15.87	22.55	28.12
Tyr	3.72	2.61	3.10	4.01	5.39	3.02	3.34	3.50	2.70	2.99	4.90	3.20	4.10	4.55	4.90	6.81	9.93	11.92	11.22
Phe	4.68	3.25	4.25	4.10	3.96	4.75	3.82	5.40	4.70	4.79	4.89	4.64	3.58	5.70	3.89	6.07	6.32	6.94	7.26
Lys	16.66	14.30	13.00	14.10	12.24	14.32	13.20	12.80	13.40	13.44	15.63	14.80	14.90	13.50	13.44	15.16	13.22	15.49	15.16
His	9.76	6.25	5.30	4.20	4.94	6.40	5.40	5.20	7.80	9.23	7.50	6.00	5.80	5.90	7.50	4.96	4.18	6.80	8.30
Try	4.09	4.23	4.00	3.98	4.43	1.50	2.70	1.10	3.20	3.79	3.79	4.21	5.50	4.15	5.68	2.67	2.34	4.75	5.07
Arg	7.76	8.20	8.00	7.43	7.98	8.56	8.20	7.50	5.30	4.16	4.16	4.50	5.12	6.00	7.48	4.19	14.56	9.14	8.60
Total amino acid	133.53	142.28	115.01	138.58	125.35	155.44	158.42	153.82	125.02	147.51	150.85	147.45	145.44	145.25	133.64	202.38	163.20	160.84	174.35
Essential amino acid	61.99	57.71	58.88	67.02	64.56	64.57	68.47	9.40	60.26	81.27	85.89	88.45	83.38	78.06	59.09	78.94	86.97	94.19	104.18
Non essential amino acid	71.54	84.57	56.13	71.56	60.79	80.87	88.95	63.42	69.76	65.14	64.96	59.00	61.61	67.19	74.55	123.44	76.23	66.65	70.17

Table 4-b

Name	H.Y	K.I				K.T				T.M					K.S				
Day	7	A	1	3	7	A	1	3	7	A	1	3	5	7	A	1	3	5	7
Cys・NH_2	0.15	0.45	0.50	0.12	0.24	0.64	0.51	0.23	0.73	0.24	0.30	0.40	0.31	0.34	0.99	0.92	0.86	0.72	0.81
Asp	0.43	0.30	0.20	0.25	0.25	0.28	0.15	0.10	0.30	0.31	0.25	0.20	0.25	0.31	0.28	0.24	0.31	0.16	0.12
Thr	26.82	24.60	23.10	21.50	26.40	35.00	31.00	28.50	24.10	22.46	23.82	23.91	14.40	16.57	24.16	23.80	23.65	24.40	25.55
Ser	11.31	10.50	9.80	10.50	14.60	10.00	8.00	7.50	6.60	14.40	12.00	10.50	14.00	13.80	13.60	13.20	12.80	13.00	14.70
Glu	2.68	4.50	3.00	3.50	3.90	4.00	5.20	4.10	4.20	5.21	48.50	4.25	4.00	4.14	4.00	3.20	2.60	3.00	6.80
Gly	13.38	9.50	10.20	12.80	10.80	15.00	11.80	9.20	11.20	9.53	8.20	8.45	8.95	8.96	7.50	8.20	6.80	6.00	9.60
Ala	14.12	20.50	17.50	16.00	17.50	28.00	24.50	19.20	18.80	14.11	13.51	9.42	9.20	10.34	12.70	12.40	11.25	10.40	12.90
Cys	2.30	3.20	1.50	2.00	2.50	2.00	4.80	3.60	2.10		2.50	3.00	4.01	4.02	5.90	6.20	6.40	5.10	6.50
Val	12.49	11.50	11.00	8.00	6.80	9.00	10.50	8.50	12.30	9.10	5.00	15.00	12.00	11.40	1.21	8.20	1.34	14.50	12.30
Met	2.28	2.28	2.10	2.07	2.25	1.00	0.58	0.40	1.50	1.38	1.37	0.96	1.06	1.30	2.30	2.80	1.80	2.50	2.30
Ileu	9.40	7.50	5.00	6.00	4.50	8.00	9.50	2.50	4.50	9.00	10.50	11.00	9.80	9.00	6.30	4.50	7.80	9.50	6.80
Leu	19.57	8.00	7.50	5.10	6.40	5.00	7.80	8.50	6.40	6.40	8.40	10.50	11.00	12.80	9.30	9.10	11.00	9.80	8.00
Tyr	10.12	4.90	3.20	3.00	6.90	3.20	3.12	3.40	4.90	4.90	4.70	3.75	3.80	3.99	3.50	4.10	5.20	4.00	4.90
Phe	6.89	9.00	5.80	6.20	4.52	6.80	6.72	4.36	6.45	4.45	4.10	3.00	3.50	4.79	8.90	7.00	7.50	9.10	6.70
															0.95				11.16
Lys	13.93	14.26	12.00	17.86	12.19	13.26	12.92	14.81	12.81	11.88	11.50	11.70	12.90	12.81	15.08	13.10	13.33	13.80	12.56
His	5.78	6.20	4.25	3.82	4.62	2.62	3.20	2.15	1.15	5.77	4.80	3.10	3.80	5.08	3.40	2.80	2.70	3.20	3.96
Try	2.22	3.26	2.86	2.10	3.17	2.65	1.20	2.10	1.89	4.80	5.20	6.10	6.40	6.58	3.03	4.78	5.10	2.50	2.84
Arg	6.01	4.10	3.50	7.80	4.99	5.23	4.60	2.50	6.65	6.40	6.68	7.00	7.20	7.48	3.24	3.04	1.05	2.00	3.33
Total amino acid	159.88	112.96	113.11	128.62	130.53	151.68	146.10	121.65	126.58	130.34	127.63	132.24	209.38	133.71	137.77	127.58	121.49	116.85	140.76
Essential amino acid	93.60	58.26	59.46	68.83	66.23	80.71	80.2	69.67	69.95	69.47	69.89	82.17	71.06	75.25	70.28	73.28	71.52	86.10	65.98
Non essential amino acid	66.28	54.70	53.65	59.79	64.30	70.97	65.88	51.98	56.63	60.87	57.79	50.07	138.32	58.46	67.49	54.30	49.97	30.75	74.78

3rd day in 1, followed by a decrease until the 7th day in all cases. In 2 cases, a decrease was seen on the 3rd day followed by an increase until the 7th day on the contrary. Values closer to normal were seen as compared with group 1.

Cysteic acid decreased on the 3rd and 5th day followed by an increase until the 7th day in 5 cases, while an increase was seen until the 3rd day followed by a decrease until the 7th day in 2 cases.

Tyrosine decreased on the 1st day followed by a gradual increase until the 7th day, approaching the normal value.

Aspartic acid increased on the 3rd day and decreased on the 7th day in 3 cases, and decreased on the 3rd day and increased on the 7th day in 3. All of them approached the normal value.

4. *Vitamin B_1 Concentration and Amino Acid Fractions* (Table 5, 6)

In order to study the interrelationship between vitamin B_1 concentration and amino acid fractions, both were determined simultaneously.

Vitamin B_1 concentration is shown in the Table 5. On the 3rd postoperative day,

Table 5 *Vitamin B_1 (Butyrylthiamine disulfide) and Amino Acid Fractions* (r/mℓ)

Name	T. H			M. Y					T. M		
	Pre. Ope	1 hour	8 day	Pre. Ope	3 hour	7 hour	24 hour	8 day	Pre. Ope	3 day	8 day
Cys・NH_2	0.49	0.49	0.47	0.97	0.90	0.97	0.49	0.24	0.24	0.40	0.34
Asp	0.31	0.31	0.30	0.31	0.31	0.62	0.31	0.31	0.31	0.20	0.31
The	22.80	10.50	17.00	28.70	28.50	26.5	36.90	26.90	22.46	23.91	16.57
Ser	12.50	11.90	11.50	13.80	11.30	14.40	10.60	13.20	14.40	10.50	13.80
Glu	5.70	2.80	3.00	5.70		6.10	2.90	5.70	5.21	4.25	4.14
Gly	9.00	16.00	19.20	6.00		6.00	7.20	6.00	9.53	8.45	8.96
Ala	16.20	14.40	16.00	14.40	14.42	14.40	14.40	18.00	14.11	9.42	10.34
Cys	4.20	4.20	4.20			4.20	4.20	4.20		4.02	3.00
Val	11.40	16.00	6.80	13.70		11.40	22.80	9.10	9.10	15.00	11.40
Met	2.38	3.15	1.38	2.50	2.30	2.50	3.15	2.80	1.38	0.96	1.30
Ileu	9.00	18.10	4.50	9.15	8.50	8.50	18.10	8.50	9.00	11.00	9.00
Leu	16.00	25.60	6.40	16.00	15.90	14.80	25.60	15.40	6.40	10.50	12.80
Tyr	4.90	4.90	4.90	4.90	4.90	4.90	4.90	4.90	4.90	3.75	3.99
Phe	4.89	5.34	3.89	3.89	3.89	3.89	4.34	3.89	4.45	3.00	4.79
Lys	15.63	12.50	13.44	25.00	28,10	18.00	15.60	37.50	11.88	11.70	12.81
His	7.50	6.93	7.50	2.89	3.46	2.89	6.35	8.66	5.77	3.10	5.08
Try	3.79	5.68	5.68	1.89	3.79	3.79	3.79	7.22	4.80	6.10	6.50
Arg	4.16	3.33	7.48	6.65	4.49	3.33	3.33	5.82	6.40	7.00	7.48
Vitamin B_1 Concentration (M_0/dℓ)	7.2	270	5.4	8.9	9.1	7.0	64	5.4	180	54	12

* TH was administrated 200 mg of vitamin B_1 at pre-operation.
MY was no administration Vitamin B_1 at Pre-Operation, but administrated 100 mg of vitamin B_1 at 1 hour after operation attack.

the blood level of butyrylthiamine disulfide was maintained higher than that of thiamine tetrahydrofurfuryl disulfide. Butyrylthiamine disulfide was therefore used in all cases in group 2. Blood concentrations in group 2 are shown in Table 13 and 14. Some relationship with the postoperative amino acid fraction was suggested.

Table 6-indicates the amino acid fraction upon changing the blood concentration of VB_1 through intravenous injection. When concentration of vitamin B_1 was elevated, concentrations of valine, methionine, isoleucine, leucine, phenylalanine, and glycine tended to rise, while serine, glutamic acid, lysine, and histidine showed a tendency of decrease. Concentrations of these amino acid might change according to the method employed and further studies are indicated.

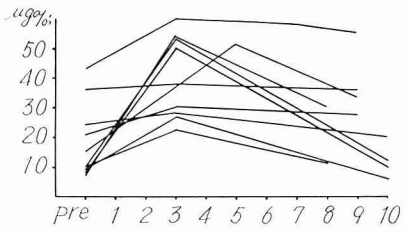
Table 6 *Vitamin B_1 Concentration* (ug/dℓ)

Name	Pre. Op	Post. Op	1	3	5	7
M.K	12.5	12.0	31.0	12.0		9.1
K.T	8.4			12.0		13.5
M.O			15.5	7.8		7.1
G.N	7.5	6.2	6.9	5.6		7.4
R.K	10.1	5.3	15.5	10.3		4.5
K.I	7.7					10.0
K.N	8.1	6.0	7.0		9.6	14.0
Y.M	9.8	9.0	26.0	15.5		5.4
F.N	10.5			7.7		2.8

administration of tetra hydro furfuryl disulfide

Name	Pre. Op	Post. Op	1	3	5	7	10
K.I	29.0	21.5	36.0	57.0		10.3	
S.Y			29.5	24.5		27.0	
S.S	9.2	9.7	12.5	280.0		15.5	
T.N	16.5	15.0	11.8	29.0		115.0	
S.S.	7.3		8.4			22.5	
Y.S	9.7			22.5		11.0	
T.H	7.2			250.0			5.4
T.M	9.6			54.0			12.0
S.T	7.2			54.0			300.0
K.S	15.5				52.0	16.0	
M.Y	8.9			27.0			5.4

administration of Butyryl thiamine disulfide



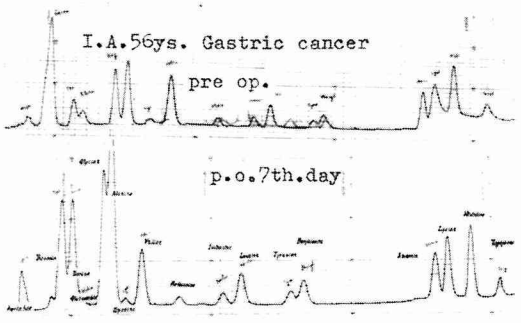


Fig. 4 Vitamin B_1 blood concentration.

5. *Addition of Amino Acid as a Counter-Measure Against Changes in Amino Acid Fractions* (Table 7 Fig. 5)

Serum total amino acid decreased on the 1st postoperative day but started to rise on the 3rd day, unlike group 2. Further increase was noted on the 5th and 7th day, giving values higher than the preoperative level.

Total essential amino acid decreased on the 1st day and further decreased on the

3rd and 5th day in some cases but a gradual increase was seen by the 7th day, returning to the preoperative level.

Total non-essential amino acid decreased on the 1st day in most cases, and showed a tendency of increase on the 3rd, 5th and 7th day. Increase started already on the 3rd day unlike group 2.

Changes in individual amino acid were as follows.

Leucine slightly decreased on the 1st day followed by a gradual increase until the 7th day in 5 cases. In 2 other cases, the elevation continued from the 1st to the 7th day. As compared with group 2, the value on the 7th day was closer to normal and the width of fluctuation was smaller.

Valine rose on the 1st day and subsequently kept small fluctuations, maintaining approximately the same level by the 7th day in 7 cases, while a considerable decrease was seen on the 7th day in 2 cases. The values were closer to normal than those in group 2.

Isoleucine decreased on the 1st day in 5 cases and decreased on the 3rd day in 1 case. Subsequent rise towards the 7th day approaching the normal level was seen in both of them. The width of fluctuaion was smaller than in group 2.

Tryptohane gradually increased from the time of admission until the 7th day in 6 cases, and gradually decreased in 2 cases. The difference from the normal value was greater than in group 2.

Lysine markedly decreased on the 1st, 3rd, and 5th day, followed by a rapid increase on the 7th day approaching the normal value in 5 cases, a slow and gradual increase until the 7th day with small fluctuations in 3 cases, and a sustained decrease until the 7th day in 1 case. Wider fluctuations were seen than in group 2.

Methionine showed an increase on the 1st day in most of the cases. Three showed a decrease on the 5th day, while other 6 showed further increase. Values were closer to normal than in group 2, representing values at the lower limit of normal range.

Threonine increased on the 1st day showing a temporary decrease on the 3rd day in all cases, followed by an increase reaching values higher than at the admission on the 7th day. Values were closer to normal than in group 2. Increase was seen in all cases in which threonine was administered.

Pyenylalanine decreased on the 1st day in 4 cases, and increased on the 1st day in 4 cases. A gradual increase was seen until the 7th day in all except for 1 case. Values were closer to normal in most of the cases than in group 2.

Alanine decreased on the 1st day, followed by an increase until the 7th day reaching values higher than the preoperative level. More cases showed normal values than in group 2.

Serine decreased on the 1st day in 4 cases, followed by an increase on the 3rd, 5th, and 7th day. Fluctuations were smaller than in group 2.

Cystine decreased on the 1st day in 2 cases followed by an increase on the 3rd, 5th, and 7th day in all except 1. Values were closer to normal than in group 2, with smaller fluctuations.

Glycine decreased on the 1st day in 4 cases, followed by increase on the 3rd day.

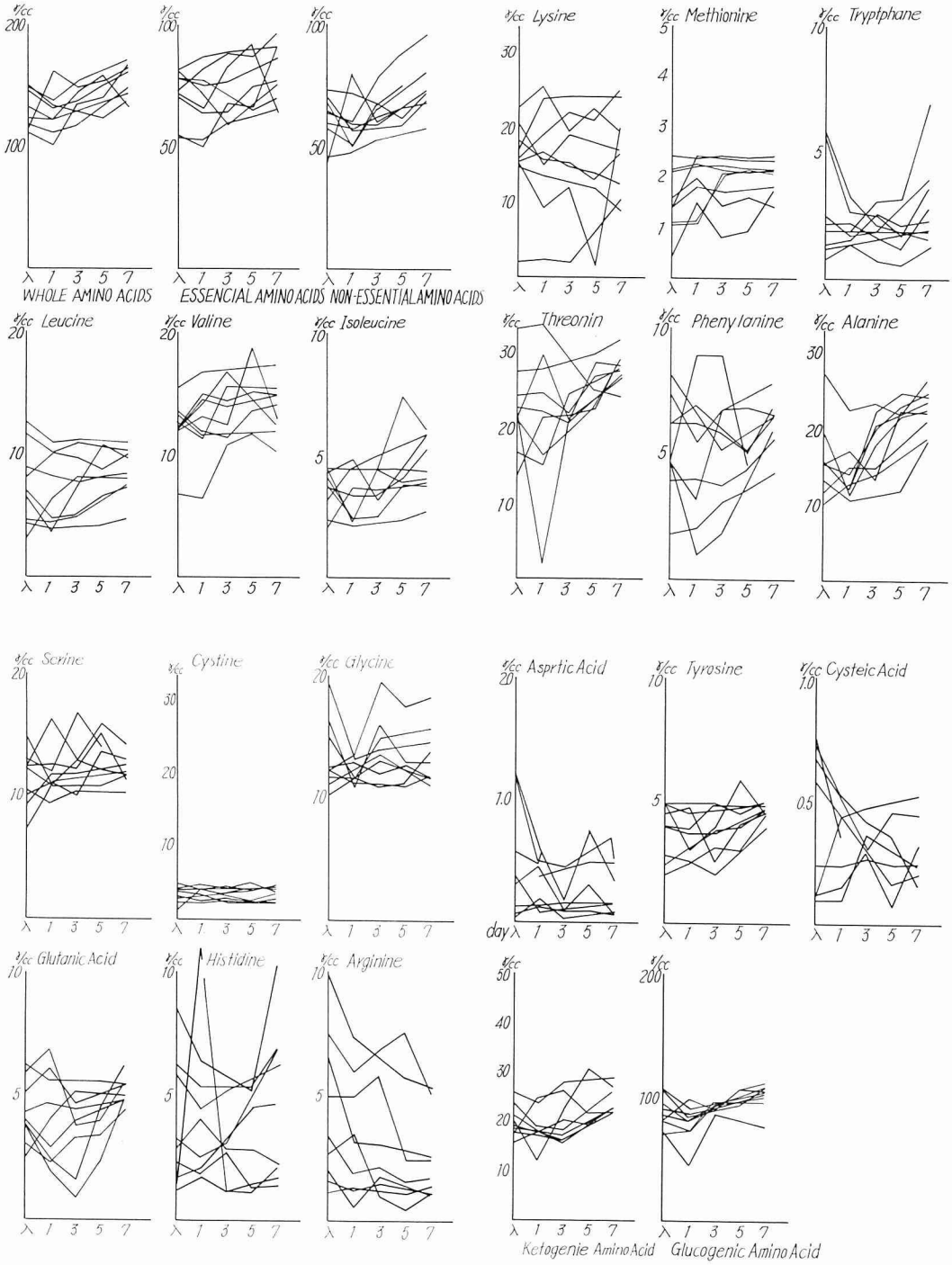

γ/cc
WHOLE AMINO ACIDS
ESSENCIAL AMINO ACIDS
NON-ESSENTIAL AMINO ACIDS
Lysine
Methionine
Tryptphane
Leucine
Valine
Isoleucine
Threonin
Phenylanine
Alanine
Serine
Cystine
Glycine
Asprtic Acid
Tyrosine
Cysteic Acid
Glutanic Acid
Histidine
Arginine
day
Ketogenic Amino Acid
Glucogenic Amino Acid

Fig. 5

Table 7-a *Changes in Postoperative Amino Acid Fraction due to Administration of a Large Amount of Amino Acid Group 3 Addition of Amino Acid as a Countermeasure Against Changes in Amino Acid Fractions* (γ/mℓ)

Name	G.T					T.S					T.T					S.T				K.F	
Day	A	1	3	5	7	A	1	3	5	7	A	1	3	5	7	A	1	3	7	A	1
Cys・NH_2	0.24	0.24	0.27	0.24	0.24	0.12	0.15	0.29	0.07	0.32	0.73	0.52	0.41	0.35	0.16	0.12	0.44	0.47	0.51	0.76	0.35
Asp	0.31	0.46	0.09	0.31	0.06	0.06	0.12	0.09	0.09	0.06	1.23	0.62	0.19	0.75	0.34	0.40	0.09	0.10	0.15	0.58	0.48
Thr	20.70	2.25	20.70	28.80	28.50	21.50	16.60	19.70	23.10	28.70	14.10	21.42	21.60	22.83	29.14	22.96	22.34	20.80	26.83	24.41	24.90
Ser	12.50	16.30	13.00	16.00	14.20	13.00	12.00	17.00	14.00	14.10	10.00	11.10	10.10	13.67	13.05	14.80	11.10	11.50	12.00	12.55	12.63
Glu	5.90	6.90	3.80	4.00	5.50	3.90	2.00	0.90	2.40	4.90	3.90	2.40	1.60	4.51	6.19	4.00	2.90	4.00	4.80	3.08	2.28
Gly	11.20	12.40	13.60	12.40	11.20	16.00	11.00	16.00	13.00	13.00	12.40	13.50	19.60	17.47	18.26	14.90	11.70	15.00	15.70	10.34	11.72
Ala	15.40	17.20	13.40	22.40	23.60	27.20	22.50	23.60	22.30	26.60	15.40	12.30	22.40	24.76	24.48	19.20	11.90	20.50	23.60	15.29	14.02
Cys	1.30	4.20	4.20	5.00	3.00	4.00	4.05	4.63	4.20	4.79	2.84	3.17	3.80	4.09	4.65	2.33	2.25	2.63	3.40	2.71	2.61
Val	12.30	14.60	16.80	14.60	12.30	12.10	13.20	12.50	18.80	13.00	6.80	6.53	10.90	11.80	10.34	15.50	16.80	17.00	17.30	13.69	11.97
Met	1.08	1.12	2.04	2.12	2.08	m2.40	2.38	2.40	2.38	2.40	0.40	1.50	0.80	0.92	1.73	1.40	1.80	1.70	1.80	1.59	1.99
Ileu	4.50	4.50	4.50	4.50	4.40	3.80	2.40	2.50	3.80	3.80	4.50	2.30	4.50	7.45	6.10	3.20	4.50	5.00	5.90	4.52	2.37
Leu	3.20	6.40	8.20	8.20	8.20	7.00	2.80	5.20	6.60	7.50	6.40	3.80	7.70	10.81	9.93	11.60	10.20	11.05	10.50	8.90	8.32
Tyr	4.90	4.90	4.90	4.50	4.90	4.50	4.75	2.50	4.00	4.50	4.90	3.00	3.90	5.92	4.48	4.00	3.90	4.84	4.80	2.42	3.03
Phe	4.89	8.90	8.90	4.50	4.50	6.20	6.20	5.80	5.00	6.70	4.50	3.10	6.70	6.80	6.54	7.20	5.40	6.70	7.80	3.19	3.94
Lys	22.50	25.60	19.40	22.50	19.40	15.60	16.90	15.00	14.10	13.66	15.60	9.40	12.30	1.70	19.70	16.90	23.80	24.10	24.10	18.37	15.74
His	2.89	4.04	2.89	2.89	2.31	1.44	12.00	1.15	1.15	2.10	2.31	1.90	2.77	1.25	1.40	5.89	4.44	5.15	6.21	8.50	6.45
Try	1.89	1.89	1.89	1.89	1.89	1.14	1.33	0.76	0.57	1.14	1.89	1.88	3.03	3.18	6.87	2.46	1.70	1.90	3.98	5.56	2.63
Arg	4.99	4.99	5.82	2.49	2.49	2.66	3.49	1.00	0.50	1.16	3.33	1.91	1.16	1.61	1.79	1.58	1.25	1.50	1.16	7.44	5.96
Total amino acid	130.69	122.22	144.40	157.34	131.31	142.62	135.87	131.02	136.06	148.43	111.23	100.35	134.46	139.88	165.15	148.44	136.61	153.94	170.54	144.62	131.39
Essential amino acid	71.06	65.26	82.43	91.51	63.81	69.74	63.81	63·86	74.34	76.90	54.19	49.93	67.53	65.49	90.35	81.22	86.54	88.25	90.41	80.75	71.86
Non essential amino acid	59.63	59.96	61.97	65.83	67.50	72.88	72.06	67.16	61.71	71.35	57.04	50.42	66.93	74.39	74.80	67.22	50.07	65.69	80.13	63.67	59.53

Table 7-b

Name	K.F			Y.S				S.O				K.D					S.Y			
Day	3	5	7	A	1	3	7	A	1	3	7	A	1	3	5	7	A	1	5	7
Cys・NH_2				0.10	0.10	0.36	0.24	1.02	0.85	0.75	0.90	0.68	0.51	0.30	0.45	0.44	0.59		0.16	0.24
Asp	1.50	2.10	0.51	0.03	0.19	0.03	0.09	1.20	0.50	0.45	0.70	0.12	0.13	0.15	0.15	0.15		0.37	0.49	0.47
Thr	22.43	27.03	27.78	21.40	29.80	21.30	26.60	16.94	15.25	24.70	28.03	27.60	28.10	29.00	30.00	31.80	33.59	33.67	25.32	23.49
Ser	12.26	15.38	11.71	10.50	9.40	10.40	10.30	9.30	11.85	11.90	12.64	7.30	11.00	13.00	12.10	11.80	12.07	10.99	10.92	12.60
Glu	3.32	3.41	4.40	2.60	4.09	5.17	5.03	4.31	4.70	4.45	4.82	5.10	6.10	4.70	5.00	5.40	6.32	5.62	5.56	5.34
Gly	11.06	11.31	13.94	11.80	11.70	13.10	11.70	19.22	13.25	14.00	14.61	12.60	13.00	12.10	12.80	12.40	12.39	11.33	1.02	12.95
Ala	20.30	23.16	24.77	10.20	12.70	14.10	19.00	11.63	15.10	14.90	21.33	10.40	11.00	18.00	22.00	22.60	13.47	10.57	12.06	24.95
Cys	2.81	3.66	3.79	4.40	4.80	4.34	4.30	3.78	3.43	2.32	3.25	3.08	31.50	3.75	4.34	4.50	4.80		2.40	3.56
Val	11.56	13.60	14.12	12.70	11.40	15.70	15.50	12.07	14.50	14.00	15.00	12.30	15.10	14.50	15.20	15.00	13.45	11.62	11.81	12.12
Met	1.42	1.58	1.42	1.05	1.07	2.08	2.14	2.11	22.21	2/23	2.15	2.15	2.23	2.15	2.11	2.12	1.39	2.41	2.22	2.33
Ileu	4.48	3.98	4.08	4.30	4.90	3.20	5.92	2.03	3.70	3.60	3.98	3.70	3.40	4.40	4.10	5.30	2.32	2.12	2.40	3.10
Leu	7.80	8.27	8.54	12.50	11.00	11.30	11.08	4.76	4.50	5.00	7.67	8.20	10.20	9.81	8.90	10.20	4.38	3.92	4.32	5.61
Tyr	3.76	3.98	4.55	2.80	2.50	2.00	3.90	3.99	3.71	3.71	4.67	2.00	2.50	3.10	3.00	4.40	4.81	4,51	4.71	5.18
Phe	3.69	4.32	5.52	4.50	0.90	1.80	5.90	8.04	6.50	5.12	6.45	1.80	2.00	3.00	3.50	4.80	6.18	6.89	5.05	7.86
Lys	15.28	13.26	16.65	20.90	15.00	19.10	16.90	2.30	2.61	2.15	10.32	15.90	19.20	22.00	21.00	24.60	14.70	13.70	12.01	16.11
His	5.81	5.26	10.22	1.17	1.75	1.17	1.75	3/23	2.51	3.14	6.93	1.70	2.10	3.20	4.50	4.67	6.24	5.37	5.38	8.37
Try	2/53	1/78	3.60	0.76	0.38	1.52	1.92	5.63	3.15	2.10	1.59	1.33	1.50	2.60	2.10	2.27	2.14	2.18	1.21	4.30
Arg	6.81	7.61	5.21	2.00	0.58	1.74	1.08	6.61	3.15	3.10	2.62	1.16	1.30	1.20	1.15	1.41	9.95	7.35	5.79	5.05
Total amino acid	136.82	149.69	160.81	123.71	122.30	128.41	143.35	118.17	111.47	117.62	147.66	117.12	160.87	146.96	152.40	163.86	148.79	132.62	122.83	153.63
Essential amino acid	59.02	62.17	65.64	78.11	74.45	76.00	85.96	53.88	52.45	58.90	75.19	72.98	81.73	87.46	86.91	96.09	78.15	76.51	64.34	74.92
Non essential amino acid	77.80	87.52	95.17	45.60	47.85	52.41	57.39	64.29	59.05	58.72	72.47	44.14	79.14	59.50	65.49	67.77	70.64	56.11	58.49	68.71

Some cases showed a slight decrease on the 5th day but an increase was seen in all cases on the 7th day. As compared with group 2, the degree of elevation was greater but values failed to reach the normal level.

Glutamic Acid showed a decrease on the 3rd day in most of the cases, followed by an increase on the 5th and 7th day. Values were closer to normal than in group 2.

Histidine decreased on the 1st day in 6 cases, on the 3rd day in 1, and on the 5th day in 1, followed by an increase until the 7th day. Values were higher than preoperative and normal level.

Arginine decreased on the 1st day in 8 cases, followed by further decrease until the 7th day, reaching values lower than preoperative values. However, fluctuations were smaller than in group 2.

Cysteic acid increased on the 3rd and 5th day followed by a decrease on the 7th day in 4 cases. In 2 cases, a decrease was seen on the 3rd day and increase was sen on the 7th day. Values were closer to normal.

Tyrosine decreased on the 1st or 3rd day, followed by a gradual increase on the 5th and 7th day in 5 cases while a slow and continuous increase from the 1st to the 7th day was seen in 3 cases. On the 7th day, values closer to normal were obtained in all cases.

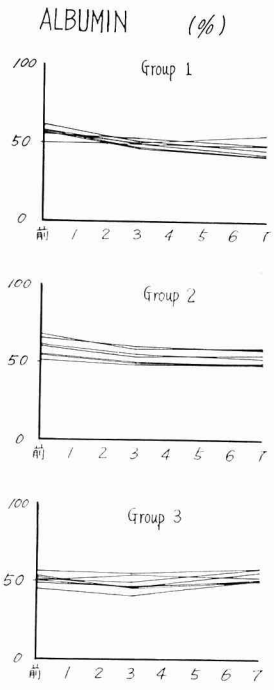


Fig. 6

Aspartic acid decreased on the 1st and 3rd day in some cases, followed by a gradual increase until the 7th day approaching the normal values.

Summary and Discussion

Lurje[21] was the first to report on the effect of operative insult on plasma amino acid level, through his observation on a temporary decrease of plasma amino acid postoperatively. According to subsequent reports by Farr[22], Peters[23], and Miwa[50], plasma total amino acids decreased immediately after the operation and stayed lower than the preoperative value even after the nitrogen balance became positive. Man found a marked decrease immediately after operation and 4 hours later[2]. The larger the operative insult, the greater the degree of the fall in plasma amino acid.

Concerning the fluctuations of individual amino acid in the immediate postoperative period, Everson[24] observed a marked fall in the plasma level of all amino acids especially threonine, valine, methionine, isoleucine, phenylalanin, tryptophane, lysine, and arginine immediately after gasterctomy and cholecystectomy. The greatest fall was found in tryptophane which became 40% of the preoperative value, while leucine show the least fall of 7%. These changes were said to be due to the increase in the secretion of adrenaline. Using paper chromatography Yamada[25] demonstrated a tendency of the fall of most of the non-essential amino acids immediately after operation, whereas essential amino acid did not change markedly, probably due to the increase in the demand of

glucogenic amino acid due to the insult.

With the use of high voltage filter paper electrophoresis, Miwa demonstrated a decrease of leucine, isoleucine, and valine fractions and an increase in alanine fraction in the immediate postoperative period, concluding that these changes were caused by a transient hepatic hypofunction secondary to a decrease in hepatic blood flow directly mediated by the endocrine system[50]. Schreier[26] found a decrease of all amino acids except leucine and isoleucine 3 hours after operation using the method with microorganism, ascribing such change to the endocrine hyperfunction especially the alarm reaction of Selye[138].

Haki[28] observed an increase of leucine and isoleucine postoperatively, while Fukuda[29] found a decrease of most of the amino acids in plasma from the immediate postoperative period to the 5th day, except for leucine and isoleucine which showed a slight increase. According to the present result, valine and alanine tended to increase 30 minutes after the operation, while all other amino acids showed a tendency of decrease.

Little doubt remains on the relationship between the immediate postoperative decrease of serum free amino acids and adrenocortical function. According to Sandberg[30] and Nogami[31] the adrenocortical function reaches its maximum 4 hours after operation, falls on the first day, returning to the normal level 5–7 days later. The degree of such change depended upon the degree of insult. Hayasaka[50] of our Department obtained similar results using various adrenocrotical function tests.

Fluctuations of serum amino acids after operation thus appears to represent part of the reaction of the body to the insult preceding the postoperative changes in adrenocortical function. According to Takada[89] of our Department, lactic dehydrogenase (LDH) and hydroxybutylic acid dehydrogenase (HBD) showed maximum fluctuation 4 to 5 hours after operation, in close relation with amino acids especially alanine, valine, leucine, isoleucine, serine, methionine, threonine, glycine, tyrosine, tryptophane, and phenylalanine. Changes in GOT and GPT also showed a peak at 4 hours after operation with some relationship to aspartic acid, leucine, isoleucine, valine, and threonine. According to Ikemoto[32] of our Department, pyruvic acid reached the maximum postoperatively slightly preceding LDH and HBD, under a close relationship with alanine, histidine, valine, leucine, isoleucine, threonine, glutamic acid and serine.

Postoperative changes in amino acids are thus intimately ralated to LDH, HBD, GOT, GPT and pyruvic acid as one of the reaction of the body to stress.

It might therefore be concluded that the reaction of the organism to stress centering at the adrenocortical function, including functional changes in the autonomic nervous system, endocrine glands, liver, and kidney as well as the decrease in nutritional supply due to operation represent the causes of the fall of serum free amino acid after operation. Scarcely any reports are available concerning the fluctuations of serum free amino acids according to the passage of time after operation. Akiyama[33] stated that all amino acids especially non-essential amino acids increased immediately after operation as the degree of operative insult became greater. The amino acids decreased on the 3rd day and again increased on the 7th day. Changes of glycine, glutamic acid, and alanine were especially pronounced. According to Tosen,[77] serum total amino acid concentration reached the maximum 3–5 days after resection of gastric ulcer, followed by a decrease

on the 7th day. Essential amino acids such as isoleucine, leucine, and valine played the main role, while non-essential fractions scarcely increased after operation. The postoperative decrease of serum total amino acid after resection of gastric cancer was greater than after resection of gastric ulcer, the recovery was slower, essential fractions increased from the relatively early period, and the pronounced decrease in non-essential fractions such as proline, glycine, and alanine was found[77]. According to Akai[49], Kuriyama[51], and Miwa[50], leucine, isoleucine, and valine reached the maximum on the 3rd postoperative day. The decrease in alanine was always seen, especially markedly after gastrectomy. Ariti[64] showed the tendency of decrease of various amino acids 3 days after operation. These amino acid returned to the preoperative value or higher level on the 7th day except of isoleucine and histidine. On the contrary., Haki[29] found the increase in leucine, isoleucine, and valine due to operative insult was not as pronounced as expected. According to Everson[24], all amino acids decreased from immediately after operation. Many returned approximately to the preoperative value on the 1st postoperative day, whereas lysine retuned on the 3rd and threonine and arginine on the 7th day. Considerable difference was thus found on the postoperative fluctuations of serum amino acid even without the use of parenteral amino acid supplement.

Various reports are also available concerning the postoperative fluctuations of amino acid upon the use of parenteral amino acid supplement. Using the parenteral supplement of 30 g of amino acid per day with the composition of FAO, Haki studied the daily changes of serum free amino acids, demonstrating a marked changes in leucine, isoleucine, and valine showing a uniform increase. The rate of utilization of various amino acid was lower than before the operation. By using 400 mℓ of 10% FAO continuously after the operation, Akiyama[33] found a decrease in urinary nitrogen excretion, followed by the change of nitrogen balance into positive on the 4th day. Urinary excretion of essential amino acids slightly increased but the excretory fractions of each amino acid did not show a marked fluctuation, indicating a normalization of protein metabolism as compared with the cases without amino acid supplement. According to Tosen[77], administration of amino acid preparation of FAO composition resulted in a diminution of the degree of the decrease of amino acid fraction in the early postoperative period and an early and marked change into positivity in patients with gastric cancer. Kuriyama[51] reported on the increase in amino acid reflecting the composition of amino acid in the fluid in serum and urine in response to postoperative amino acid supplement.

In the present study, daily administration of the small dose of 200 mℓ and the large dose of 600 mℓ were used in the postoperative amino acid supplementation and fluctuations of individual amino acids were determined. Upon administ ration of a small dose, the concentration of leucine, valine, isoleucine, tryptophane, arginine and cysteic acid rose on the 3rd or 5th day reaching the maximum. showing a tendency of decrease until the 7th day, while lysine, methionine, alanine, serine, cystine and histidine decreased on the 3rd and 5th day and tended to increase on the 7th day. Threonine, glycine, and glutamic acid showed a slow and persistent decrease from the immediate postoperative period through the 3rd, 5th and 7th day, while phenylalanine showed a slow increase

from the immediate postoperative period through the 3rd, 5th and 7th day. On the other hand, in cases given a large amount of 600 mℓ, a rise was seen in leucine, valine, isoleucine, tryptophane, lysine and arginine immediately after the operation, reaching the maximum on the 3rd and 5th day, followed by a tendency of decrease until the 7th day. Methionine, threonine, phenylalanine, alanine, serine, cystine, glycine, glutamic acid, histidine, and tyrosine, on the contrary decreased from the immediate postoperative period, reaching the bottom on the 3rd and 5th day, followed by an increase until the 7th day. Concerning the postoperative fluctuation of leucine, valine, isoleucine, and alanine, our results agreed with those of Akai, Miwa, and Kuriyama only with regard to the administration of a large and small amount of amino acids. When the approach of the value on the 7th day was taken as the sign of good recovery, methionine, threonine, phenylalanine, serine, glycine, glutamic acid, histidine, tyrosine, arginine, and aspartic acid showed a better result upon administration of a large amount, and cystine also gave similar result despite considerable fluctuations. Valine and lysine showed a more pronounced decrease upon administration of a large amount than in administration of a small amount.

Leucine, isoleucine, alanine and cysteic acid also gave wider fluctuations and poorer results upon administration of a large amount than in administration of a small amount. When such a comparison was carried out between administrations of large and small amounts keeping other conditions constant, most of the amino acid behaved better upon administration of a large amount, although valine, lysine, leucine, isoleucine and alanine gave poorer results. This is naturally due to the composition of the administered amino acids, being not exactly adequate for the demand of the body. Althouge the author has attempted the study of prescribing each adequate amino acid in the parenteral fluid during the last few years using high voltage paper electrophoresis, inability of measuring individual amino acid precluded the success[52].

As stated before, even administration of potent amino acid mixture was able to change the amino acid fractions only slightly in patients with gastric cancer showing an amino acid fractions characteristic to gastric cancer, and the percentage was scarecely changed. When certain amino acid fraction showed a pathological decrease below the normal level, the metabolism of this substance in the tissue is either increased or stopped regardless of the amount of urinary excretion. The requirement of amino acid fraction by individuals is thus influenced by the minimum amino acid showing a pathologically low level. Consequently the limiting factor in the parenteral fluid varies from person to person. Administration of amino acid mixtume of identical composition therefore seems to be a waste. In group 3, therefore, two or three such minimum amino acids were added to raise the threshold of such limiting factor to improve the supplementary effect. In group 3, leucine, alanine, serine, cystine, glycine, glutamic acid, histidine and tyrosine decreased on the 1st day followed by an increase by the 7th day, while isoleucine and aspartic acid showed a decrease on the 3rd day followed by an increase. Methionine, lysine, tryptophane and phenylalanine showed a persistent increase from the 1st day while a persistent decrease from the 1st to the 7th day was seen in arginine.

Threonine increased on the 1st day, temporarily decreased on the 3rd day followed by an increase. Valine showed an increase from the immediate postoperative period until the 3rd day, maintaining the similar value subsequently. The behavior of these amino acids was slightly different from that in group 1. Valine, leucine, isoleucine, lysine, and alanine which showed a poor result in group 2. approached the normal value, showing excellent results together with other amino acids. On the contrary, histidine, aspartic acid, and tryptophane showed poorer results than in groop 2, tryptophane showed poor results in both groups 2 and 3. Arginine kept decreasing from the immediate postoperative period until the 7th day, suggesting poorer level than the normal values together with aspartic acid, although the constant and smooth movement of urea cycle under an intimate relationship with the TCA cycle might well lead to paralleled lower values of aspartic acid and arginine. In any case, the values of these amino acids apart from normal might provide a problem for further study. As the 2 or 3 minimum amino acid added, lysine, threonine, methionine, arginine, aspartic acid, and tryptophane were mainly selected. The addition of these amino acids gave favorable effect on the corresponding amino acids in serum, but not always a good effect on others. The effect on arginine, histidine, aspartic acid, and tryptophane especially gives a problem on the ratio of amino acids.

In case the addition of amino acids creates an imbalance for the body, this amino acid fluid represents an unbalance for the body. According to Takeda of our Department[71], a certain ratio exists among acid, neutral, and alkaline amino acids. This ratio must be maintained upon parenteral amino acid supplementation. The problem of addition will therefore become an important problem together with the problems of imbalance and unbalance. In the initial stage of the studies on parenteral amino acid supplementation, Peters[34], Willkinson[35], Moore[67], Riegel[36], Grossman[37] and Brown[38] were of the opinion that parenteral nutrition is not able to prevent the postoperative nitrogen loss even with the use of high caloric, high protein fluid, and the early turning to positivity of nitrogen balance is impossible. However, along with studies on amino acid metabolism, Akiyama[33] was able to change the nitrogen balance into positivity on the 4th postoperative day with the use of only 400 mℓ of fluid containing amino acids. Ariti[64] reported the facilitation of postoperative anabolism in an early stage with the combined use of growth hormone. Takayama[39,40] and Higasa[41,42] reported on the necessity of intravenous fat emulsions as the indispensable means of inducing early change into positivity of nitrogen metabolism in the postoperative state. Takayama[43] suggested the combined use of anabolic hormone as indispensable together with administration of a large amount of amino acid from the preoperative stage. Elman[44] pointed out the participation of electrolytes especially K in the assimilation of amino acid. Takayama[45] demonstrated the uselessness of the administration of a large amount of amino acid in hypomagnesemia, even if other conditions were satisfactory, in his studies on postoperative magnesium metabolism. From the standpoint of protein sparing reaction, Maeda[46] obtained a favorable result with sorbitol than with sugar[47,48]. We have also reported the necessity of the presence of certain amount of various vitamins for a significant treatment. The relationship between vitamin B_1 and amino acid was demonstrated in this

paper. Aoyama[49] of our Department studied the relationship between each amino acid fraction and serum vitamin B_{12}, the indispensable nature of which in the postoperative stage was emphasized. Takayama[51] and Kodeki[52,53] reported on the necessity of aspartic acid and ornithin, non-essential amino acids, for the purpose of improving the rate of utilization of the infused amino acids. Takayama[54] stressed the importance of cytochrome on the postoperative assimilation of amino acids.

The present experiments in 2 group has demonstrated the occurrence of postoperative changes in amino acid fractions even upon administration of a large amount of amino acid in the presence of all the factors required for the assimilation of amino acids. Nakayama[55] reported a favorable result in postoperative aasimilation obtained by the addition of glycine a non-essential amino acid, to Moriamin-S prepared according to the Vuj standard. Tosen[77] pointed out a diminution in the postoperative fluctuatuations of amino acid and decrease of each amino acid as well as the early onset of the change to increase upon the use of amino acid mixture with addition of lysine. Kuriyama[51] removed leucine, isoleucine, valine from the commercial amino acid preparation and added glycine and obtained a favorable result. Hirai[29] pointed out the decrease of threonine, lysine, and cystine in the plasma of patients in the terminal stage of cancer and administered amino acid preparation with addition of lysine and tyrosine, achieving an approach of the plasma amino acid fractions of patients in the terminal stage of cancer to normal. This represent the closest method to our concept.

Despite such a large number of reports, individual amino acid has not been discussed until the present report. Determination of each individual amino acid and addition of 2 or 3 minimum amino acid seems to be most desirable.

Fukuda[56] also pointed out the difficulty in correcting the disorder in amino acid fractions in each disease with the conventional crystal amino acid solution alone. Some day amino acid solution should be prepared according to the individual diseases.

Conclusion

No definite conclusion has been established concerning the effect of operative insult on the changes in amino acid fractions. No treatment has yet been established for such postoperative fluctuations.

The authors have studied these problems and obtained following conclusions.

1) Due to the operative stress, most of the amino acids decrease.

2) In the group with postoperative administration of a small amount of amino acid, the level of leucine, valine, isoleucine, tryptophane and arginine rose on the 3rd and 5th day reaching the peak, followed by a decrease until the 7th day. Lysine, methionine, alanine, serine, cystine, and histidine decreased on the 3rd and 5th day reaching the minimum level, followed by an increase by the 7th day.

3) Even if a large amount of amino acids was administered together with all the facotors required for the postoperative assimilation of amino acids, an unfavorable influence was noted in valine, lysine, alanine, leucine, isoleucine, and cysteic acid as compared with the group given a small dose, while a beneficial influence was noted on other amino acids.

4) A favorable response on individual amino acid other than arginine, tryptophane, cysteic acid, and aspartic acid was noted upon addition of 2 or 3 minimum amino acids selected by measuring the concentration of individual amino acids and calculating as the percentage of the normal level.

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