TABLE IV. Excretion of Phenylalanine and Phenylpyruvic Acid in the Sweat (mg/100 cc).

Patient	N, mg/100 cc	Phenylalanine, mg/100 cc	Phenylpyruvic acid, mg/100 cc
A.	61	2.3	20
B.	100	3.4	15
C.	57	1.6	19
F.	44	1.6	6
K.P	54	1.4	13
K.A.	56	2.4	56
M.M.	76	2.7	25
M.E.	140	4.4	33
N.	84	3.5	21
R.	152	9.6	47

individuals this amount of phenlypyruvic acid is usually completely metabolized.

From these feeding experiments it would appear that some quantitative changes in the excretion of phenyl compounds should be expected when foods with different phenylalanine content are ingested by the patients. However, since the ratio of phenylalanine to nitrogen in various proteins and foods does not show conspicuous variations(19), the amount of phenyl compounds excreted per g of nitrogen, as expressed in Table I, is probably little affected by the quality of ingested food.

In view of the findings of urinary excretion of phenyl compounds, it was considered of interest to investigate the excretion of these metabolites in sweat. Accordingly, sweat was collected as directed by Hier *et al.* (20) from 10 patients and determinations were performed on suitable dilutions following the procedure described for urine. The patient was bathed before the collection of sweat. Phenyllactic acid was not found in measurable amounts. The data concerning phenylalanine and phenylpyruvic acid are shown in Table IV. The values for the amino acid were somewhat above those reported by Hier *et al.*(20) in the normal individual. Phenylpyruvic acid is not found in the sweat of normal subjects. It would appear, therefore, that a small amount of phenylalanine and its derivative is eliminated by way of sweat.

Summary. Quantitative data are presented on the urinary excretion of phenylalanine, phenylpyruvic acid and phenyllactic acid in twenty patients affected with phenylpyruvic oligophrenia. The values, expressed in mg per g of total nitrogen, show inconspicuous differences from patient to patient kept on similar diets. High protein diet or the ingestion of phenylalanine and phenylpyruvic acid result in an increased daily output of phenyl compounds. Data on sweat excretion of phenyl compounds are also presented.

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Oligophrenia Phenylpyruvica. II. Constancy of the Metabolic Error. (18109)

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In phenylpyruvic oligophrenia mental deficiency is accompanied by faulty phenylalanine metabolism. The metabolic error is manifested by the urinary excretion of large amounts of phenylalanine, phenyllactic acid, and phenylpyruvic acid, and by an elevated phenylalanine concentration in the blood. The genetic analysis strongly suggests that this disease is inherited as an autosomal Mendelian recessive and that; therefore, the mental and metabolic disturbance may be caused by the same gene. The question arises whether both abnormalities, when

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TABLE I. Concentration of L-phenylalanine (PA) and Phenyllactic Acid (PL) in Serum and Spinal Fluid of Patients with Phenylpyruvic Oligophrenia.

			Sample I		Sample II		Sampel III		Sample IV		Spinal fluid
Patient	Age	I.Q.	PA + PL mg %	PA mg %	PA + PL mg %	PA mg %	PA + PL mg %	PA mg %	PA + PL mg %	PA mg %	PA mg %
1	28	5	32	31	39	38	33	33	33	34	7.7
2	42	46	29	29	33	32	31	28	33	30	7.6
3	41	11	27	27		34					
4	32	7	33	32	31	29					
5	29	47	33	35	38	36	34	32			7.8
6	26	7	27	27	33	31					
7	15	35	31	31							7.5
8	17	12	33	33							
9	23	7	30	29	34	34	33	33			7.9
10	30	38	27	27							
11	26	10	26	26							
12	6	14	29	27							
13	5	24	27	26							
14	19	9	24	26	29	31	32	31			8.2
15	29	5	33	29							
16	5	24	25	24							
17	27	40	24	22							6.2
18	8	10	21	19							
19	22	6									6.1
20	20	7									6.3

fully developed, are correlated in their quantitative aspects. It has recently been suggested(1) that a positive correlation exists between the degree of mental deficiency and the metabolic disturbance as measured by the excretion of phenylpyruvic acid. Since the excretion of phenylalanine and its metabolic derivatives may only be secondary to the abnormally high blood concentration of the amino acid, it was considered of interest to determine whether a correlation exists between this value and the degree of mental deficiency.

In this report quantitative data on the phenylalanine concentration of the blood and spinal fluid of phenylketonurics are presented.

Experimental. Microbiological determinations of phenylalanine and phenyllactic acid in serum ultrafiltrates and in urine were carried out on 18 phenylketonuric fasting patients as described previously(2). Microbiological determinations of phenylalanine in the spinal fluid were carried out on 9 patients according to the directions of Solomon *et al.*(3).

Suitable dilutions were made in each sample in order to bring the concentration of the amino acid within the range of the microbiological method. Urinary phenylpyruvic acid was determined according to the method of Friedeman and Haugen(4).

Results and discussion. The concentration of L-phenylalanine alone and of the sum of phenyllactic acid and phenylalanine in blood serum was determined in some of these subjects with phenylpyruvic oligophrenia at intervals of several months. It may be seen (Table I) that the difference between the sum of phenyllactic acid and phenylalanine and the amino acid alone was not significant. It may, therefore, be concluded that only traces, if any, of the hydroxy-acid circulate in blood. Although there was considerable variation of the values taken at different times in the same individuals, it would appear that the intraindividual variations were significantly smaller than those found among individuals ($P<0.05$). This result would indicate that there was a characteristic blood level of phenylalanine for each individual.

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TABLE II. Blood Serum and Urine Concentration of Phenylalanine (PA), Phenyllactic Acid (PL), and Phenylpyruvic Acid (PP), After Intravenous Administration of 1.6 g of L-Phenylalanine.

Patient	Min.	Serum PA + PL mg %	Urine ml	Urine PA + PL mg %	Urine PP mg %
R	0	34	—	—	—
	20	38	—	—	—
	40	36	—	—	—
	60	38	—	—	—
	120	42	—	—	—
S	0	39	250	120	160
	10	43	55	128	115
	20	40	25	85	73
	35	41	75	58	90
	120	40	155	62	181
B	0	33	—	—	—
	10	36	—	—	—
	30	34	—	—	—
	120	34	—	—	—
Control	0	2.0	100	0.5	0
	10	7.7	75	0.6	0
	20	5.4	60	1.5	0
	30	6.1	25	1.4	0

It is clear that there is no correlation between the phenylalanine level in serum and the mental performance expressed as I.Q. score.

The relative constancy of the phenylalanine level in serum offers an explanation for the findings of a relative constancy of the ratios of urinary phenyl compounds to urinary total nitrogen(5). Since the amount of phenylalanine circulating through the kidney will determine the amount of the amino acid and its metabolic derivatives excreted in the urine, it is not surprising that the ratio of phenyl compounds to total nitrogen excreted should be a relatively constant value.

The phenylalanine content of spinal fluid as of the serum of phenylketonurics did not differ greatly among patients (Table I). The increase of phenylalanine over the normal values of spinal fluid was of an order of magnitude similar to that observed in the blood.

To two fasting phenylketonurics and to one control (also a mental defective) 1.6 g of L-phenylalanine was administered intravenously. As seen in Table II, the phenylalanine disappeared very rapidly from the blood into the tissues of the phenylketonuric and the non-phenylketonuric defectives. It was apparently released slowly from the tissues since the urine samples obtained simultaneously with the blood samples did not show a significant change in the content of phenyl derivatives during the first 2 hours after the administration of phenylalanine. However, preliminary analyses of the urine indicate that the total amount was excreted within 48 hours.

Since the phenylalanine level in the blood of phenylketonurics is a relatively constant value which shows no correlation with the mental state, it is of interest to inquire into the mechanism which determines the blood level of the amino acid in this disease. It is probable that the major portion, if not all, of the phenylalanine ingested with the food, is excreted as such or as one of the derivatives in the urine. Small amounts of an amino acid excreted by glomerular filtration would be reabsorbed within the kidney tubuli. In the case of phenylpyruvic oligophrenia the nonutilization of phenylalanine leads eventually to a blood level beyond the ability of the tubuli to reabsorb it. The critical blood level at which phenylalanine is excreted in the urine is not known but the maximal rate of tubular reabsorption in dogs is not exceeded by an increase of the phenylalanine content of plasma by a factor of 10(6). It has to be assumed that in phenylketonurics the inability to metabolize phenylalanine causes a level of the amino acid in blood and consequently in the glomerular filtrate to be established which overwhelms the tubular reabsorption. Although the cause of the increased phenylalanine level as such is the metabolic error, it appears that its quantitative expression is determined by the reabsorptive power of the kidney tubuli. Whether this function of the tubuli is normal in phenylpyruvic oligophrenia or is modified by the disease cannot be decided at present.

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Summary. The serum level of free phenylalanine and phenyllactic acid was determined in 18 patients suffering from phenylpyruvic oligophrenia. No significant amounts of the hydroxy acid were found. The concentration range of the amino acid was between 19 and 38 mg per 100 ml of serum with larger inter- than intra-individual variations. No correlation exists between the degree of mental deficiency and the concentration of phenylalanine in serum. Phenylalanine concentration in the spinal fluid varied from 6.1 to 8.2 mg/100 cc.

It is suggested that although the increased amount of phenylalanine is caused by the metabolic error, its blood plasma level is determined by the ability of the kidney tubuli to reabsorb the amino acid.

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Comparison of Influenza B Virus Strains from the 1950 Epidemic with Strains from Earlier Epidemics. (18110)

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Shortly after the discovery of influenza B virus(1,2), antigenic differences between strains of the agent were noted(3,4). Numerous reports have appeared in which serological studies revealed antigenic differences between strains which had been passed in series in the mouse lung or between such strains and strains which had been maintained by passage only in the chick embryo (3-9). In general, new strains have been compared with the Lee strain or with other strains obtained from the same epidemic. It should be emphasized that the Lee strain which was recovered in 1940(1) had been through many mouse lung passages. In the past, when egg strains have been compared with each other(8), they have tended to show closely similar antigenic patterns. If the so-called adaptation of strains of influenza B virus to the mouse lung is associated with unpredictable alterations in antigenic pattern, as occurs with strains of influenza A virus(10,11), then antigenic differences between mouse lung strains of the former virus might be more apparent than real.

During February and March, 1950, there occurred in the New York area, as elsewhere in various parts of the United States, an epidemic of influenza. From some patients studied in the Hospital of the Rockefeller Institute, influenza B virus was recovered; from others, influenza A virus was obtained. Investigations with acute and convalescent sera from the various patients confirmed these findings; certain patients clearly had influenza B, others had influenza A. Because all strains obtained from the 1950 epidemic in this laboratory were recovered after inoculation of chick embryos and because a number of earlier egg strains of influenza B virus were available, an opportunity was provided to compare various strains recovered since 1945, none of which had ever been passed in the mouse lung. The results of serological studies with these strains indicate that egg strains

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