account for complete closure of the aqueduct. As pointed out by Russell(11), gliosis is evoked in subependymal tissues by distension of the ventricles and destruction of the ependymal epithelium. This presumably arises as a reaction to pressure and tends to counteract pressure of fluid from within the ventricle. Bruemmer *et al.*(12) found a 15% increase in the number of nuclei/g of tissue in brain homogenates from Vit. B_{12} deficient offspring. There was no difference in the amount of deoxyribonucleic acid per nucleus, but the amount of pentose-nucleic acid per cell was decreased. It was concluded that the average brain cell in the deficient animal is smaller than normal, resulting in an increased number of cells per unit volume.

Summary. Female rats deficient in Vit. B_{12} produced offspring with a high incidence of hydrocephalus. The cerebral cortex of hydrocephalic brains was decreased in thickness and in some areas the ependyma was missing. Ependymal and choroid cellular morphology was deranged and the cells had accumulated lipide. Tall columnar-type cells normally present as an intact layer in the roof of the third ventricle and aqueduct of control rats were occasionally found in hydrocephalic brains with occluded aqueducts.

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Nicotinic Acid—Tryptophan Metabolism in Certain Diseases.* (23647)

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Biosynthesis and metabolism of nicotinic acid has been extensively studied(1-6) in animals and in normal humans but comparatively little work has been done on this subject in persons suffering from diseases. Conflicting claims have been made regarding the principal site of synthesis of nicotinic acid. Liver(7-11), intestinal bacteria(12-16), and body tissues(17-21) have been suggested as the major site of this vitamin formation. The present communication deals with studies on the urinary excretions of nicotinic acid and amide, quinolinic acid, N'-methylnicotinamide (N'MN), 6-pyridone, tryptophan, kynurenin, anthranilic acid and 3-hydroxyanthranilic acid in patients suffering from typhoid fever, cholera, small pox, liver cirrhosis, and infective hepatitis before and after feeding of tryptophan with a view to study the metabolism of nicotinic acid and its site of synthesis from tryptophan. For the sake of comparison similar studies were made on normal men also.

Methods. Ten male patients suffering from each disease who were admitted in the N. R. Sircar Medical College Hospital, Calcutta

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were selected for the study. Only those cholera patients were taken who had just passed the anuric phase. Small pox patients were in the eruptive stage. All cirrhosis patients were complicated by some degree of ascites. Patients suffering from hepatitis had marked icteric tinge. Patients suffering from typhoid fever were not given chloromycetin. The patients were fed hospital diets which did not vary from day to day during the experimental period. The 24-hour urine was collected in a bottle containing 10 cc toluene. Urinary excretions of different metabolites were determined for 2 consecutive days. At the end of second day's collection they were fed 5 g DL-tryptophan and 24-hour urine collected daily for 3 subsequent days and analysed for constituents mentioned above. Ten normal persons were also studied similarly. However, to patients suffering from typhoid fever 5 g DL-tryptophan was fed on 2 consecutive days. Nicotinic acid and amide was estimated by the method of Banerjee *et al.*(22) as modified by Nandi & Banerjee(23). Quinolinic acid was estimated after autoclaving urine in normal sulphuric acid at 15 lb. pressure for one hour and estimating the nicotinic acid formed. Quinolinic acid values were calculated by the method of Sarett(24). N'MN was estimated by the method of Carpenter and Kodicek(25) slightly modified. 6-pyridone was estimated according to the method of Rosen *et al.*(26). Tryptophan, kynurenin, anthranilic acid and 3-hydroxyanthranilic acid were separated by paper chromatography and the chromatograms treated with Ehrlich's reagent according to the method of Dalgleish(27). The colour intensity of the spots in the chromatogram was estimated with a photoelectric densitometer to give fairly quantitative results.

The results are given in Table I.

Discussion. In the diseased conditions studied urinary excretion of tryptophan was less than normal both before and after the feeding of tryptophan. This might be due to diminished absorption, increased incorporation into the body tissues, increased conversion into nicotinic acid, or increased oxidation in the tissues.

Cholera: The absence of kynurenin but appearance of 3-hydroxyanthranilic acid following tryptophan feeding suggests that kynurenin is metabolised to 3-hydroxyanthranilic acid at a very rapid rate. The synthesis of nicotinic acid proceeds at a subnormal rate. This might be due to deficient absorption of tryptophan from the intestine, or deficient synthesis of nicotinic acid by the intestinal bacteria which have been washed away by purging or deficient synthesis of nicotinic acid from tryptophan in tissues.

Small pox: Urinary excretion of different metabolites of nicotinic acid was very high both before and after administration of tryptophan. Possibly the breakdown of body tissues due to toxaemia makes available additional sources of tryptophan for synthesis of nicotinic acid. Higher quantities of N'MN and 6-pyridone excretions indicate an attempt on the part of body to get rid of extra load of niacin in the process of detoxication. *Liver cirrhosis*: The absence of 3-hydroxyanthranilic acid but increase in urinary excretion of nicotinic acid and its derivatives after tryptophan feeding suggests that the compound is too rapidly transformed into nicotinic acid derivatives. The increase in the values of nicotinic acid and its derivatives after tryptophan feeding indicates that synthesis of nicotinic acid is not disturbed in this disorder. Gabuzda *et al.*(28) have reported urinary excretion of tryptophan to be slightly higher than normal in this condition; our findings, however, do not agree with them. *Infective hepatitis*: Synthesis of nicotinic acid proceeds almost normally in this disease. *Typhoid*: Synthesis of nicotinic acid and its final disposal proceeds normally though at a slightly accelerated rate.

Since synthesis of nicotinic acid follows almost the normal pattern in liver cirrhosis and hepatitis, it is unlikely that liver is the organ mainly concerned with this function. This agrees with the observation of Banerjee and Basak(29) who reported that liver poisoned with carbon tetrachloride injection in rhesus monkeys did not result in reduction of nicotinic acid synthesis. Diminished synthesis and metabolism of nicotinic acid in cholera suggests many possibilities already mentioned. In typhoid where the intestine is the chief site of lesion, the synthesis of nicotinic acid

TABLE I. Average 24-Hour Urinary Excretions of Metabolites of Nicotinic Acid and Tryptophan in mg by Each 10 Patients Suffering from Different Diseases.

			Nicotinic acid and amide	Quinolinic acid	N'MN	6-pyridone	Tryptophan	Kynurenin	3-hydroxyanthranilic acid
Cholera	Before feeding tryptophan		1.5 ± .23*	2.3 ± .56	2.3 ± .22	2.38± .53	17.5 ± 2.5	0	0
	Days after feeding 5 g DL-tryptophan	1	2.57 ± .34	5.04 ± .48	4.21 ± .31	13.6 ± 2.3	161.5 ± 46.1	0	34.0 ± 4.5
		2	2.01 ± .24	3.90 ± .41	3.71 ± .22	12.2 ± 1.5	60.7 ± 3.9	0	16.1 ± 1.4
		3	1.68 ± .19	3.02 ± .45	2.85 ± .27	6.4 ± 1.0	22.0 ± 2.4	0	0
Small pox	Before		11.3 ± .94	12.5 ± 1.0	15.7 ± 1.2	9.0 ± .7	0	0	0
	After	1	20.8 ± .75	27.5 ± 1.4	32.9 ± 1.5	45.5 ± 2.6	165.6 ± 3.5	100.8 ± 4.0	40.6 ± 2.5
		2	14.6 ±1.1	17.5 ± 1.6	28.6 ± 1.8	35.9 ± 1.3	55.0 ± 2.1	0	0
		3	11.7 ± .9	13.4 ± 1.2	21.8 ± 1.3	20.4 ± 1.5	13.2 ± 1.0	0	0
Cirrhosis of liver	Before		2.51 ± .09	2.44 ± .39	4.35 ± .4	2.46 ± .56	37.1 ± 2.6	0	0
	After	1	5.08 ± .47	6.14 ± .60	9.15 ± .48	16.6 ± 2.0	723.1 ±32.6	53.8 ± 3.2	0
		2	4.08 ± .43	4.85 ± .47	7.37 ± .62	14.6 ± 1.6	71.0 ± 4.5	0	0
		3	2.91 ± .14	3.18 ± .42	5.22 ± .56	6.86 ± .92	49.6 ± 2.8	0	0
Hepatitis	Before		3.43 ± .36	2.92 ± .24	7.21 ± .48	1.88± .3	0	0	0
	After	1	6.98 ± .59	9.51 ± .62	12.8 ±1.0	17.7 ± 1.4	459.0 ±30.6	52.4 ± 3.7	67.4 ± 3.5
		2	5.38 ± .37	6.32 ± .42	9.78 ± .48	12.8 ± 1.3	58.2 ± 4.4	0	0
		3	3.9 ± .41	3.58 ± .35	7.69 ± .23	6.0 ± .91	14.2 ± 1.1	0	0
Typhoid fever	Before		5.23 ± .49	8.29 ± 1.3	11.89 ± .87	4.03 ± .84			
	After	1	10.19 ± .63	14.24 ± .80	19.27 ± 1.32	37.61 ± 4.49			
		2	12.47 ± .57	17.86 ± 1.1	26.54 ± 1.82	53.68 ± 5.81			
Normal	Before		4.53 ± .21	3.76 ± .50	7.1 ± .41	3.3 ± .82	63.2 ± 2.6	0	0
	After	1	7.84 ± .29	10.39 ± .59	13.9 ± .78	45.3 ± 6.7	1007.0 ± 36.2	270.5 ± 25.8	171.6 ± 11.4
		2	6.16 ± .31	4.76 ± .38	10.3 ± .56	30.2 ± 4.4	233.4 ± 18.2	0	0
		3	5.03 ± .27	4.08 ± .22	7.6 ± .47	18.9 ± 2.5	121.5 ± 9.4	0	0

* Mean ± S.E. Anthranilic acid was absent from urine in all subjects.

proceeds quite normally, which contradicts the belief that nicotinic acid is mainly formed in the gut. The enhanced rate of conversion of tryptophan into nicotinic acid and its final disposal in small pox indicates that body tissues are more concerned in the synthesis of this vitamin.

Summary. 1. Urinary excretions of nicotinic acid and amide, quinilinic acid, N'-methylnicotinamide, 6-pyridone, tryptophan, kynurenin, anthranilic acid and 3-hydroxyanthranilic acid were estimated in normal men and in patients suffering from typhoid fever, cholera, small pox, cirrhosis of liver and infective hepatitis both before and for 3 days after the feeding of tryptophan. 2. Excretion of tryptophan both before and after feeding diminished in all the diseases studied. Kynurenin which was absent initially in the urine of patients appeared in urine collected for 24 hours after the feeding of tryptophan in small pox, liver cirrhosis and hepatitis but not in cholera. 3-hydroxyanthranilic acid appeared in urine after tryptophan was fed in cholera, small pox and hepatitis but not in cirrhosis of liver. In all diseased conditions studied, except in typhoid and small pox, urinary excretion of nicotinic acid and its metabolites was greatly diminished. After administration of tryptophan urinary excretion of nicotinic acid metabolites increased in all diseases but the increase was least in patients suffering from cholera. 3. Patients suffering from small pox excreted increased amounts of nicotinic acid and its derivatives both before and after tryptophan feeding as compared to normal men.

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