averages. The latter varied from 22% to 109%. The individual adrenal weights of the injected rats were consistently heavier than the control weights within a given litter. Some atrophy of the adrenals of the injected rats did occur because glands from normal rats at the time of operation weighed from 16 to 20 mg, depending on the age of the rat. Most all of the injected rats gained in body weight or lost only a few grams. There did not seem to be any definite correlation between body weight changes and the degree of adrenal involution in these preliminary experiments. Histologically, the cortex appeared more normal in the injected rats, and the general appearance and yellowish color of the fresh adrenals were like that of normal rats.

Three similar experiments were carried out except that an interval of 7-9 days was allowed before beginning injections. The results were rather equivocal as adrenal weight differences in 3 litters of 5, 4 and 4 rats were respectively 0%, 33% and 56%. The adrenals of the injected rats were heavier than those of the controls in the two latter cases.

Male hormone substances have been reported not to affect the adrenals of hypophysectomized rats,[3] or mice[4] which is similar to the reported non-effect of progesterone[5] and cortical hormones.[6,7] Atwell[8] stated that the adrenal cortical cells of hypophysectomized larval *Rana sylvatica* were somewhat restored by cortical extract. In the annual breeding ground squirrel, the adrenal cortex hypertrophied along with sex organs on experimentally induced sexual recrudescence.[9]

Summary. Injections of large doses of male hormone partially prevent the atrophy of the adrenal cortex which normally follows hypophysectomy in the immature male rat.

[3] Walsh, E. L., Cuyler, W. K., and McCullagh, D. R., *Am. J. Physiol.*, 1934, **107**, 508.

[4] Nelson, W. O., and Merckel, C. E., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 737.

[5] Selye, H., *Anat. Rec.*, 1940, **78**, 253.

[6] Atwell, W. J., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1259.

[7] Ingle, D. J., *Am. J. Physiol.*, 1938, **124**, 369.

[8] Atwell, W. J., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 621.

[9] Moore, C. R., Simmons, G. F., Wells, L. J., Zalesky, M., and Nelson, W. O., *Anat. Rec.*, 1934, **60**, 279.

13949

Nitrogen Balance in Human Tryptophane Deficiency

WARREN M. COX, JR., ARTHUR J. MUELLER AND DALLAS FICKAS.
From the Laboratories of Mead Johnson and Company.

Many reports on the inadequacy of tryptophane-deficient protein hydrolysates in animal nutrition are available. With the exception of the recent report of Holt and coworkers,[1] we have been unable to find any report of tryptophane deficiency in man.

In February, 1940, we had the opportunity of studying a patient with a gastrostomy. The patient, a 65-year-old woman with cancerous occlusion of the esophagus, had, of necessity, reduced her food intake progressively during the 6 months prior to admission to the hospital. Difficulty in swallowing was progressive. For the week preceding operation she had been unable to swallow any food by mouth; and could retain but little fluid. A gastrostomy opening was made under local anesthesia on January 27th and the second day thereafter studies on nitrogen balance were begun.

Because of the long-continued protein starvation, nitrogen was not given at a basal level. None the less, we hoped to make observations on tryptophane deficiency in a

[1] Holt, L. E., Jr., Albanese, A. A., Brumback, J. E., Jr., Kadji, C., and Wangerin, D. M., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 726.

TABLE I.
Nitrogen Balances on Milk, and Enzymic and Acid Hydrolysates of Casein.
Patient F.N. Weight 41 kg. Gastrostomy performed 1/27/40.
(Expressed as g per kilo per day.)

Period	Date	Supplement	Total nitrogen intake	Output		Balance	Plasma	
				Feces	Urine		Protein g %	Albumin g %
1	1/30/40	None	None	.009	.063	—.072		
2	31	Enzymic	.195	.008	.088	+.099	6.45	4.08
	2/1	Hydrolysate	.184	.050	.070	+.064		
	2		.197	.010	.109	+.078		
		Avg	.192	.023	.089	+.080		
3	3	Milk	.194	.036	.111	+.047	6.10	3.46
	4		.196	.012	.097	+.087		
	5		.199	.002	.127	+.070		
		Avg	.196	.017	.112	+.068		
4	6	Enzymic	.211	.007	.153	+.051	6.21	3.52
	7	Hydrolysate	.218	.019	.151	+.048		
	8		.207	.011	.143	+.053		
		Avg	.212	.012	.149	+.051		
5	9	Milk	.197	.043	.142	+.012	6.06	3.73
	10		.198	.023	.100	+.075		
	11		.192	.011	.108	+.073		
		Avg	.196	.026	.117	+.053		
6	12	Acid	.203	.005	.253	—.055	6.65	3.57
	13	Hydrolysate	.214	.012	.199	+.003		
	14		.214	.012	.208	—.006		
		Avg	.210	.010	.220	—.019		
7	15	Enzymic	.204	.013	.202	—.011	6.53	3.57
	16	Hydrolysate	.206	.009	.139	+.058		
	17		.207	.016	.155	+.036	6.18	3.30
		Avg	.206	.013	.165	+.028		

human (*cf.* our earlier report),[2] as well as to determine the relative value of hydrolyzed and unhydrolyzed protein in the maintenance of nitrogen equilibrium.

A diet complete in nutritive elements was prepared in the form of a thin starch paste, divided into 7 portions, and given by gravity, through the gastrostomy opening. The formula for the feeding was: Water *ca.* 800, corn starch 40, dextrose 55, Dextri-Maltose 55, olive oil 55, enzymic or acid hydrolyzed casein 68, yeast 2, NaCl 5, ferrous ammonium sulfate 0.3, dibasic calcium phosphate 1 g, nicotinic acid 40, riboflavin 2, thiamine 6, ascorbic 100 mg and Oleum Percomorphum 20 drops. Using a mechanical stirrer, the water-soluble substances (except vitamins) were first dissolved in the hot water, starch added to gelatinization, and the two oily substances stirred in. The vitamins were added to the almost cool suspension. The formula with milk was made by substituting 692 cc of evaporated milk for the olive oil, protein hydrolysate, calcium phosphate salt, and most of the water. Urine was collected in the usual manner and an s.s. enema in the morning constituted the fecal collec-

2 Cox, W. M., Jr., and Mueller, A. J., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 658.

tion. Three nitrogenous supplements were given: milk, casein hydrolyzed by enzymes* and by acid.†

Daily balances for 6 periods of 3 days each were accomplished before the patient was discharged. Three periods were supplemented with enzymic casein hydrolysate, 2 with milk, and one with the acid hydrolysate (Table I). Nitrogen retention was initially avid, but with time more normal retentions were observed. Thus the 3 periods on the enzymic hydrolysate (level 0.2 g N per kilo) showed decreasing retentions of +.080, +.051, and +.028 g per kilo body weight daily. The 2 periods with milk gave values of +.068 and +.053. These are all exceptionally high retention figures and express the intensity of the patient's need. The 2 supplements are apparently equally effective as nitrogen sources.

The effect of the tryptophane-deficient hydrolysate is of principal interest. The first day of supplementation resulted in a very large urinary nitrogen loss—considerably greater even than the nitrogen intake. The volume of urine for the day was double the usual excretion, and for the period was greater than the previous periods by an average of 700 cc daily. This reversal followed 12 days of large positive retention, and since there was no change in fluid intake, must be attributed to the incompleteness of the acid hydrolysate. Severe loss did not continue, however, since on the second and third day of the period a small positive and small negative balance occurred. These data suggest that the body was able to adjust itself to partially use the deficient mixture. The small net loss, for the 3-day period, —.019 g per kilo, is considerably less than the loss during complete protein starvation (Period 1), and confirms similar observations in rats[2] that even an incomplete source of nitrogen is preferable to no nitrogen at all.

Summary. An enzymic digest of casein may be as effective as milk protein in promoting nitrogen retention, while an acid hydrolysate deficient in tryptophane will not effect nitrogen equilibrium.

* Hydrolyzed with fresh pancreas,[3] known under the trade name of Amigen.

† This has previously been shown adequate for growth in rats when supplemented with 2% tryptophane.

[3] Mueller, A. J., Kemmerer, K. S., Cox, W. M., Jr., and Barnes, S. T., *J. Biol. Chem.*, 1940, **134**, 573.

13950 P

Effects of Lesions of the Periaqueductal Gray Matter in the Cat*

PERCIVAL BAILEY AND EDWARD W. DAVIS.

From the Department of Neurology and Neurological Surgery, University of Illinois College of Medicine.

The great epidemic of lethargic encephalitis directed the attention of neurologists to the region of the midbrain and hypothalamus. A long series of experimental and pathological studies has demonstrated the importance of the gray masses which surround the inferior and posterior parts of the third ventricle, but the posterior extension of the juxta-ventricular gray matter, which surrounds the aqueduct of Sylvius in a cylinder of considerable size, has been neglected. This periaqueductal gray matter is of such a shape, and so located, as to make its destruction very difficult by the usual means—such as the Horsley-Clarke machine—without such extensive damage to neighboring structures as to obscure the interpretation of results.

After much experimentation we developed an electrode which could be inserted by an opening in the occipitoatlantoid ligament

* Aided by a grant from the American Medical Association.