TABLE IV. Effect of Pyrazinamide on Nicotinamide Growth Response in Chicks.

Level of nicotinamide, γ daily	Level of pyrazinamide, γ daily	Initial wt and No.	Avg gain and No. alive ( ) 2 wk	4 wk
50		40 (27)	17 (22)	41 (14)
50		42 (10)	40 (10)	80 (9)
100		40 (28)	35 (25)	99 (21)
200		39 (37)	45 (37)	166 (30)
	200	40 (8)	4 (6)	— (0)
	1 mg	39 (9)	25 (8)	44 (6)
	10	40 (19)	19 (15)	35 (7)
	100	38 (10)	9 (8)	40 (7)
200	1	39 (9)	37 (8)	111 (7)
50	10	42 (10)	28 (10)	57 (9)
100	10	42 (10)	38 (8)	82 (8)
200	10	40 (19)	46 (18)	119 (17)
100	100	38 (10)	28 (9)	96 (9)
200	100	38 (10)	30 (10)	126 (10)

is improbable that large enough doses could be given to animals to induce pellagra, if its inhibition index for *L. arabinosus* is an indication of the amount required.

Summary. 1. Of a series of 37 compounds tested, pyrazinamide, pyrazinoic acid and 2-sulfanilamide-5-nitropyridine were found to be nicotinamide antagonists for *L. arabinosus*. 2. Pyrazinamide was not an antagonist for rats or chicks.

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1. Bills, C. E., McDonald, F. G., and Spies, T. D., *Southern Med. J.*, 1939, v32, 793.

2. Dann, W. J., Kohn, H. I., and Handler, P., *J. Nutrition*, 1940, v20, 477.

3. Waisman, H. A., Mickelson, O., McKibbin, J. M., and Elvehjem, C. A., *J. Nutrition*, 1940, v19, 483.

4. Bonner, J., *Plant Physiol.*, 1940, v15, 555.

5. Koser, S. A., and Kasai, G. J., *J. Inf. Dis.*, 1948, v83, 271.

6. Koser, S. A., Dorfman, A., and Saunders, F., PROC. SOC. EXP. BIOL. AND MED., 1940, v43, 391.

7. Moller, E. F., and Birkower, L., *Ber. deut. chem. Ges.*, 1942, v75, 1108.

8. Coté, L., and Oleson, J. J., *J. Bact.*, 1951, v61, 463.

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Changes in Glucose Tolerance as an Index of Improvement after Electroshock Therapy. (19649)

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Impairment of glucose tolerance in many patients with manic-depressive, involutional and schizophrenic psychoses is well known. An attempt was made to evaluate the possible use of changes in glucose tolerance after electroshock therapy as an objective index of clinical improvement.

Material and methods. Twelve patients, ranging in age from 32 to 73 years, were the subjects; 10 were women. One of the patients was known to have had diabetes mellitus for a decade; the disease was discovered here in 2 others. The patients were given 3 electroshock treatments weekly in the numbers indicated (Table I). All patients were much improved following treatment. Studies of the blood sugar were made after oral administration of 100 g of dextrose before the first and again 5 to 10 days after the last treatment; the method of Folin and Wu(1) was used.

TABLE I. Diagnoses of Patients and Treatments Given.

Case	Age	Sex	Treatment, shocks	Diagnosis
A	65	♀	5	Involutional psychosis; melancholia
B	44	♀	6	Schizophrenia, paranoid
C	66	♀	5	Manic depressive, manic
D	54	♀	10	Involutional psychosis; melancholia
E	72	♀	12	" " "
F	40	♀	13	Schizophrenia, paranoid
G	54	♀	9	Paranoid condition
H	32	♀	4	Manic depressive, depressed
I	56	♂	4	" " "
J	59	♀	7	Involutional psychosis; melancholia
K	73	♂	7	" " "
L	58	♂	5	Manic depressive, depressed

Observations. Insignificant changes in glucose tolerance occurred in 3 patients (Fig. 1, Cases A, B, I) following a course of treatments. Slight impairment of glucose tolerance was noted in 2 instances (Fig. 1, Cases C, G), and a notable lowering of the level of the curve occurred in 4 (Fig. 1, Cases D, E, F, H). Improvement in sugar tolerance occurred after shock therapy in 2 of the 3 diabetic patients; this was definite in one instance (Fig. 2, Case K) and questionable in the other (Fig. 2, Case L).

Discussion. The observations made here show no consistent change in glucose tolerance in patients who improved clinically after a course of electroshock therapy; while the glucose tolerance may improve somewhat in some diabetic and non-diabetic psychotic patients treated with electroshock therapy, this change was inconstant. It is evident even from the results in this small group of patients that changes in glucose tolerance cannot be used as an objective index of improvement after electroshock therapy.

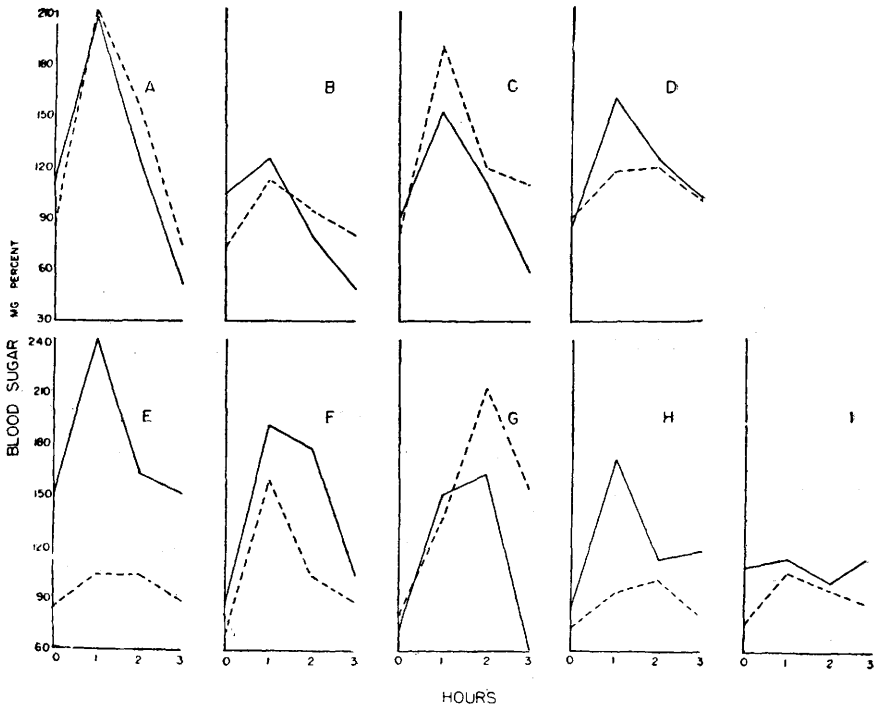

FIG. 1. Oral glucose tolerance tests before (solid line) and after (broken line) a course of electroshock therapy.

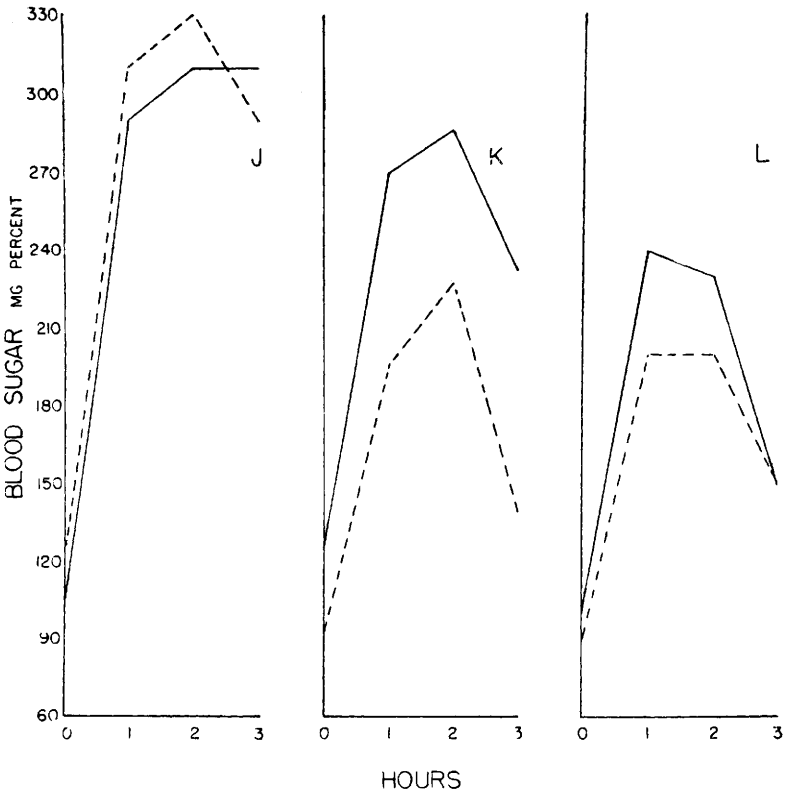

FIG. 2. Oral glucose tolerance tests in 3 diabetic patients before (solid line) and after (broken line) a course of electroshock therapy.

A number of factors may influence glucose tolerance in untreated patients with mental disease: these include metabolic changes associated with the mental illness itself, abnormal absorption from the gastrointestinal tract(2), and starvation. Hyperactivity of the adrenal cortex that occurs early in the course of electroshock therapy tends to depress glucose tolerance, but the hyperactivity induced by shock therapy wears off as treatment continues (3). However, the effect of adrenal cortical hormones on sugar tolerance may persist for weeks(4). In addition, the state of the sodium metabolism appears to have a profound influence on utilization of glucose when the adrenal cortex is stimulated(5); marked changes in sodium metabolism occur during the course of shock therapy(6,7). The effect of electroshock therapy on sugar metabolism is the resultant of the effects of changes in adrenal-cortical function, amelioration of mental disease, improvement in nutritional status, modification of electrolyte metabolism, and possibly other factors. These factors vary in different patients; the large number of irregularly variable factors involved makes correlation between changes in glucose tolerance and in clinical state a poor one.

Summary and conclusions. The effect of electroshock therapy on glucose tolerance was studied in 12 psychotic patients who improved with electroshock therapy. Changes in sugar tolerance varied in direction and degree; there was no correlation with clinical improvement.

1. Peters, J. P., and Van Slyke, D. D., *Quantitative Clinical Chemistry*, Vol. II Methods, Baltimore, The Williams & Wilkins Co., p. 456.

2. Parsons, E. H., Gildea, E. F., Ronzini, E., and Hulbert, S. Z., *Am. J. Psychiat.*, 1949, v105, 573.

3. Altschule, M. D., and Parkhurst, B. H., *Arch. Neurol. Psychiat.*, 1950, v64, 516.

4. Bunim, J. J., *Bull. N. Y. Acad. Med.*, 1951, v27, 75.

5. Ransohoff, W., Brust, A. A., Reiser, M. F.,

Mirsky, I. A., and Ferris, E. B., *Proc. Second Clin. ACTH Conf.*, 1951, v1, 160.

6. Altschule, M. D., and Tillotson, K. J., *Am. J. Psychiat.*, 1949, v105, 829.

7. Grunebaum, H., and Altschule, M. D., *Arch Neurol. and Psychiat.*, 1950, v63, 444.

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Significance of Intermedin Activity in Adrenocorticotropic Hormone Preparations.* (19650)

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Recent investigations by Johnsson and Högberg(1) and by Sulman(2,3) have suggested that intermedin and adrenocorticotropic hormone (ACTH) were closely related or identical, and that assay of melanophore expansion activity in the frog could be employed as a convenient test for ACTH. In addition, the physico-chemical properties(4) of the melanophore expanding hormone are in many respects similar to those reported for ACTH. The following experiments were designed to demonstrate whether the adrenal ascorbic acid depleting activity of various ACTH preparations is correlated directly with intermedin activity.

Assay methods. Hypophysectomized frogs, *Rana pipiens,* were employed for intermedin assay in most of these studies. In one series of experiments *Rana catesbiana* was employed. Quantitation of melanophore expansion was made on an arbitrary 1+ through 4+ scale, in addition to the determination of the minimal effective dose (m.e.d.) necessary to produce a 1+ reaction. Readings were made at half hour intervals for a 4 hour period after injection of the test solution (0.1 ml) into the dorsal lymph sac. Adrenocorticotropic hormone preparations were assayed by the adrenal ascorbic acid depletion test(5).

Results. The investigation proceeded along 5 separate lines. The first approach involved the determination of both types of activity in a number of ACTH preparations(6). The results of this series of experiments are presented in Table I. It is obvious that no direct correlation exists between the ACTH and intermedin activities of the various preparations. As a matter of fact, the few preparations tested show an inverse correlation.

TABLE I. Adrenocorticotropic and Intermedin Activities of ACTH Preparations.

Preparation, ACTH	ACTH activity, I.U./mg	Intermedin activity (m.e.d.), μg
L 2317 H	35	.5
M	30	.1
L 2316 C*	200	5

* Partial acid hydrolysate of L 2317 M(6).

The second series of experiments was undertaken in the hope of demonstrating a chemical separation of the adrenocorticotropic and intermedin activities. Fractions with highly potent adrenocorticotropic activity, obtained from a method using charcoal chromatography (7), exhibited a marked concentration of intermedin activity as well, and no separation was achieved. Definite separation was obtained, however, with fractions isolated from cellulose columns by a discontinuous pH gradient. As has been reported previously(8), almost all of the adrenocorticotropic activity resides in the second of three peaks obtained by this method. Intermedin activity, on the other hand, was almost completely concentrated in the first peak (Table II). Thus, an effective

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