living conditions prevailing by the time of the ancient Aleut settlements. This is one chief objective of the current Aleutian project at Michigan.

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The Effect of Insulin Coma on Uropepsin Excretion[1]

James S. L. Jacobs, Clinton E. Tempereau, and Philip M. West

Departments of Psychiatry and Investigative Medicine, Long Beach Veterans Administration Hospital, Long Beach, California,* and *Department of Infectious Diseases, University of California Medical School, Los Angeles

Uropepsin excretion determinations were performed on 10 schizophrenic patients who underwent insulin coma therapy. No patients were included who exhibited gastrointestinal, neoplastic, or other physical diseases that might influence uropepsin excretion. Control periods of at least one week were observed before and after therapy. Comparable studies were obtained with subshock insulin and electroconvulsive treatments. For each determination, the measured urine specimen covered the period of actual therapy, was of about 4 hr duration, and corresponded diurnally to the controls. All specimens were obtained between 7:00 A.M. and 11:00 A.M. Uropepsin determinations were performed according to P. M. West's modification (*1*) of Sylvest's technique (*2*). The results have been quantified in units/hour; the reproducibility of the method is approximately 2%.

The generally irregular and fluctuating, abnormally high concentrations of uropepsin during the control periods conformed to the pattern usually found in schizophrenic psychotics (*3*). The characteristic response to the intramuscular administration of regular insulin was an increase in uropepsin output. The magnitude of this reaction did not correlate with the form of schizophrenia, the dosage of insulin, the stage of insulin treatment, the occurrence of coma, or the duration of therapy. The unit dosage at which the first significant increase in output occurred varied between 40 and 600; that for the maximum increase varied between 80 and 900. The maximal outputs were from 1.5 to 5 times the control levels (Fig. 1), might occur

[1] Reviewed in the Veterans Administration and published with the approval of the chief medical director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinions or policy of the Veterans Administration.

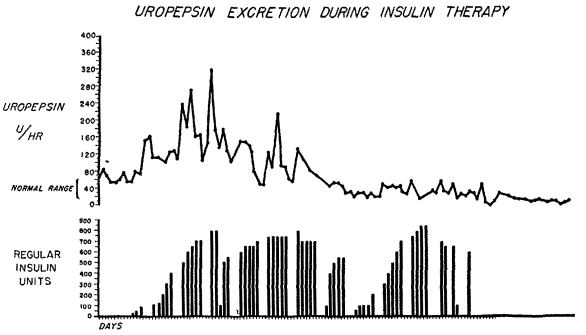

FIG. 1. Effect of regular insulin administration on the excretion of uropepsin. Coma occurred at the 21st dose (650 μ). Note that insulin dosage was deliberately reduced twice thereafter in order to evaluate the effect upon uropepsin excretion.

at any point in therapy, were not sustained, and could not be reproduced with comparable or larger doses of insulin. In those instances in which electroconvulsive therapy preceded insulin coma, and in control studies with electroconvulsive therapy alone, the increase in uropepsin excretion was smaller and evanescent during the electroconvulsive treatments and did not affect the response to insulin.

The problem of quantifying certain adrenocortical functions in schizophrenic psychotics in the resting state, and under the influence of insulin and other physical therapies, proved to be a difficult one until the discovery of what is evidently a simple and quantitative measure of this activity, namely, uropepsin (*4*).

Eosinophil counts taken prior to the injection of insulin and immediately after the termination of each treatment revealed changes which consistently indicated adrenocortical stimulation. Reduction of the number of circulating eosinophils varied from 50% to 90% during insulin therapy (*6*). The stimulating effect of insulin upon adrenocortical activity has been demonstrated by other investigators (*7–10*). Although the mechanism is uncertain, it has been suggested that the release of adrenalin and its effect upon the pituitary-adrenal axis is partially responsible; and this occurs despite the recognized antagonism between insulin and adrenocortical hormone upon the hexokinase system.

The consistent daily occurrence of eosinopoenia in response to insulin administration implies that the concomitantly increased uropepsin excretion during a course of insulin coma therapy furnishes here, as it does under other circumstances (*4*), a quantitative measure of adrenocortical activity. Although the eosinophil count furnishes a satisfactory test of adrenocortical *reactivity,* it does not provide a quantitative measure of the day-to-day fluctuations of adrenocortical function.

Our investigations of adrenocortical function and proteolytic enzyme kinetics have shown a great individual variability in the schizophrenic group and indicate a pronounced tendency toward hyperadrenocorticism and unstable protein metabolism, both at

rest and under physical and emotional stresses. Hence, the observed effects of insulin and electroconvulsive therapies upon uropepsin excretion assume considerable theoretical significance.

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Biosynthesis of the C^{14}-Labeled Form of Dextran[1]

Norbert J. Scully,[2] Homer E. Stavely,[3] John Skok,[2] Alfred R. Stanley,[3] J. K. Dale,[3] J. T. Craig,[3] E. B. Hodge,[3] William Chorney,[2] Ronald Watanabe,[2] and Robert Baldwin[3]

Argonne National Laboratory, Chicago, Illinois, and Research and Development Laboratories, Commercial Solvents Corporation, Terre Haute, Indiana

Dextran is a polysaccharide, made up solely of glucose units, produced by bacterial fermentation of sucrose. Only the glucose portion of the sucrose molecule is utilized in the biosynthetic process. Dextran of suitable molecular size and purity is currently of interest as a synthetic plasma volume expander, particularly for use in event of large-scale catastrophe in which natural blood plasma supplies might be limited. Dextran has been tested clinically with success, but its metabolic fate in the body is inadequately known, since the best analytical procedures account for only about half of injected dextran. It was concluded that these metabolic questions could best be resolved through the use of an isotopically labeled form of dextran.[4]

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[2] Argonne National Laboratory, Chicago, Illinois.

[3] Commercial Solvents Corporation, Terre Haute, Indiana. The following Commercial Solvents Corporation personnel also assisted with various phases of the program: Robert Cundiff, L. R. Jones, and Dona Graam.

[4] The metabolism studies are being conducted by various investigators, at the direction of the Subcommittee on Shock, National Research Council.

Argonne National Laboratory and Commercial Solvents Corporation, at the request of the Office of the Surgeon General of the U. S. Army, and under the direction of the Subcommittee on Shock, National Research Council, cooperated in biosynthesizing C^{14}-labeled dextran at two different levels of activity, one designed for use in animal experiments, the other for human clinical experiments. Since 1949 the Research and Development Laboratories, Commercial Solvents Corporation, have conducted a dextran research program and at present have developed a successful clinical grade of dextran. The present report outlines the experimental procedures and results incident to the successful completion of the biosynthesis program.

Essentially, the problem involved the biosynthesis of labeled C^{14} sucrose, followed by the biosynthesis of labeled dextran through fermentation of this sugar. The quantity and absolute activity of labeled dextran required for proposed laboratory and clinical experiments necessitated the handling of approximately 0.3 c of radiocarbon. In order to determine the adequacy of both proposed experimental equipment and procedures, a small quantity of low absolute activity C^{14} dextran was biosynthesized. As soon as these studies were evaluated large-scale biosyntheses were initiated.

C^{14} sucrose was biosynthesized by allowing carbohydrate-depleted, excised *Canna* leaves to photosynthesize in the presence of $C^{14}O_2$ in a 38-liter hermetically sealed, leaf-chamber system.[5] This plant was selected because of its reported high efficiency in converting $C^{14}O_2$ to sucrose during photosynthesis (*1*). A total of 309.7 mc of $C^{14}O_2$ was generated from $BaC^{14}O_3$ in eight experiments employing a total of 30 leaves, weighing 208.8 g fresh. The separate photosynthesis periods varied from 6 to 24 hr and resulted in fixation of 308.0 mc in the leaves, or 99.4% of that generated.

A total of 175.2 mc of C^{14} sucrose was biosynthe-

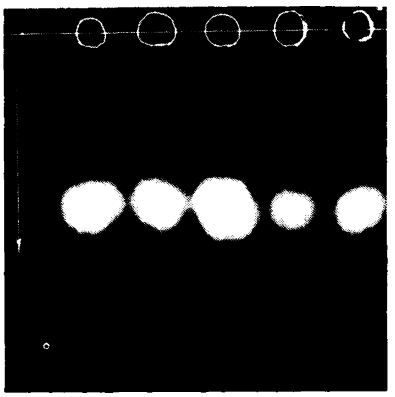

Fig. 1. Radioautograph of paper chromatogram of five separate lots of C^{14} sucrose showing their lack of contamination. Paper partition chromatogrammed for 48 hr at 20° C with BuOH : EtOH : H_2O (45 : 5 : 50) as irrigating solvent. Radioautographed for 30 days using Eastman No-screen x-ray film.

[5] The detailed experimental methods utilized for the biosynthesis and isolation of C^{14} sucrose and other plant fractions from Canna leaves are to be presented elsewhere.