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TO: Committee on Use of Isotopes in Human Beings

FROM: W.W. Shreeve, M.D., Ph.D. and R. Schwartz, M.D.

SUBJECT: Use of $Na^{24}$ and $Na^{22}$ in Combination as Tracers in Diabetic Patients

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GENERAL STATEMENT

In previous studies we have observed an early (15 minute) effect of intravenous insulin on decreasing the arterio-venous difference in specific activity of $Na^{24}$ and of $C^{14}O_2$ in the forearm of diabetic patients. This change may be due to increased blood flow caused by epinephrine response to hypoglycemia. However, it may also be related to a more direct effect of insulin on cell permeability to electrolytes. This study aims, therefore, at a more basic understanding of the effect of insulin on cell membranes and cellular transport as well as electrolyte derangements in diabetes.

Diabetic patients will be used because they are most useful for study of the electrolyte metabolism in the insulin-free state. Adult diabetics over age 30 and without restriction as to sex, life expectancy, or reproductive capacity will be studied.

Previous studies at Brookhaven with human beings have utilized $Na^{24}$ (Proj. H-32) and $Na^{22}$ (Project H-54) in single intravenous injections. We have previously employed $Na^{24}$ in doses (50 $\mu c$) well below those authorized in Project H-32 and have obtained adequate counting in the well-type scintillation counter. The turnover half-time of sodium in the whole body is generally about 10-25 days (1) and may be markedly increased or decreased by changes in dietary intake of sodium chloride (Dahl, L.K. and Gordon, W.H., Jr., Project H-54). Smilay et al (2) indicated that the half-time could be reduced to 13 days by 10 gm. daily NaCl intake and to 6 days by a 30 gm. intake. Similar effects were indicated by Sackner et al (3).

In our course of study we will first inject intravenously in the fasting insulin-free subject a tracer amount of $Na^{24}$ followed by sampling of the artery at the antecubital fossa of one arm and the vein at the same site of the other arm with collections at intervals of a few minutes. Approximately one hour after the $Na^{24}$ injection there will be administered intravenously .1$\mu$ unmodified insulin/kg. Five minutes later another tracer dose of $Na^{22}$ will be given intravenously and the process repeated. The $Na^{24}$ will be counted promptly after the study and the $Na^{22}$ some days later after the $Na^{24}$ has decayed to negligible values. Urine samples will be collected at intervals for determination of catechol amines and blood for glucose analysis.

It is not expected that this study will be repeated in the same patient. At present one patient, , aged 60, has been designated for this study. It is proposed that a dose of 50 $\mu c$. $Na^{24}$ and 6 $\mu c$. $Na^{22}$ be given this patient and generally to patients aged 45 or over. In younger patients both doses will be reduced to half these amounts.

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ISOTOPE

Sodium 24 is produced in the Brookhaven graphite reactor with a specific activity of about 50 millicuries/40 mg. It decays almost entirely by $\beta^-$ emission with maximum energy of 1.39 MEV. Two gamma rays with energies of 2.76 and 1.38 MEV are also emitted (4). The half-life of $Na^{24}$ is 15 hours. Sodium 22 is produced by cyclotron bombardment and is available as carrier-free material with 99% chemical purity from Nuclear Science and Engineering Corporation of Pittsburgh (2). It has a physical half-life of 2.6 years. It decays mainly by $\beta+$ emission with maximum energy of .542 MEV together with a gamma ray of 1.277 MEV (cf. Project H-54). Both radioisotopes are routinely assayed before use in the Medical Research Center. Samples for injection will be taken up in pyrogen-free isotonic saline and sterilized by autoclaving.

RADIATION DOSAGE

It has been estimated that the total dosage from administration of 3$\mu$. $Na^{22}$ will provide ca. .15 rads at a biological half-life of 30 days (Project H-54). With a dose of 6 $\mu$cs. the radiation would be .30 rads, but it is suggested that our patients can be given, after study, a high salt intake, e.g. 10 gm. daily, which would decrease the half-life to about 15 days (2) and thus provide only .15 rads from 6 $\mu$c. Present evidence indicates (2) that only about 1% of injected sodium remains for an appreciably longer half-life than 20 to 30 days.

It has previously been calculated that the combined beta and gamma whole body radiation dosage from $Na^{24}$ injected intravenously would be .114 rep/$\mu$c./kg. (Project H-32). This is approximately .114 x .9 = .103 rads. Therefore a dose of 50 $\mu$c. to a 70 kg. man would provide approximately

$$.103 \times \frac{5}{7} = .074 \text{ rads.}$$

The total maximum dosage from 50 $\mu$c. $Na^{24}$ and 6 $\mu$c. $Na^{22}$ would thus be

$$.074 + .150 = .224 \text{ rads.}$$

National Bureau of Standards Handbook 69 states that 10 microcuries of $Na^{24}$ is the maximum permissable continuous body burden while for $Na^{22}$ the value is 7 $\mu$. Thus, the proposed dose of $Na^{22}$ is less than the MPD and the 50 $\mu$c. dose of $Na^{24}$ would in a period of a little more than two half-lives, i.e., 1.5 days, be less than the MPD.

HEALTH PHYSICS

High activity sodium sources are prepared for use, assayed and transported with proper lead shielding. The levels used in the patients require no special disposal of excreta or shielding, but blood and urine samples sent to clinical and research laboratories will be marked as containing $Na^{24}$ and $Na^{22}$ in microcurie amounts or less.

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1. Veall, N. and Vetter, H.

Radioisotope Techniques in Clinical Research and Diagnosis,

Butterworth & Co. Ltd., 1958

2. Smilay et al

J. Lab. and Clin. Med. 58, 60 (1961)

3. Sackner et al.

Proc. Soc. Exp. Biol. and Med. 106, 514 (1961)

4. Kamen, M.D.

Isotopic Tracers in Biology

Academic Press Inc., Third Ed., 1957

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