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Publication Date

1949-07-15

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Contract No. W-7405-eng-48

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by

J. Govaerts

Berkeley, California

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July 15, 1949

ABSTRACT

The fate of C^{14} fixed by the lungs as barium carbonate has been studied to evaluate the hazards which the use of the radiocarbon isotope C^{14} might present to laboratory workers who used this material. The results obtained indicate that C^{14} introduced into the lungs as a fine suspension either by intravenous injection or by insufflation in the form of $BaC^{14}O_3$ is very rapidly excreted. The overall retention of C^{14} is less than 15% twelve hours after administration. At the same time, it appears from these data and from those obtained by other workers that the dangers that might be encountered by those who work with C^{14} are not as great as expected.

* The work described in this paper was sponsored by the Atomic Energy Commission.

** While on leave from the Laboratory of Radioactivity and Nuclear Physics, University of Liege, Liege, Belgium.

THE RATE OF ELIMINATION OF C^{14} ADMINISTERED AS $BaC^{14}O_3$ *

by

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A problem of particular importance is the evaluation of the hazard of the long-lived radiocarbon isotope C^{14} . Armstrong and associates (1) have studied the rate of elimination of C^{14} by rats after intraperitoneal injections of sodium carbonate containing C^{14} . The incorporation of C^{14} could be detected in the muscle and liver by implantation of $CaC^{14}O_3$ in the peritoneal cavity and maintaining the isotopic inorganic C^{14} content of the body fluid at a high level over a longer period of time. A comparison was also made between the elimination of the C^{14} from the tissues by mature and growing rats (2). In general, the rate of excretion of the isotope is very fast. The specific activities of the tissues of the growing rats greatly exceeded those of the mature animals. The overall retention of C^{14} , however, was greater in the mature rats. In the latter, no significant change in the C^{14} retention was observed from the fifteenth day after injection, while an appreciable decrease in the C^{14} retention was observed in growing animals. A rapid excretion of C^{14} has been ob-

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(1) W. D. Armstrong, J. Schubert and A. Lindenbaum, Proc. Soc. Exp. Biol. and Med., 68, 233 (1948).

(2) J. Schubert and W. D. Armstrong, J. Biol. Chem., 177, 521 (1949).

served by Gould and Associates (3) after intraperitoneal injection of labeled sodium bicarbonate, acetate or succinate. After four hours the cumulative excretion of carbon dioxide was 95% for bicarbonate, 87% for acetate and 86% for succinate.

Barium carbonate is the most suitable and common chemical form in which C^{14} is measured, but while handling this material there is a possibility of dusting and consequent inhalation by laboratory workers unless adequate precautions are taken. There is very little information in the literature with respect to the danger that might be encountered by those who work with $BaC^{14}O_3$, and the following experiments were performed in order to determine the rate at which C^{14} is eliminated by mice when introduced into the lungs as $BaC^{14}O_3$.

EXPERIMENTAL

The ideal experiment would have been to keep the mice in an atmosphere in which a dust of $BaC^{14}O_3$ was continuously maintained. Under these conditions experimental difficulties would be encountered, particularly the need for a large amount of barium carbonate of high specific activity. For these reasons, intravenous injections of a fine suspension of $BaC^{14}O_3$ in isotonic glucose solution were tested in order to deposit the barium carbonate in the lungs of mice. In preliminary experiments the lungs were tested 3-60 minutes after the injection, and we could observe that the $BaC^{14}O_3$ is rapidly fixed by the lungs and no significant

(3) R. Gould, F. Sinex, I. Rosenberg, A. K. Solomon and A. B. Hastings, J. Biol. Chem., 177, 295 (1949).

activity is found in the soft tissues. So, as expected, most of the injected suspension of $\text{BaC}^{14}\text{O}_3$ is deposited in the lungs.

Each mouse was placed in a metabolic cage for the duration of the experiment. The cage was swept with a continuous stream of air that was bubbled through a tower filled with sodium hydroxide solution in order to fix the expired carbon dioxide. Before admitting the air to the cage it was made CO_2 -free by passing it through a tower containing moistened soda lime. The expired carbon dioxide was fractionated and the urine and feces were collected. The mice were sacrificed by ether and the thorax was immediately opened. The lungs, kidney, liver and spleen were removed, dried and weighed for separate assay. The tissues and excreta were dried in vacuo for two days at room temperature.

The expired carbon dioxide was precipitated as barium carbonate which was filtered, dried and weighed. The excreta and internal organs were combusted according to the Van Slyke-Folch method (4); the carbon dioxide produced was absorbed and treated in the same manner as expired carbon dioxide.

Most of the barium carbonate samples were counted as $\text{BaC}^{14}\text{O}_3$ plates using either a thin mica-window Geiger-Mueller tube or a Nucleometer (Radiation Counter Laboratories, Chicago, Illinois), depending on the specific activity of the sample. Some very low specific activity samples were measured using an ionization chamber with a vibrating reed electrometer. The total radioactivity of each sample was determined and the percentage of the activity in the initial dose recovered was calculated. In some cases, the radioactivity of the remaining carcass was determined.

(4) D. D. Van Slyke and J. Folch, J. Biol. Chem., 136, 509 (1940);
H. E. Skipper, C. E. Bryan, L. White, Jr. and O. S. Hutchison,
J. Biol. Chem., 173, 371 (1948).

RESULTS AND DISCUSSION

The representative findings concerning the cumulative excretion of C^{14} as carbon dioxide are represented in Fig. 1. These typical data obtained from three mice indicate that C^{14} appears in the expired carbon dioxide immediately after injection. The excretion by the lungs of the injected C^{14} is very rapid; about 45% of the injected dose is expired during the first hour after administration. Later, the excretion is slowed down progressively, and after twelve hours about 85% of the dose is excreted as $C^{14}O_2$. In these animals no significant activity is found in the tissues collected and the same observations have been made for the excreta collected during the experiment. About 88-99% of the total activity was recovered. Since the amount of residual C^{14} in the body of the mice at the time of sacrifice was very small, the failure to find measurable amounts of C^{14} in the tissues is not to be interpreted as evidence that none was there.

The injections of barium carbonate produced an increase of the total quantity of carbon dioxide expired by the mice as shown in Fig. 2. After administration the carbon dioxide (total) expired becomes 3-5 times higher than the normal value, the latter being reached only several hours after the administration.

The half-life of retention by the body can be estimated from a plot of the data on semi-logarithmic paper in which the percentages of the injected dose remaining in the animal are plotted on the logarithmic axis and time on the regular axis. As shown in Fig. 3, it is possible to obtain curves analogous to radioactive decay curves. The curves obtained

present two processes corresponding to two biological half-lives of one and nine hours, respectively. So, we observe first a rapid excretion of the injected C^{14} followed by progressively slower excretion. It is clear that the biological half-lives reported here apply only to the particular experimental condition reported in this paper.

In order to obtain more information about the mechanism of excretion of radiocarbon by the lungs, some experiments were performed by injecting intravenously sodium carbonate containing C^{14} . The curves representing the cumulative excretion of C^{14} in the form of $C^{14}O_2$ are very similar to those obtained with barium carbonate injections. About 70% of the injected dose is excreted during the first three hours following administration. After that time, negligible amounts of radiocarbon are expired by the lungs. If the data are plotted on semi-logarithmic paper, only one biological half-life of about one hour is obtained; most of the C^{14} is expired following a half-life of one hour. Comparing these results with those obtained with barium carbonate injection, we find, again, only the first process concerning the rapid injection of C^{14} as $C^{14}O_2$. With sodium carbonate injections also no detectable activity could be found in the liver, spleen, lungs, kidney and excreta. The fact that in these experiments all the radiocarbon was not recovered can be explained by a loss of material during the injections of the small amounts of solutions.

Fig. 4 represents the typical data obtained when C^{14} is introduced into the nose in the form of $BaC^{14}O_3$. The results are expressed as accumulated activity in disintegrations per minute expired as carbon dioxide. Because experimental difficulties were encountered, it was

rather difficult to know the exact total dose given to the animal. However, an estimation can be made indicating that up to 70% of the administered dose is excreted within the first four hours following administration.

From these data we may conclude that most of the C^{14} absorbed by the organism as barium carbonate is expired by the lungs as $C^{14}O_2$.

Acknowledgment: - The author takes pleasure in acknowledging his gratitude to Prof. M. Calvin whose suggestions and encouragement made this work possible and for the opportunity to work in the Radiation Laboratory. The author is grateful to Dr. B. M. Tolbert and Dr. H. B. Jones for continued interest and assistance. The program has been greatly aided by help from Mrs. Govaerts and thanks are also due to Mrs. Yvonne H. Stone and Mrs. C. Jane Krone for making radioactivity measurements.

SUMMARY

The fate of C^{14} fixed by the lungs as barium carbonate has been studied to evaluate the hazards which the use of the radiocarbon isotope C^{14} might present to laboratory workers who used this material. The results obtained indicate that C^{14} introduced into the lungs as a fine suspension either by intravenous injection or by insufflation in the form of $BaC^{14}O_3$ is very rapidly excreted. The overall retention of C^{14} is less than 15% twelve hours after administration. At the same time, it appears from these data and from those obtained by other workers that the dangers that might be encountered by those who work with C^{14} are not as great as expected.

FIG. 2

FIG. 3

Fig.

FIG. 4