

terminologies are too confusing to exist side by side. Eventually one or the other must achieve universal acceptance. The Fisher-Race terminology (2, 3) is familiar to everyone. There are many reasons why it is easier to teach and learn.

For example, Wiener (9) must use a different set of terms for the genotypes and the phenotypes (Rh_1 , Rh_0 , and R_1 , R_0 , etc.). So the worker in the field must learn another terminology. This is obviated in the British system.

$\frac{CDe}{CDe}$ clearly indicates all the information necessary.

Another point is that the symbol Rh_1 does not indicate whether the individual referred to is homozygous or heterozygous (4, 8, 9). The corresponding symbol of Race (3) does, $\frac{CDe}{CDe}$ or $\frac{CDe}{ede}$. The importance of this can be seen in the following example. In the mating of two individuals—one, Rh_1 , the other, rh —the possible progeny are Rh' , Rh_1 , Rh_0 , and rh . (It reminds one of multiplying with Roman numerals, i.e., $XIV \times VIII = CXII$!) One must memorize the entire table (9); one cannot easily work out the genotypes involved. There are also multiple matings possible, but the Wiener terminology does not take that in consideration. When he feels additional explanation of a phenotype is needed, he mentions it in a footnote (11).

TABLE 1

Wiener		Race		Proposed	
Antigen	Agglutinin	Antigen	Agglutinin	Antigen	Agglutinin
Rh_0	Anti Rh_0	D	Anti D	D	Anti d
rh'	Anti rh'	C	Anti C	C	Anti c
rh''	Anti rh''	E	Anti E	E	Anti e
Hr_0	Anti Rh_0	d	Anti d	D'	Anti d'
rh'	Anti rh'	c	Anti c	C'	Anti c'
rh''	Anti rh''	e	Anti e	E'	Anti e'

How much simpler is the Fisher-Race nomenclature: The Rh_1 individual is either homozygous $\frac{CDe}{CDe}$ or heterozygous $\frac{CDe}{ede}$, and in matings with an rh $\frac{ede}{ede}$ individual, the results would be (in the first mating) $\frac{CDe}{ede}$; in the second mating: $\frac{CDe}{ede}$ or $\frac{ede}{ede}$. There is nothing esoteric or far-fetched about it.

But the Fisher-Race nomenclature has still some confusing terms. The use of the lower case letters c, d, and e, to denote the Hr antigens leads to ambiguity when it is remembered that in the major groups, a and b indicate agglutinins. It is therefore proposed that the lower case letters be reserved for agglutinins, leaving the capital letters to indicate antigens.

Table 1 will clarify the proposed change. The advantages are quite obvious. No confusion can exist in either the reading or the speaking of these terms. Allowance is made for the discovery and naming of new antigens and agglutinins. Also their reciprocal relation is retained: D and D'; e and e'.

Conclusion. The great contributions made by Dr. Wiener in the field of immunology cannot be denied. However, although a subject must necessarily be scientifically correct, it must also be as clear and intelligible as possible. The adoption of the Fisher-Race terminology is a step forward, but there is still some confusion. It is hoped that the proposed changes will also lead along the same path to a clearer understanding.

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Rate of Elimination of C^{14} Administered as $BaC^{14}O_3$ ¹

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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 his associates (1) 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 long period of time. A comparison was also made between the elimination of C^{14} from the tissues by mature and growing rats (3). In general, the rate of excretion of the isotope was very fast. The specific activities of the tissues of growing rats greatly exceeded those of mature animals. The over-all retention of C^{14} , however, was greater in mature rats. In the latter, no significant change in the C^{14} retention was observed from the 15th day after injection, whereas an appreciable decrease in the C^{14} retention was still observed in growing animals. A rapid excretion of C^{14} has been observed by Gould *et al.* (2) after intraperitoneal injection of labeled sodium bicarbonate, acetate, or succinate. After 4 hr the

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cumulative excretion of CO_2 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 $\text{BaC}^{14}\text{O}_3$ 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 $\text{BaC}^{14}\text{O}_3$.

In an ideal experiment, mice would be kept in an atmosphere in which a dust of Ba^{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.

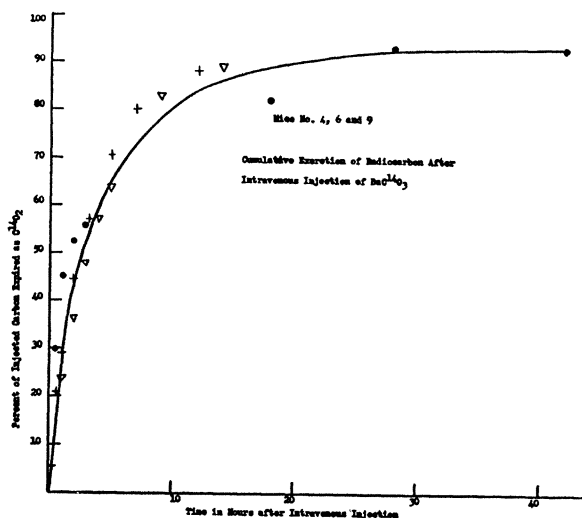


FIG. 1.

For this reason intravenous injections of a fine suspension of $\text{BaC}^{14}\text{O}_3$ in isotonic glucose solution were given in order to deposit the barium carbonate in the lungs of mice. In preliminary experiments, 3–60 min after injection the $\text{BaC}^{14}\text{O}_3$ was rapidly fixed by the lungs and no significant activity was found in soft tissues. 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 NaOH solution in order to fix the expired CO_2 . 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 CO_2 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 vacuum for two days at room temperature.

The expired CO_2 was precipitated as barium carbonate, which was filtered, dried, and weighed. The excreta and

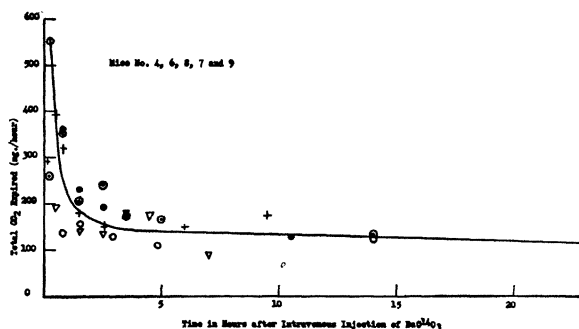


FIG. 2.

internal organs were incinerated according to the Van Slyke-Folch method (4, 5); the CO_2 produced was absorbed and treated in the same manner as expired CO_2 .

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

The representative findings concerning the cumulative excretion of C^{14} as CO_2 are represented in Fig. 1. These typical data obtained from three mice indicate that C^{14} appears in the expired CO_2 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

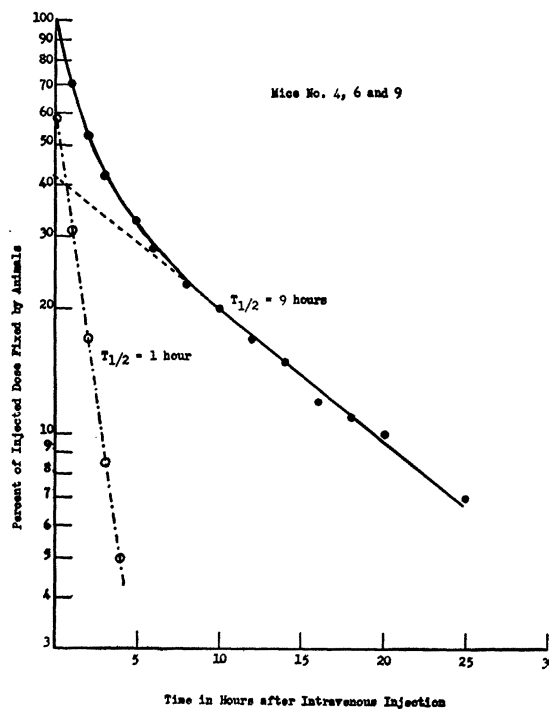


FIG. 3.

the first hour after administration. Later, the excretion is slowed down progressively, and after 12 hr 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 at the time of sacrifice was very small, 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 CO_2 expired by the mice as shown in Fig. 2. The total CO_2 expired becomes three to five times higher than the normal value, which is reached only several hours after injection.

The half-life of retention by the body can be estimated from a plot of the data on semilogarithmic 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

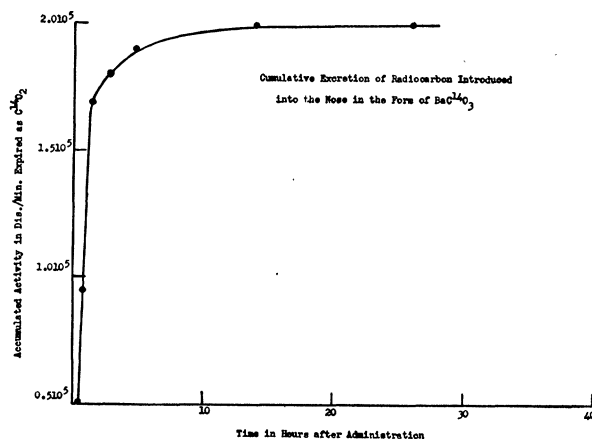


FIG. 4.

to obtain curves analogous to radioactive decay curves. The curves obtained present two processes corresponding to two biological half-lives of 1 hr and 9 hr, respectively. We observe first a rapid excretion of the injected C^{14} , followed by progressively slower excretion. The biological half-lives reported here apply only to the particular experimental conditions described 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 mice intravenously with 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 3 hr following administration. After that time, negligible amounts of radiocarbon are expired by the lungs. If the data are plotted on semilogarithmic paper, only one biological half-life of about 1 hr is obtained; most of the C^{14} is expired following a half-life of 1 hr. Comparing these results with those obtained with barium carbonate injections, we find again the rapid excretion by the lungs of C^{14} as $C^{14}O_2$. As with

sodium carbonate injections, 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 min expired as CO_2 . Because experimental difficulties were encountered, it is 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 4 hr 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 $C^{14}O_2$, and that the dangers to those who work with C^{14} are not as great as expected.

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Studies on the Metabolism of Administered Cytochrome C by the Aid of Iron-labeled Cytochrome¹

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This journal repeatedly has been the site of discussion of the therapeutic and prophylactic value of cytochrome C injections (3, 6, 8–10, 13). It may, therefore, be of interest to report here some recent findings on the metabolism of administered cytochrome C as traced by the fate of its constituent iron. The production of Fe^{55} -labeled cytochrome C has been reported previously (1). The purity of this preparation based on spectrophotometric analysis and protein dry weight determination was 73%; noncytochrome iron present was less than 2.5% of cytochrome iron. Two male albino rats were injected intravenously with this preparation and exposed immediately thereafter to a simulated altitude of 20,000 ft. Twenty-four hours after injection about 10 ml of blood was drawn by heart puncture, and the animal was decapitated. Cytochrome was isolated from kidney, liver, spleen, and heart, according to Rosenthal and Drabkin (12), and from muscle by a procedure similar to that of Keilin and Hartree (5). A fractionation for ferritin, according to Granick (4), was carried out on portions of the livers and on the kidneys of one of the animals. Fractions obtained and organs were treated according to Peacock

¹ The radioiron used in this investigation was supplied by Carbide and Carbon Chemicals Corporation, Oak Ridge, Tennessee, on allocation from the Isotopes Division, U. S. Atomic Energy Commission.