THE FIRST RADIOINDICATOR STUDY IN THE LIFE SCIENCES WITH A MAN-MADE RADIONUCLIDE

Four decades have elapsed since the use of a man-made radioindicator in biomedicine first was described in print (1). That succinct disclosure in 800 words is reproduced below just 40 years later to commemorate this pivotal event in the history of nuclear medicine.

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Radioactive Indicators in the Study of Phosphorus Metabolism in Rats

Recent progress in the production of radioactive isotopes by neutron bombardment makes the radioactive isotope of phosphorus $_{15}P^{32}$ easily accessible. This isotope, which has a half-life value of 17 days, can be utilised as an indicator of inactive phosphorus in the same way that the radioactive isotopes of lead, bismuth and so on were formerly used as indicators of these elements. If, for example, we add active $_{15}P^{32}$ to 1 mgm. of inactive phosphorus in such quantity that the Geiger counter registers 1,000 impulses per minute, carry out with the phosphorus activated in this way any sort of chemical or biological reaction and then find that the product obtained gives 1 impulse per minute, we may conclude that 1/1,000 mgm. of the phosphorus originally introduced is present in the product investigated.

Rats were fed with a few milligrams of sodium phosphate containing $_{15}P^{32}$ as indicator. The radioactive phosphorus present in the urine and faeces was then investigated for a period of a month. The result is shown in Fig. 1, which shows the percentage of the 2 mgm. of phosphorus taken, found daily in the excrements. The rat was killed, and, after ignition, the phosphorus content of the different organs was investigated. The result of an experiment in which the rat was killed 22 days after being fed on active phosphorus is seen in the first column in Table 1. The largest part of the phosphorus taken is present in the bones, and the smallest in the kidneys. When, however, we take into account the very different weights of the different organs and calculate the phosphorus content of the latter per gram after drying, we obtain a very different picture, as seen from the second column in Table 1. The spleen, kidneys, and the brain are found to contain per gram most of the active phosphorus. During one of the experiments, the rat produced six offspring on the seventh day, of which five were eaten by the mother; this caused a large increase in the active phosphorus content of the excreta in the following three days. The presence of 2 per cent of the 2 mgm. active phosphorus taken by the mother was revealed by the analysis of the remaining offspring.

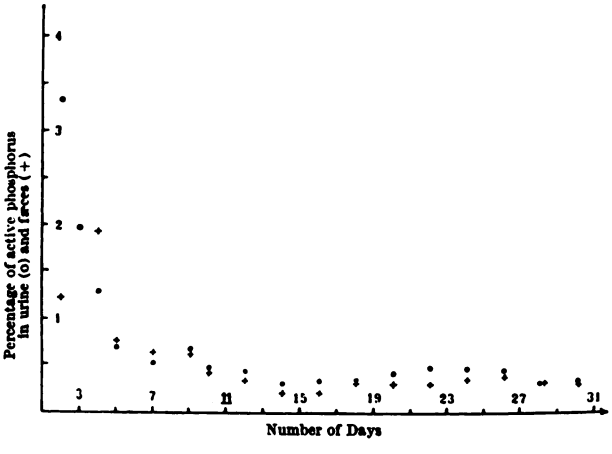

FIG. 1. On the first day, 7.4 per cent of phosphorus was found in the faeces and 5 per cent in the urine.

TABLE 1. Distribution of the active phosphorus in the rat

	Per cent	Per cent per gm.
Urine	26.3	
Faeces	31.8	
Brain and Medulla	0.5	14.7
Spleen and Kidneys	0.2	18.2
Liver	1.7	13.9
Blood	0.4	1.8
Skeleton	24.8	2.8
Muscles and fat	17.4	7.4

The active phosphorus content of the urine and faeces shows great fluctuations during the first few days after the intake of the preparation. Later, it becomes fairly constant; and we have obviously to deal with the excretion of phosphorus which has already been deposited for a while in the skeleton, the muscles, or other organs, and which has been displaced again. From our experiments, it follows that the average time which a phosphorus atom thus spends in the organism of a normally fed rat is about two months. This is also supported by the fact that rats killed about a month after the intake of phosphorus contain only about half the active phosphorus found in those killed after a week's time. This result strongly supports the view that the formation of the bones is a dynamic process, the bone continuously taking up phosphorus atoms which are partly or wholly lost again, and are replaced by other phosphorus atoms. In the case of an adult rat, about 30 per cent of the phosphorus atoms deposited in the skeleton were removed in the course of twenty days.

In another set of experiments we investigated the different parts of the skeleton. No conspicuous differences in the active phosphorus content could be found, with the exception of the teeth. The front teeth, which grow rapidly in rats, contained a larger part of the 2 mgm. phosphorus taken than the average of the whole skeleton, the ratio being about 10:1 in the case of adult and 6:1 in that of half-adult rats, whereas the molar teeth took up less than the average per gram of the skeleton, the ratio being 1:2 in the most extreme case. A detailed account of these and further results will be published elsewhere.

We wish to express our thanks to Prof. Niels Bohr for the kind interest he has taken in this work. For the preparation of the radioactive sources, and helpful assistance in making the measurements, we would also like to thank Mr. J. Ambrosen and Mr. S. Høffer-Jensen.

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Professor Hevesy kindly paused sufficiently long for me to make the photograph on the right when Doctor Paul C. Aebersold and I visited his laboratory in Stockholm in August 1950. He had been awarded the Nobel Prize for Chemistry 7 years before, in 1943 (*2*). This was just 30 years after Fritz Paneth and he published an account of their first use of a naturally occurring radionuclide, 21-year ^{210}Pb (Ra D), as a radioindicator in chemistry (*3*). Ten years later, in 1923, Hevesy was first to use 10.6-hr ^{212}Pb (Th B) as a radioindicator in studies in plants (*4*). And the following year he collaborated in the initial uses of radioindicators in animals with 5-day ^{210}Bi (Ra E), as well as ^{210}Pb again. Thus, Hevesy was well prepared promptly to embrace the opportunities provided by the discoveries of radioindicators of many physiologic elements that soon followed the announcement of artificial radioactivity in Paris in 1934 (*5*).

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He related to Aebersold and me how the ^{32}P was generated for these studies, carried out with Chievitz in Copenhagen the following year. Apparently, the α-particles emitted by 3.8-day ^{222}Rn (harvested from