

Phosphorus Metabolism in Normal, Rachitic and 'Treated' Rats

IN a letter to NATURE¹, Chievitz and Hevesy made a provisional communication on the use of radioactive indicators in the study of phosphorus metabolism in rats. In a recent paper to the Royal Society of Copenhagen², a detailed account of these investigations was given. Since 1936, we have been making experiments on phosphorus metabolism in normal, rachitic and 'treated' rats, utilizing also a radioactive phosphorus isotope as an indicator³. Although the detailed figures will be published shortly in the *Proceedings of the Royal Academy* at Amsterdam, we think a brief review into our experiments may be of general interest.

In six series with about sixty rats, we tried to investigate the absorption, retention and deposition in bone of normal, rachitic and 'treated' animals. The 'treated' rats are those rachitic rats, which received a dose of halibut oil a few hours before the oral administration of the radioactive isotope.

In our experiments the 'labelled' phosphorus was administered as sodium phosphate in an aqueous solution of pH 6-7. For that purpose, in four series, a fixed quantity of the radioactive solution was inserted by an exactly calibrated pipette into the stomach of the rat through a small stomach tube. In the fifth and sixth series the radioactive solution was injected in the tail vein.

A certain time after the administration of the active sodium phosphate—in our experiments after 1, 2, 8 and 8½ hours—the rats were decapitated and then quickly sectioned. The oesophagus was ligatured near the pro-stomach, whereas the ileum was doubly ligatured close to the caecum. Then the oesophagus was cut orally to the ligature, the ileum between the two ligatures. The limb bones were then dissected and cleaned, and the residue of the body with the head was collected. Now the preparations of the several organs to be measured were made. The determination of the radioactivity of the samples of blood, small and large intestine, faeces, urine, bones and residue was done with the compensation ionization chamber, whereby the ionization current produced by the radioactive preparations was compared each time with the ionization current of a constant source⁴.

The first series of experiments, in which the rats were decapitated after one hour, showed that the blood in normal and rachitic rats contains scarcely any radioactive phosphorus, perhaps a little in the rachitic rats, whereas the skeleton contains sometimes a considerable amount. The 'treated' rats, on the contrary, contain a large quantity of the labelled phosphorus in the blood. The rapid entrance of the phosphorus isotope into the bone is perceptible as well in the normal and rachitic rats as in the 'treated' rats³.

In the second series the rats were decapitated two hours after the administration of the active sodium phosphate. The radioactivity of the residue was also determined, and it was found that we could recover fully the whole of the quantity of the radioactive isotope administered. So our technique is reliable. But significant differences between the three groups of rats could not be found. The variation in the figures is too large to permit reliable conclusions.

Therefore in the third series the rats were decapitated after 8 hours, and here we think we can see small differences in the distribution of the labelled

phosphorus in the body of the three groups. The deposition in normal rats averaged 55 per cent, whereas in rachitic rats the deposition of the active phosphorus averaged 75 per cent. These figures also show a large variation, so that we are convinced that many experiments are necessary to make a significant difference certain. This fact is clearly shown in the fourth series; the rats were decapitated after 8½ hours; but we could not confirm the results of the third series.

In the fifth and sixth series the active phosphorus was injected into the tail vein. Here it is to be noted that, one hour after the injection, a considerable amount of the labelled phosphorus could be detected in the small intestine.

Summarizing, we can say that the distribution in the organism of the active phosphorus could be followed up easily. Of the labelled phosphorus administered, nearly 100 per cent could be recovered in our experiments. Both by administration with the stomach tube, and by injection in the tail vein, a very rapid entrance of the active phosphorus into the bone was perceptible. Furthermore, it was observed that one hour after the injection into the tail vein, a considerable amount of the radioactive phosphorus was re-excreted into the small intestine. This re-excretion can only happen with the digestive juices, after the labelled phosphorus had been moved with the blood stream and deposited in the several organs. So far as the gross absorption is concerned, that is the difference between the quantity of phosphorus administered and the quantity present in the stomach and small intestine after a certain period, we could not see any difference in the period between 1 and 8 hours after the administration in the normal, rachitic and 'treated' rats. The same can be said about the re-excretion into the gut. A characteristic mode of action of vitamin D on the absorption or re-excretion into the gut from the administered phosphorus could not be demonstrated.

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¹ Chievitz, O., and Hevesy, G., NATURE, **136**, 754 (1935).

² Chievitz, O., and Hevesy, G., *Kgl. Danske Vid. Selsk., Biol. Medd.*, **13**, 9 (1937).

³ Dols, M. J. L., VI Weltgeflügelkongress, Berlin-Leipzig, *Kongressber.*, **3**, 198 (1936).

⁴ Sizoo, G. J., and Koene, C. P., *Physica*, **3**, 1053 (1936).

Œstrogenic Activity of *p*-Hydroxy Propenyl Benzene (Anol)

FOLLOWING the publication of our letter in NATURE of April 10, p. 627, concerning the high Œstrogenic activity of anol, we have received information from some workers who have confirmed our observations, and from some others who have been unable to demonstrate activity with doses very much greater than those described by ourselves.

A re-investigation of the problem has indicated to us that some batches of apparently pure anol, melting