The Retention of Radioactive Phosphorus When Administered in Different Chemical Forms*†

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The efficacy of radioactive phosphorus as a therapeutic agent in some types of leukemia and allied diseases has been demonstrated by Lawrence and others (3, 2, 4). The form in which radioactive phosphorus has thus far been administered is the dibasic sodium phosphate. This was used at first orally and then intravenously (6).

That radioactive phosphorus may be administered safely in this form ($Na_2HP'O_4$) either orally or intravenously has been thoroughly established. With the development of greater efficiency in the cyclotron and particularly with the utilization of iron phosphide probes within the cyclotron rather than red phosphorus in the target field for bombardment, it has become possible to obtain phosphorus of very high specific activity, often approximating 1 mc. per mgm. of phosphorus.

Therefore, it seemed feasible to give therapeutic doses of radioactive phosphorus in varied chemical forms, since the total amount of phosphate-containing compound administered would be very small and well below the threshold of any harmful effect. Probably ionization of the phosphate compounds occurs promptly, and any therapeutic effect depends not on the particular form in which the radioactive phosphorus is administered, but rather on the radioactive phosphorus itself.

Since dibasic sodium phosphate is not readily prepared chemically from iron phosphide, since the half life of radioactive phosphorus is limited (14.3 days), and since the services of skilled chemists are difficult to obtain at the present time, it has become of practical importance to determine whether or not other more easily prepared forms containing the phosphate acid radical are satisfactory for therapeutic use.

Through the courtesy of Dr. John Irvine of the Massachusetts Institute of Technology, we obtained supplies of radioactive phosphorus in the form of magnesium ammonium phosphate and of phosphoric acid. Owing to the fact that phosphoric acid was diluted with 0.85 per cent of sodium chloride for the purpose of intravenous injection, it is probable that some formation of sodium salts may have taken place. The magnesium ammonium phosphate ($MgNH_4PO_4$) is insoluble in water or in alkaline solutions. In the very small amounts necessary for injection, it was soluble at pH 6.5 in 0.85 per cent sodium chloride and 5 per cent glucose. This solution can be autoclaved without caramelization and proved harmless, first to experimental animals, and then to human beings.

No reactions have been encountered with the intravenous administration of radioactive phosphorus in the form of phosphoric acid or of magnesium ammonium phosphate. Some pyrogenic reactions resulted from the intravenous use of lots of dibasic sodium phosphate of low specific activity that had not been completely freed from impurities. In recent months, since the preparation of magnesium ammonium phosphate entails more chemical manipulations than does that of phosphoric acid, the use of magnesium ammonium phosphate has been abandoned and phosphoric acid used entirely.

The amounts of radioactive phosphorus administered ranged from 130 to 3,850 μc. in the case of $Na_1HP'O_4$, from 1,100 to 3,900 μc. in the case of $MgNH_4P'O_4$, and from 1,000 to 4,000 μc. in the case of $H_3P'O_4$. All measurements represent microcurie equivalents and were made with a modified Geiger counter checked against the Lauritsen type electroscope as modified by Hudson and Cowing (1).

The therapeutic effect of these three compounds in the treatment of leukemia has been indistinguishable. The concentration of equivalent doses of the different compounds in separated and ashed leukemic cells has been similar within the limits of experimental

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error. The excretion rates have been essentially the same in all three, and conversely, the amount of retention in the body.

In order to demonstrate this point clearly, a set of three "scatter" graphs has been plotted, one for each of the three compounds. Fig. 1 [1] represents the percentage of retention of P^{32} administered as $Na_2HP'O_4$. Fig. 2 represents that for $MgNH_4P'O_4$. Fig. 3 represents that for $H_3P'O_4$. Each point on the graph represents a single determination of the percentage of the original dose of radioactive phosphorus administered retained in the body at that given time. The calculations have been carried out to allow for both excretion from the body and decay of radioactivity. It will be noted that the three graphs are essentially similar and might well be superimposed.

The case showing the relatively low retention in Fig. 1 has already been commented upon (5). This was a case of benzol poisoning simulating leukemia. Whether the poorer retention was chance or characteristic of the disease has not been determined, as further studies were not carried out.

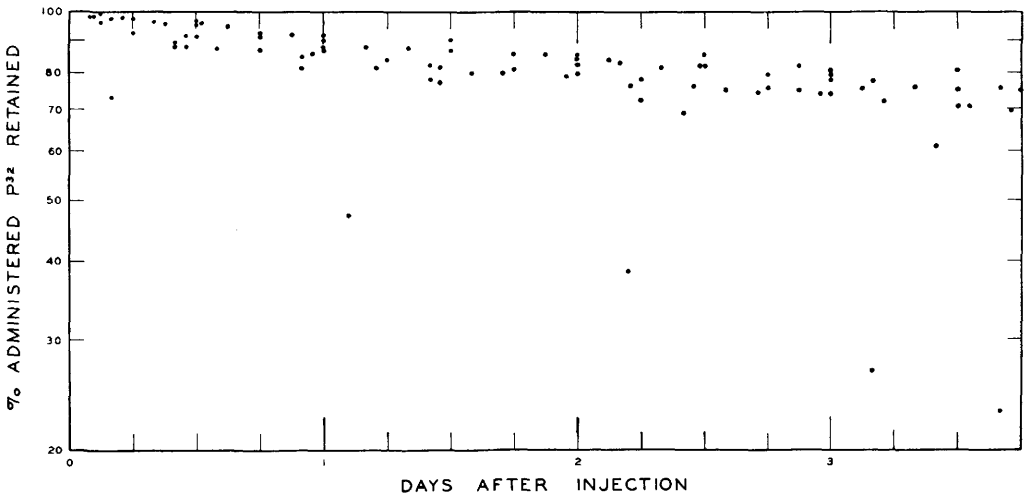

FIG. 1.—Percentage of retention of radioactive phosphorus when administered intravenously as $Na_2HP'O_4$.

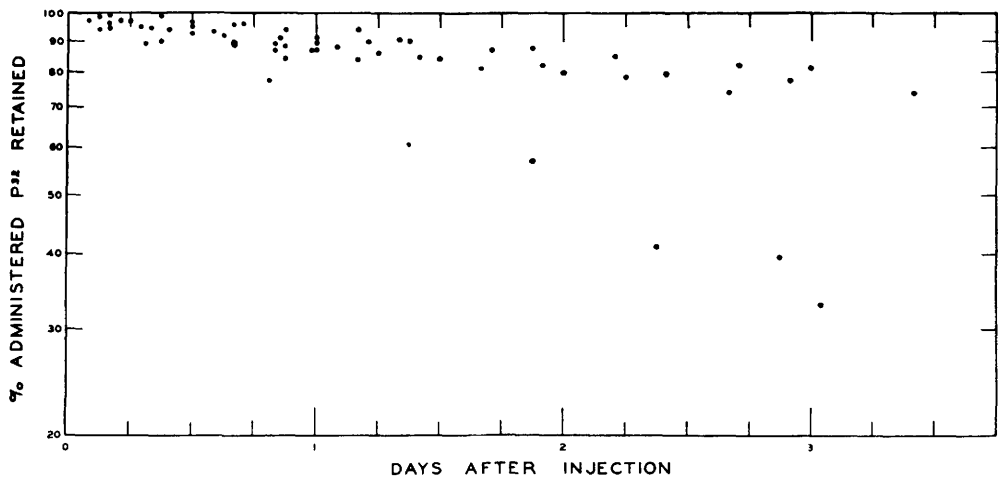

FIG. 2.—Percentage of retention of radioactive phosphorus when administered intravenously as $MgNH_4P'O_4$.

In Fig. 2 a single case shows rapid excretion. This was a dose of 3.9 mc. equivalents administered to a patient with subacute lymphatic leukemia. The patient was having severe intestinal hemorrhages. The increased loss was due to large amounts of radioactive phosphorus present in the stools, which also contained large amounts of blood. It is probable, therefore, that this does not represent loss due to true excretion, but

[1] Fig. 1 has been used in "The Retention of Radioactive Phosphorus in Leukemic Patients" (5).

loss due to hemorrhage into the gastrointestinal tract. On the administration of a number of other doses subsequently, when the clinical condition of the patient had improved and the intestinal hemorrhage was not present, the percentage of retention was indistinguishable from that of other cases.

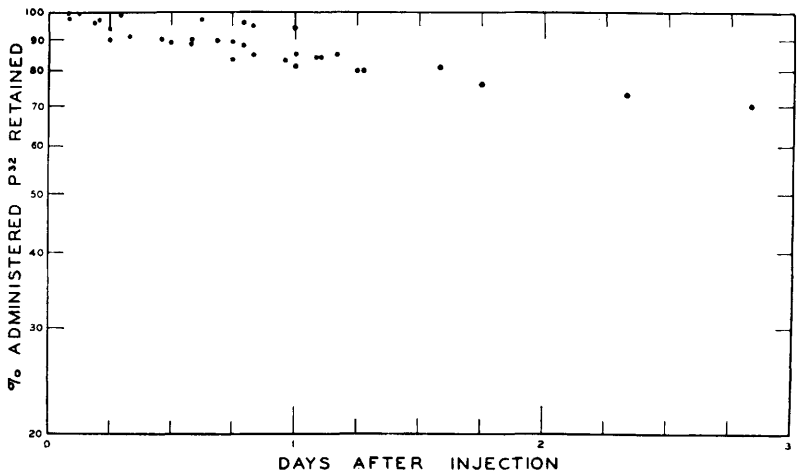

FIG. 3.—Percentage of retention of radioactive phosphorus when administered intravenously as $H_3P'O_4$.

SUMMARY

1. Small amounts of radioactive magnesium ammonium phosphate and also phosphoric acid of high specific activity may be administered safely intravenously, dissolved in 250 to 350 cc. of 0.85 per cent NaCl and 5 per cent glucose.

2. The retention of the radioactive phosphorus was practically identical regardless of which of the three compounds was used.

3. In the case of dibasic sodium phosphate and in the case of phosphoric acid one instance each of poor retention was encountered, in the former unexplained, and in the latter due to extensive intestinal hemorrhage.

4. If it is necessary to conserve time in chemical manipulations in the preparation of radioactive phosphorus for therapeutic use, H_3PO_4 or $MgNH_4PO_4$ may be substituted for $Na_2HP'O_4$ as the vehicle of administration.

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