The Retention of Radioactive Phosphorus in Leukemic Patients*

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The use of radioactive phosphorus in the therapy of leukemia (1) is based on several considerations. The radioactive phosphorus gives off beta radiations, to which the leukemic cells are more sensitive than are many of the normal body cells. Its concentration in the tissues is relatively greater in rapidly proliferating cell groups such as leukemic infiltrations than in most normal tissues. The tissues that normally take up relatively larger amounts of P³² are those in which leukemic deposits tend to occur, such as liver, kidney, and bone. The half life of radio active phosphorus (14.3 days) is of convenient length for carrying out the necessary chemical manipulations in the preparation of the material and for delivering an adequate dosage of radiation without subjecting the tissues to radiation for months and years after its administration, as in the case of radium salts. P³² after giving off beta radiation changes to sulfur. The amount of phosphorus administered, usually as Na₂HPO₄, has no demonstrable effect aside from its radioactivity.

The present study, based on 69 cases, is planned to make available data on the effective radiation obtained by various doses of radioactive phosphorus.

The materials used in these observations have been prepared in two ways—by bombardment of red phosphorus by the cyclotron, or by the bombardment of an iron phosphide probe, placed in the beam of the cyclotron.

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The materials used in these observations have been prepared in two ways—by bombardment of red phosphorus by the cyclotron, or by the bombardment of an iron phosphide probe, placed in the beam of the cyclotron. This latter method is preferable in that it gives a higher specific activity of the phosphorus. In several of the lots used, the activity has been of the order of 1 mc. per mgm. Even in the samples of relatively high specific activity, it must be remembered that only a small portion of the phosphorus present is radioactive.

Two facts must be kept in mind in attempting to evaluate radiation by P³². First, although the measurements are expressed in millicuries, the radiations are actually beta rather than gamma, and hence not comparable directly with the gamma radiation of radium or radon; second, the range of the beta particles may vary materially, a very few penetrating tissue as far as 13 mm. from the atoms which are their source, while most have only a very short range. A further difference between the radiation administered by the conventional x-ray therapy apparatus and that administered by means of artificially radioactive phosphorus is that in the case of radiation from the x-ray tube there is appreciable variation in the amount of effective radiation with the depth of a given tissue beneath the skin; whereas with ingested or injected temporarily radioactive materials, the distribution of radiation is homogeneous throughout the body except as influenced by the specific affinity of certain tissues for the material.

In most of the cases studied in this series each gram of body tissue would receive about 120 ergs in the first 24 hours, assuming a homogeneous distribution of the phosphorus. The "threshold" dose of P³², so far as effect on the blood cells is concerned, is said to be 0.006 to 0.009 μc. per gm. of body weight.

Two methods of administration of radioactive phosphorus have been utilized, the oral and the intravenous. I have customarily used the intravenous method and have used oral administration only to obtain comparative data. My preference for the intravenous method is based on the following considerations: first, the loss of about 20 per cent of the administered radioactive phosphorus due to precipitation and failure of absorption in the gastrointestinal tract is eliminated; second, the dosage can be determined accurately since all the material given reaches the blood stream; third, a higher level of concentration in the blood relative to the dose administered may be reached than is achieved by the oral method.

For intravenous administration a desired dose of P³² in the form of disodium phosphate is dissolved in 200 to 300 cc. of 5 per cent glucose and 0.85 per cent saline solution, or of normal saline solution alone. In

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1 I am indebted to the Harvard Cyclotron Committee, to Professor Robley D. Evans, of Massachusetts Institute of Technology, and to Professor Ernest O. Lawrence for supplies of P³².

2 Based on calculations by Low-Beer, Lawrence, and Stone (2).
should be pyrogen free and autoclaved. If radioactive

case of infants or children, it is dissolved in from 25
to 100 cc. of normal saline solution. The solution
should be pyrogen free and autoclaved. If radioactive
phosphorus obtained from the bombardment of red
phosphorus is utilized, one or more recrystallizations
as disodium phosphate are desirable in order to purify
the compound. Sometimes traces of indicator left
over from the chemical manipulations are present,
which, in my experience, have been associated with
febrile reactions on administration. There should be
no untoward reaction to intravenous administration
of properly prepared solutions.

The rate of administration may be fairly rapid, up
to 10 or 15 cc. a minute in the case of adults. No spe-
cial precautions are needed for the protection of the
personnel administering the intravenous solution, since
the bulk of radioactivity is screened out by the glass-
ware and tubing, and they are in contact with even
this weak source of radiation for only a short period
of time.

I have not deemed it necessary to maintain the pa-

tients on a low phosphorus or low calcium diet when
the intravenous mode of administration is utilized.

When P\(^{32}\) is to be administered orally, I have com-

monly given it in 200 cc. of orange juice.

In any studies of excretion, the difficulty of obtain-
ing all the urine and feces from a given patient can
be readily appreciated. Fortunately, the personnel in
this hospital has been thoroughly drilled in the accu-
rate and complete collection of excretions because of
the large number of diabetic patients that have been
treated here over many years. I believe that our
figures on excretion, even though some of them cover
a period of a month or more, are fairly accurate.

The measurements of radioactivity have been carried
out on urine by determinations of dried aliquot
samples; on blood and its constituents by drying the
entire sample obtained and then measuring its activity;
the measurements on feces have been made after ash-
ing the entire fecal mass. Most of the measurements
have been made on a modified type of Geiger counter,
the remainder on an electroscope. A number of the
samples have been read on both instruments with
satisfactory checks obtained. The determination is
accurate within 10 per cent as low as 0.001 \(\mu\)c.

Several leukemic patients had long-continued ob-

servation in the hospital in the course of treatment.
One of these was followed for 33 days and one for
19 days. The results of the determinations on these
patients are presented in the form of graphs on semi-
logarithmic paper, the total radioactivity remaining in
the body being expressed as percentages of the initial
total dose plotted against time. (Figs. 1 and 2). The
sharp rises in the graphs represent the effect of sup-
plemental doses of P\(^{32}\). The rate of fall represents both
excretion and decay of radioactive phosphorus.

It will be seen that the rate of fall in the amount of
material retained is fairly constant, and the downward
slope of the graphs essentially similar following each
injection. At the end of 3 days about 75 per cent of
the dose is still present. This is in keeping with the
results obtained by Low-Beer and Treadwell (3).

The essential similarity of the amount retained at
a given time after initial dosage is shown by Fig. 3,
case 39 (chronic myelogenous leukemia), in which
the percentage of retention of material administered
is plotted against time. Here 8 doses ranging from
2,300 \(\mu\)c. to 130 \(\mu\)c. given a single patient are shown.
The essential similarity of the slopes, in spite of wide
variations in the amounts administered and the clini-
cal condition of the patient, is clearly shown. Two
of these doses, those of October 31 and November 11,
1942, were oral. The rest were intravenous.

Thus in case 39 an average of 87 per cent of the
dose of radioactive phosphorus administered is present
at the end of 24 hours, 80 per cent at the end of 48
hours, 75 per cent at the end of 72 hours, 63 per cent
at the end of 120 hours, and 52 per cent at the end
of a week. During the time that these doses were ad-
ministered the patient's condition ranged from mori-
bund to moderate activity, and the white blood cell
count from 350,000 to 23,500. The red blood cell
count ranged from 1,290,000 per cu. mm. to 4,400,000
per cu. mm.

The fastest excretion, September 28, 1942, was from
a dose that was given at a time when the patient's
white cell count was falling rapidly, from 310,000 per
cu. mm. to 122,000 in 3 days. On the third day a blood
transfusion of 500 cc. was given. The blood trans-
fusion and rapidity of the destruction of the white
cells may account for the greater excretion of this
particular dose than the others.

The fairly constant rate of excretion is further shown
in Fig. 4, case 34 (chronic myelogenous leukemia).
In Fig. 5 are presented 91 determinations of radio-
activity of the blood made on 7 leukemic patients.
This shows the fairly uniform rate of loss of radioac-
tive material from the body when it is administered
intravenously. The low points in Fig. 5, representing
rapid excretion, were obtained from a patient with
benzol poisoning and a leukemoid blood picture. The
diagnosis of subacute leukemia had been made at one
hospital and a diagnosis of myeloid metaplasia at
another. In order that the discrepancy shown by this
patient from the clearly leukemic group may be pre-

tended more plainly, 3 successive injections are pre-

icted in Fig. 6, illustrating not only the definite varia-
tion from the bulk of the leukemic patients, but also
the variation from one dose to another.
Fig. 4

Fig. 5

Fig. 6
The amount of fecal excretion is practically negligible when $^{32}P$ is injected intravenously. This is brought out by random selection of sample determinations, given in Table I. If hemorrhage occurs into the gastrointestinal tract, the amount of $^{32}P$ in the feces will be increased.

### Table I: Fecal Excretion Following Intravenous Administration

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Dose, $\mu$g</th>
<th>Feces collected, days</th>
<th>Total $^{32}P$ in feces, $\mu$g</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>1,214</td>
<td>5</td>
<td>4.45</td>
</tr>
<tr>
<td>24</td>
<td>666</td>
<td>6</td>
<td>4.90</td>
</tr>
<tr>
<td>27</td>
<td>1,550</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>33</td>
<td>3,080</td>
<td>3</td>
<td>12.1</td>
</tr>
<tr>
<td>34</td>
<td>1,710</td>
<td>4</td>
<td>4.5</td>
</tr>
<tr>
<td>45</td>
<td>1,240</td>
<td>2</td>
<td>3.9</td>
</tr>
<tr>
<td>69</td>
<td>2,550</td>
<td>6</td>
<td>6.6</td>
</tr>
</tbody>
</table>

Although a slight amount of $^{32}P$ is excreted in the saliva, this is usually swallowed and the major part reabsorbed. In case 1 the saliva contained 0.042 $\mu$g per cc, 1½ hours after injection of a dose of 2,606 $\mu$g, when the blood level was 0.04 $\mu$g per cc.

### SUMMARY AND CONCLUSION

1. The retention of radioactive phosphorus when administered intravenously in cases of leukemia is relatively constant, amounting on the third day to 75 per cent of the original dose and on the seventh day to 52 per cent.

2. The rate of excretion of $^{32}P$ by leukemic patients does not vary significantly with variation of doses within the therapeutic range, nor with the clinical condition of the patient.

3. A blood dyscrasia of undetermined nature gave abnormally rapid excretion rates.

4. The amount lost in the feces is negligible when radioactive phosphorus is administered intravenously.

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### REFERENCES


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