

DOCUMENT SOURCE	
Lawrence Berkeley Laboratory Archives and Records Office	
Records Series Title	Scientists' Papers - John Lawrence
Accession No.	42-90A-0168
File Code No.	19-14-16
Carton No.	(9)
Folder No.	5-3-1962
Notes	Studies with Zn ⁶⁵
Found By	Raven Holmes
Date	

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with criteria for patient selection

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J. Parker
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BERKELEY: DONNER LABORATORY AND DONNER PAVILION

August 28, 1962

DR. JOHN H. LAWRENCE

Dear Dr. Lawrence:

Some time ago Dr. Linfoot and I discussed briefly with you our interest in studying the turnover of Zn⁶⁵ in patients using the whole body counter. We have reviewed the literature, and I wish to summarize this for you briefly and to describe the plan of our experiments.

Zinc is an integral part of a number of known enzyme molecules, for instance, and in animals it is taken up first in pancreas, liver, and pituitary; subsequently large amounts are transferred to bone. Zn⁶⁵ has been used in studies of serum zinc in diabetics, but results have been inconclusive, probably because zinc is removed so rapidly from serum even in normals. I believe that with the whole body counter we might find something more significant because we measure a different compartment(s) than simply serum. Even if zinc is not involved in diabetes, patients who have been taking zinc-insulin for many years might have an excessive zinc load, and their turnover can be compared with diabetics on non-zinc insulin and with those who do not require insulin.

Dr. Tai-June Yoo, working with Dr. Gofman, has found reduced serum zinc levels in patients with Xanthoma tuberosum, while patients with Xanthoma tendinosum have normal zinc levels. He wants to find out whether there is a demonstrable zinc abnormality which might be part of the genetic aspect of this disease. He is ready to begin whole body counter studies with μc of Zn⁶⁵ as soon as possible on these patients.

In animals excessive zinc loads have been shown to produce pancreatic fibrosis, and something similar might occur in zinc-loaded diabetics. It is known that zinc is concentrated in the pancreas, and is passed into the GI tract with digestive enzymes. Thus we might also usefully study zinc turnover in patients with pancreatic insufficiency.

In chronic lymphatic and myelogenous leukemia, the zinc level in leucocytes falls to 10% of normal, returning to normal with successful therapy. Since we have such patients available, I think we should study whole body zinc turnover in a few as a pilot study. The procedure is very simple, and patients could be counted usually as part of their regular clinic visits. Since zinc ultimately is lodged in bone, we

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should also study some of our pituitary patients with bony metastases.

Zinc is also concentrated in the prostate, and has been found to be abnormally low in tumors of the prostate. Zinc is also apparently necessary for spermatogenesis. Studies on zinc turnover in conditions involving these organs are interesting possibilities for later study.

Zn⁶⁵ has a 245 day physical half-life, about 400 day biological half-life, with an effective half-life in the body of 150 days. The maximum permissible body burden for continuous exposure is 60 microcuries, and we wish to give patients 1uc or 1.7% of this, a total dose of 40mr. We will give the Zn⁶⁵ intravenously, and count a patient every day for the first week, then each week for a month, then each month for a year or longer. We will attempt to resolve the excretion curve into a series of exponentials, to see if we can detect differences in compartment sizes or turnover times. Eventually we will want to study a group of five paid volunteers for Zn⁶⁵ turnover using 0.1uc or 0.17% of maximum permissible, a total dose of 4 mr. Craig and Siegel at Montefiore Hospital in New York have used doses of 50 to 100uc of Zn⁶⁵ in cancer patients. If it seems interesting, there are positron-emitting isotopes of zinc which we can make in the cyclotron and use with Hal's camera.

In summary, we wish to study Zn⁶⁵ turnover in the following types of patient, which we have available to us:

1. Diabetics on zinc-insulin, non-zinc insulin, and no insulin.
2. Patients with Xanthoma tuberosum and Xanthoma tendinosum.
3. Chronic lymphatic and myelogenous leukemia, treated and untreated.
4. Patients with bony metastases or primary bone tumors or other conditions involving bone metabolism.

Patients who might be studied later if they can be obtained would be:

5. Pancreatic insufficiency and pancreatic fibrosis.
6. Prostate carcinoma.

Ultimately it will be necessary to study a few paid volunteers, if the results on patients appear to be interesting.

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The dose will always be less than 2% of maximum permissible
in patients, and one-tenth of this for normals.
(0.1%)

Please let me know if I can give you further information, especially how much more, if any, information is required for submission to the human use committee. I will be on vacation and at the Chicago symposium until September 10. Perhaps if you think it is o.k., Howard Parker could circulate a letter to the Human Use Committee for their consideration.

Sincerely,

Tony Sargent

Tony Sargent

cc J. A. Linfoot
J. W. Gofman
H. G. Parker

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