

DOCUMENT SOURCE Lawrence Berkeley Laboratory Archives and Records Office <i>R & D Administrative Files</i> <i>Life Sciences Division</i>	
Records Series Title	
Accession No.	<i>434-90-02116</i>
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Carton No.	<i>(2)</i>
Folder No.	<i>Donner Found. Grants</i>
Notes	<i>1954-63</i>
Found by	<i>Karen Holmes</i>
Date	

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September 1, 1954

Mrs. Rodgers Denckla
Southampton
Long Island, N. Y.

BEST COPY AVAILABLE

Dear Mrs. Denckla:

This is in further reply to your letter of August 13, 1954. I am very glad to prepare for you a brief outline of the work that has been carried out in the Donner Laboratory on leukemia. As you know, this has been one of our principal efforts since the founding of the laboratory by the Donner Foundation.

Our general approach to this problem has been an effort to learn more about this condition from the fundamental standpoint of tissue growth and secondly, to gain further experience and knowledge in diagnosis and treatment, which has been so poor in the past. For these reasons, we have been engaged in a number of separate studies on various aspects of this disease, all of which are tied in together in the overall approach to the problem.

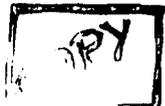
When it became known that phosphorus could be made radioactive by bombardment in the cyclotron, it then became possible to study the metabolism of phosphorus in experimental animals. Our early studies in animals showed that an appreciable concentration of radioactive phosphorus could be achieved in the bone marrow. It has long been known that x-ray could be used for the treatment of leukemia. It was our hope that we could deliver a sufficient amount of radiation to the leukemic tissues, the radioactive phosphorus serving as a vehicle for the carrying of the beta rays to the involved tissues. Following this, we started studying the metabolism of P-32 (radioactive phosphorus) in patients. We studied the excretion and blood and tissue P-32 levels. These confirmed our animal findings and showed us that we did have a method for delivering radiation to the bone marrow. We therefore embarked on a study, which is continuing, of the treatment of leukemia.

For therapy after the diagnosis has been made, these patients have been treated with P-32 as it may be needed. We have found that this is the most satisfactory method of therapy currently available in comparison with other methods, and have increased the duration of life considerably.

Over the past 20 years we have had an opportunity to follow 400 patients with leukemia. By careful examination and follow-up of each individual patient, we have been able to increase considerably

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Mrs. Danckla

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our knowledge of the clinical manifestations of this disease. We have also had excellent cooperation and rapport with our patients so that they come back to visit us at frequent intervals in order that we may follow their course. At present, in addition to studying new patients, we are continuing to see our old patients to evaluate the effects of therapy with regard to the life expectancy. We have been able to show in lymphatic leukemia that the life expectancy is considerably increased while in myelogenous leukemia, the life expectancy has been increased, but not as much. As an example of the benefit of our ability to have a long term follow-up on our patients, we have found very striking differences between the sexes with regard to duration. Males with chronic lymphatic leukemia have a longer life span than do females, while in chronic myelogenous leukemia women have a longer life span than men. In both groups of patients, we have been able to greatly modify the course of their disease so that where formerly these patients had symptoms such as fatigue, tiredness, inability to do their work, we now find that we are able by treatment to carry these patients along for many years so that they are able to work and hold a job. Actually, if you could see most of our patients, you would not suspect that they are ill.

At the same time that we are continuing to treat these patients, we have carried out a number of special studies, some of which are:

1. The bone marrow. Leukemia is essentially a disease of the bone marrow. We have been able to gain some idea as to the effectiveness of treatment and some idea as to the correlation between the findings in the bone marrow and the results of treatment. We have studied the bone marrow by two techniques; the older technique consists of aspirating bone marrow and studying the individual cells. In the last three years, we have, in addition, combined this with studying small fragments of the bone marrow tissue as we obtain them with a needle. At present, it is too early for us to give a clear cut answer as to our ability to correlate changes in the marrow with the clinical course of the disease. We have, however, observed in the patients with myelogenous leukemia who have responded satisfactorily to therapy, changes in the bone marrow smears which indicate a return toward the normal state. In lymphatic leukemia, the situation is somewhat more complicated and there is no uniformity of pattern of response.

2. Because many of these patients are thought to be anemic, we carried out a study of the blood volume using radioactive phosphorus labeled red cells. It has been found in this laboratory and in others that if one mixes red cells with P-32 some of the radioactive phosphorus will go into the red cells. These labeled cells can be injected into the patient to determine the blood volume. These studies have been of great help to us in determining the degree of anemia when it is present. We have shown that in myelogenous leukemia, patients who have a large spleen often have a very marked increase in their

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plasma volume and although their red count may be low, they have a normal total number of red cells. In lymphatic leukemia the same may also be observed. When these patients are treated, we have found that the blood volume often returns to a more normal state.

3. Some of these patients are anemic. In the past this has been thought to be due to a crowding out by the leukemia tissue of the red cell forming elements of the bone marrow. With the development in Donner Laboratory of the radioactive iron method for determining the rate of production of red cells, we have been able to show that in 90% or more of the patients that the red cell production is normal; thus this older theory was conclusively shown to be incorrect.

4. At the same time by following the distribution of radioactive iron by placing sensitive counters over the liver, spleen and bone marrow, we have been able to show that in myelogenous leukemia the patients produce red cells not only in the bone marrow, but also in the spleen. We have also been able to show by this technique that some patients prematurely destroy their red cells in the spleen, thus contributing to the anemia sometimes seen in this disease. Such studies have considerably advanced our understanding of the basic nature of leukemia.

5. We have also made direct studies of the life span of the red blood cell using several techniques, all of which show that the red cell life span in some patients with leukemia may be considerably shortened. Therefore, we have worked out the mechanisms for development of anemia in this disease and are in a position to make further investigations as to the effects of therapy on the mechanisms producing this anemia, and on the cause of this shortened red cell life, which is really the serious problem in leukemia.

6. The pituitary gland, the small gland at the base of the brain, has been shown over the past years to be one of the most important endocrine glands in the body, has recently come under investigation in this laboratory with respect to the production of a hormone by this gland which influences the rate of red cell formation. Studies started five years ago have shown that in the experimental animal removal of the pituitary, results in an anemia which can be corrected by an extract of the pituitary. We are now engaged in studies of the purification of this extract and are attempting to obtain a pure substance which has the effect of increasing the rate of red cell formation. It is our hope that this hormone will prove to be of value in treatment of patients with anemia, not only due to leukemia, but other disease states.

7. The pituitary also produces various hormones which influence growth in experimental animals, and which can induce tumors. We are, therefore, starting to carry out investigations in dogs with leukemia on the effect of irradiation of the pituitary. These dogs are brought to the animal clinic of the University by their owners, after they have become ill. The 184 inch cyclotron produces a beam of high

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energy particles which is ideally suited for the radiation of a very small volume of tissue so that in an animal as small as a rat, the pituitary gland which may be only a 16th of an inch or so in size can be selectively removed by external radiation without harming the animal. We are extending these studies to the removal of the pituitary in this case in the dog. I have previously sent you a copy of a letter written to Mr. Joseph Donner regarding the application of this technique to patients.

I hope that I have been able to present to you in this brief outline form the work that we have done and are currently carrying on and what we plan to do in the future. If you have any questions regarding this, please feel free to call on me as I shall be very happy to go over in detail or to write up for you in detail any particular aspect of this work in which you might be interested.

I hope you will visit us sometime soon.

Very sincerely,

John H. Lawrence

John H. Lawrence, M. D.

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