ever, since it is already known that pregnancy can occur in very rare instances in spite of the coil, our findings may be an example of such a rare occurrence.

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19 November 1964

Lymphocyte Lifetime in Women

Abstract. *The lifetime of the lymphocyte in hematologically normal women is 530 ± 64 days. This estimate, made from studies on 25 women who had received radiation therapy for cervical carcinoma, is based on the rate of disappearance of lymphocytes with acentric chromosome fragments.*

Ottesen (*1*) studied the incorporation of P^{32} into the DNA of the lymphocytes of two hematologically normal women. He found that the lymphocytes could be separated into two groups: a minor one with a survival time of 3 to 4 days, and a major one with a survival time of 100 to 200 days. Hamilton (*2*) studied the incorporation of adenine-8-C^{14} into the DNA of patients with chronic lymphocytic leukemia and also found two rates of disappearance of radioactive DNA; the slower rate indicated a half-life of about 300 days. However, Hamilton (*2, 3*) has pointed out that the length of survival of the radioactive DNA may be due to reutilization of the DNA rather than to a long-lived lymphocyte. We have measured the lifetime of the lymphocyte in hematologically normal women by another method and obtained a value for the average life of the lymphocyte of 530 ± 64 days. This value indicates a longer lifetime for the normal lymphocyte than had been supposed.

Our method is based on the fact that radiation produces acentric chromosome fragments in the lymphocytes. Such chromosome fragments are almost never found except in the cells of people who have been exposed to radiation. Moreover, since acentric fragments lack the centromeres that control chromosome movement on the mitotic spindle, they will not be distributed by the spindle to the daughter cells; indeed they will be lost to the nuclei and degenerate in the cytoplasm (*4*) at the first cell division after radiation. Thus an acentric chromosome fragment in the lymphocyte is assumed to mean that the lymphocyte has not divided between the time the patient was exposed to radiation and the time of observation; and the rate of decrease of lymphocytes with acentric fragments provides a direct measure of the lifetime of the lymphocyte.

The 25 patients in this study had all been treated for cervical carcinoma by delivery of 6 to 8000 rads of radiation to the paracervical triangle over a period of about 1 month. From samples of peripheral blood the leukocytes were cultured for 72 hours, and chromosome preparations were made by standard techniques. Linear regression analysis of the relation between lymphocytes with acentric chromosome fragments and time after radiation therapy (Fig. 1) shows that the percentage of lymphocytes, y, with acentric fragments is related to the number of days, x, after therapy by the equation

$$y = (16.5 \pm 1.2) \exp[-(0.00189 + 0.00023)]x$$

From this relation we obtain the estimate of an average life of 530 ± 64 days or about 18 ± 2 months.

Buckton *et al.* (*5*) have described the persisting of chromosome aberrations in patients who have received radiation therapy for ankylosing spondylitis. The extent of their data on cells with acentric chromosome fragments does not allow a good estimate of the lymphocyte lifetime. Their data on the rate of decrease of so-called unstable cells—cells with acentric fragments, dicentrics, or rings—is extensive, but there is a significant probability that the dicentrics and rings will survive one or more cell divisions; therefore, the average life of 29 months of the unstable cells shown by their data must be taken as an upper limit for the lifetime of the lymphocyte. The average life of 18 months, estimated from the rate of disappearance

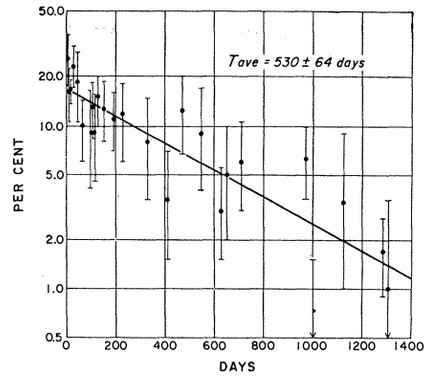

Fig. 1. Percentage of lymphocytes with acentric chromosome fragments plotted against the time after the end of radiation therapy. The vertical lines through each point are the 80 percent confidence intervals.

of lymphocytes with acentric chromosome fragments, is about 40 percent lower than the upper limit of 29 months, estimated from the rate of disappearance of unstable cells. The discrepancy between the two estimates can be accounted for by assuming a probability of about 40 percent per cell division that a dicentric or ring chromosome will survive intact. A preliminary estimate of this probability based on our own data is 33 percent.

A minor lymphocyte component with a survival time of 3 to 4 days (*1*) would not be detectable from our data, which were obtained after the end of a relatively long therapy period. To the extent that an undetected short-lived lymphocyte did influence our data, its effect has been to cause an underestimate of the average lifetime of the long-lived lymphocyte.

Whether the average life of the long-lived lymphocyte is a function of sex, age, or other conditions in man remains to be determined.

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24 December 1964