

Effect of Small Measured Doses of Radiation on Lymphocyte Morphology in Man. (23221)

R. LOWRY DOBSON AND MARY M. CHUPP (Introduced by J. H. Lawrence)

Donner Laboratory of Medical Physics and Biophysics, and Radiation Laboratory, University of California, Berkeley.

Ingram and Barnes(1) reported an increased incidence of bilobed and binucleated lymphocytes in the circulating blood of cyclotron workers. When these observations came to our attention a program was initiated at this laboratory to investigate the phenomenon on a quantitative basis. A study was carried out that same year on 5 groups of laboratory personnel comprising 34 persons(2). The results suggested an increase in incidence of binucleated lymphocytes in individuals exposed intermittently or chronically to radiation at levels below 300 mr per week. Animals given doses of x- and γ -rays from 2 to 75 r have also shown this response(3,4,5). Ingram *et al.*(6) presented additional data on the original group of cyclotron workers, and demonstrated a decrease in abnormal lymphocytes following shielding of the accelerator.

Presented here are results of a study of the binucleated lymphocyte response in normal individuals chronically exposed to low doses of ionizing radiation, predominantly x- and γ -rays.

Methods. The incidence of binucleated lymphocytes in the peripheral blood of 8 accelerator operators was determined within a few hours to a few days after exposures of 80 to 200 mr. Comparison was made with the incidence in a closely matched control group of 7 persons receiving no known radiation exposure above background levels. Intermittent and chronic exposures to x- and γ -rays were measured with electroscopes and film badges. These values were checked with independent measurements of radiation fields in work areas. The average exposure level of the accelerator operators during the year prior to sampling was 110 mr per week. During the week prior to and including the taking of blood samples the average for the group was 190 mr. The neutron fields to which these persons were exposed were low in comparison. In the one instance where neutrons could be

considered to have contributed significantly to the total exposure the individual received on the average only 13% of the maximum permissible weekly neutron dose. The other individuals in the group received considerably lower neutron exposures, of the order of 3% to 6% of the maximum permissible weekly exposure. Measurements were made by comparing track counts in the emulsion of neutron film badges to emulsions exposed to a standard Po-Be source. The maximum permissible weekly dose was taken as 4.3×10^6 Po-Be neutrons per square centimeter. Using a relative biological effectiveness of 10 this represents a dose of 300 mrem per week.

Results. The lymphocyte data presented in Fig. 1 represent the counting of more than one million white blood cells. An average of 58,000 cells per person was examined in the exposed group, an average of 77,000 cells per person in the control group. Counts were made from stained blood smears. At least 5 individual counts were taken from each person at various times of day and totaled. Only binucleated lymphocytes with 2 completely separate nuclei or with 2 non-overlapping nuclei connected by a thin hair-like filament were recorded. Cells not meeting these criteria and lymphocytes with bilobed nuclei were not considered in this study. In order to avoid possible artifactual changes, concentration methods and anticoagulants were not used.

It is apparent that the incidence of binucleated lymphocytes is low, and that more of these cells were seen in the exposed individuals than in the controls. The mean in the exposed group was 5.9 per 50,000 white blood cells with a range of 3.4 to 7.6; it was 1.4 per 50,000 in the control group with a range of 0.4 to 2.5. The difference is highly significant by statistical tests.

In an attempt to explore the pattern of this lymphocyte response to individual and cumulative exposures, several persons were studied

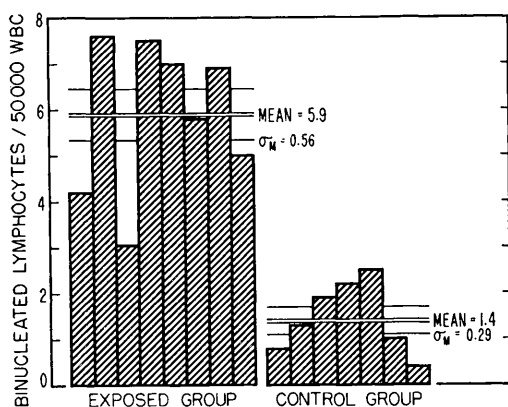


FIG. 1. Incidence of binucleated lymphocytes in peripheral blood of 7 normal unexposed individuals and of 8 normal persons exposed to levels of ionizing radiation of the order of 200 mr per week.

over periods of many months. On one of these persons 17 counts, each consisting of at least 5 hourly samples were taken during a 90-day period shortly after he began working with radiation. These data from the counting of 936,000 white blood cells are of interest because his average radiation exposure was 239 mr per week; and during this period he received 4 individual daily exposures exceeding 200 mr. While the first 2 counts showed only 1.5 and 0 binucleated lymphocytes per 50,000 white cells respectively, the incidence during the rest of the interval fluctuated about a mean of 6 per 50,000. In general larger numbers were seen several days after exposures to 200 mr or more. Daily counts were taken frequently during a 10-day period following a single dose of 264 mr on the eightieth day. Forty-eight hours after this exposure the incidence of binucleated lymphocytes was 15 per 50,000 white blood cells; 10 days after exposure it was 17 per 50,000; the average daily count between these 2 times was 3.5 per 50,000. It does not appear possible at this time to adequately relate a pattern of the binucleated lymphocyte response to individual radiation doses; however, such a relationship is suggested by these observa-

tions and is currently under study.

Discussion. Binucleated lymphocytes occur in small numbers in the peripheral blood of normal individuals. High numbers have been seen in patients with lymphatic leukemia; they may be elevated in hepatitis, and probably in other abnormal conditions. The data reported here were obtained from persons in good health. Physical findings, laboratory data and medical histories were reviewed in each case. It must nevertheless be borne in mind that this response is not specific to ionizing radiation. Murphy and Sturm(7) described seeing large numbers of these cells in the blood of animals after heat treatments. The possible relationship of these cells to the "stress lymphocytes" of Frank and Dougherty(8) is being investigated.

Summary. In the study reported here a significant increase in incidence of binucleated lymphocytes is demonstrated in persons exposed to ionizing radiation at levels of the order of 200 mr per week.

1. Ingram, M., and Barnes, S. W., *Phys. Rev.*, 1949, v75, 1765.
2. Dobson, R. L., Section in Monthly Progress Rep., Univ. of California, Radiation Lab., Rep. No. UCRL-560, 1949. Declassified 1956.
3. Bellack, S., and Storer, J. B., Army Med. Research Lab., Fort Knox, Ky., Rep. No. AMRL-162, 1954.
4. Worman, F. C. V., and Carter, R. E., Univ. of California Los Alamos Scientific Lab. Rep. No. LA-1494, 1952.
5. Ingram, M., and Barnes, S. W., *Science*, 1951, v113, 32.
6. Ingram, M., Adams, M., Coonan, L., Jespersen, J., Nielsen, G., Piatt, D., and Yettewich, G., *ibid.*, 1952, v116, 706.
7. Murphy, J. B., and Sturm, E., *J. Exp. Med.*, 1919, v29, 1.
8. Frank, J. A., and Dougherty, T. F., *Fed. Proc.*, 1953, v12, 45.

Received April 15, 1957. P.S.E.B.M., 1957, v95.