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Studies of Leukemia $L_2C$ in Guinea Pigs*, **

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With 1 Figure

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In 1954, Congdon and Lorenz (1) described several forms of acute lymphocytic leukemia which originated in an inbred strain of guinea pigs, known as strain No. 2. The disease occurred after X-irradiation, or spontaneously, in 3.6% of 112 animals after 1 year of age. The leukemia was transmissible within the inbred strain by transplantation of tumor tissue-lymph nodes, spleen, whole blood, resulting in widespread leukemic involvement of the entire hematopoietic system, with high blast cell counts in the peripheral blood. Following serial passage, the incubation period shortened to about 14 days in 2 of these leukemias, $L_2B$ and $L_2C$, and morbidity and mortality rates were 100%.

Further progress in the study of this leukemia was seriously hampered by the short supply of inbred strain No. 2 guinea pigs which are not available on the open market. Under these circumstances, little attention was paid to the nature of the etiological agent until it became known that the disease can be transmitted, in its fully virulent form, to first generation hybrids born from crossmating susceptible with resistant guinea pigs (2).

It is the purpose of this paper to report the results obtained in a systematic study of leukemia $L_2C$ over a period of 3 years. The investigation

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includes: 1) experiments on the nature of the leukemogenic agent, 2) a study of some genetic aspects of the host, and 3) attempts to trace the fate of the leukemia-transmitting agent in susceptible and in resistant animals during the incubation period of the disease.

**Materials and Methods**

Leukemic materials used were leukemic tissue cells, leukemic white blood cells, extracts prepared from leukemic tissues, and leukemic plasma or serum. The experimental animals were F_1 hybrids born from crossmating susceptible male strain No. 2 guinea pigs with resistant female Hartley guinea pigs; the animals ranged in age from 1 to 3 months. Injections of leukemic preparations were by sc, ip, or ic routes. Beginning about 1 week after injection, daily blood counts were made of each animal to follow the course of the leukemia. Guinea pigs which developed leukemia showed a progressive steep rise in the white cell count as early as the 11th day, leading after 4 to 5 days to terminal counts between 200,000 and 350,000 cells per cmm, with over 90% immature blast cells. All leukemic animals died with typical autopsy findings, i.e. massive splenomegaly, enlarged liver, hyperplastic lymph nodes and multiple lymphomata in the peritoneal cavity. In many respects, leukemia L_2C represents an ideal model for the study of an experimental malignant tumor because: a) susceptible animals may be raised in a cross-breeding colony; b) the leukemia can be diagnosed unequivocally, has a brief incubation period and a peracute clinical course, and is invariably fatal; c) spontaneous leukemia has not been observed in guinea pigs under 1 year of age, and d) there is no evidence of subclinical latent immunization.

**Nature of the Leukemogenic Agent**

1. *Transmission of leukemia with leukemic tissue extracts*

We have previously reported preliminary results which suggest that leukemia L_2C is transmissible with presumably cell-free leukemic spleen extract or with leukemic plasma (3). In order to define more clearly the conditions under which such material is capable of transmitting the disease, it became necessary to repeat these experiments on a larger scale, using a variety of different methods in preparing the leukemic tissue extracts.

Leukemic spleens were harvested from routine passage animals at the height of the disease. Leukemic brains were harvested from guinea pigs which had developed systemic leukemia following intracerebral injection of leukemic spleen extract. Leukemic cells were disrupted by any one of 4 different methods: a) grinding the tissue in a chilled mortar for 5—10 minutes or until an even pulp is obtained, b) homogenizing the tissue in a Waring blendor for 3 minutes at 15,000 r. p. m., c) breaking up the membrane of cells in suspension by osmotic shock produced by 3-times repeated cycles of quick freezing and thawing in a solid CO_2-alcohol bath, and d) exposing a cell suspension for 30 minutes to the destructive effect of ultrasonic waves generated by a Raytheon sonic oscillator (Model DF101, 250 W; 10 Kc, 1.5 amps.; 9000 cycles per second). Suffi-