

Reduction of Leukemia Incidence following Splenectomy in the Rat¹

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SUMMARY

Mononuclear cell leukemia occurs spontaneously in 24.2% of inbred Fischer and 17.9% of inbred Wistar Furth rats. Splenectomy at 1 and 2 months of age greatly reduced the incidence of leukemia in these animals.

INTRODUCTION

A unique form of mononuclear cell leukemia occurs spontaneously in 17.9% of inbred W/Fu² and 24.2% of inbred Fischer rats (3, 4). In preliminary studies, when young Fischer rats were splenectomized, no leukemias developed (2). Further studies confirmed that splenectomy in young Fischer and W/Fu rats greatly decreased the incidence of leukemia. The results of these experiments are reported in this communication.

MATERIALS AND METHODS

The rats used in these experiments were inbred Fischer (Dunning's 344 Fischer line) and inbred W/Fu rats obtained from commercial suppliers at age 2 to 4 weeks. Animals were maintained 2 in a cage and fed Purina laboratory chow and water *ad libitum*. Rats were splenectomized at 1, 2, and 2.5 months as noted below. Operative mortality was less than 1% and splenectomized animals lived a normal life-span. Following splenectomy, at the age of 2 months, 50 W/Fu rats were fed 4 mg of MCA in sesame oil by stomach tube daily, for a total of 40 mg. All rats were examined and weighed once a week. Before splenectomy, white blood cell counts and differentials were obtained from tail blood. These studies were repeated 1 week after splenectomy and 1 week after the last dose of MCA. Subsequently, leukocyte counts and examination of Wright-stained peripheral blood smears were carried out at monthly intervals. If animals became sick or if abnormalities were noted in the leukocyte count or peripheral blood smear, blood studies were done weekly or as frequently as indicated. Animals in a terminal state were sacrificed by ether anesthesia

in order to obtain adequate blood specimens and fresh tissues for histological and cytological preparations. Grossly, the size and weight of the liver and spleen and presence of tumors were especially noted. Tissues were fixed in 10% unbuffered formalin solution and stained with hematoxylin and eosin. At time of sacrifice, imprint and paint brush smears were obtained on coverslips from the bone marrow, liver, spleen, enlarged lymph nodes, and tumors, if present. Smears were air dried and stained with Wright-Giemsa.

RESULTS

Among 301 conventionally raised inbred W/Fu rats, followed throughout their life-span, there were 54 leukemias (17.9%), all of the mononuclear cell type (Chart 1). Of 136 inbred Fischer rats raised and followed in a similar manner, 33 developed mononuclear cell leukemia (24.2%) (Chart 2). Attempts at investigation of the early phase of leukemia were carried out with serial liver biopsies and splenectomies. Among the 1st 50 Fischer rats splenectomized when 2 months old, no leukemias occurred. Subsequently, a total of 150 Fischer rats were splenectomized when 1 and 2 months old; only 3 leukemias developed. The incidence of leukemia was reduced in these animals from 24.2 to 2% ($p < 0.001$) (Chart 3). In W/Fu rats, a preliminary experiment on 50 animals splenectomized between 2.5 and 3 months of age resulted in only a slight reduction in the expected incidence of leukemia (17.9 to 14%). However, when 50 W/Fu rats were splenectomized when 2 months old, only 2 leukemias were noted. In another experiment, 50 W/Fu rats were splenectomized at the age of 2 months and then fed MCA by stomach tube. Prior experiments had established that administration of MCA to young W/Fu rats greatly increased the incidence of leukemia (2). In this experiment only 1 rat developed leukemia. Splenectomy at age 2 months in W/Fu rats reduced the incidence of leukemia from 17.9 to 3% ($p < 0.001$) (Chart 4; Table 1).

DISCUSSION

The mechanism of leukemogenesis in the rat is unknown. Although viral particles have been described in leukemic rat tissues, the disease has not been successfully passaged in the rat by cell-free extracts (1, 5). Our observations suggest that the spleens of young W/Fu and Fischer inbred rats may be the

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² The abbreviations used are: W/Fu, Wistar Furth; MCA, methylcholanthrene.

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Table 1
Effect of splenectomy on the incidence of leukemia in Fischer and W/Fu rats

No. of rats	Bred	Age at splenectomy (mo.)	No. of leukemias	% leukemias
301	W/Fu		54	17.9
136	Fischer		33	24.2
100	Fischer	2	2	2
50	Fischer	1	1	2
50	W/Fu	2.5	7	14
50	W/Fu	2	2	4
50 ^a	W/Fu	2	1	2

^a Treated with 40 mg MCA postsplenectomy.

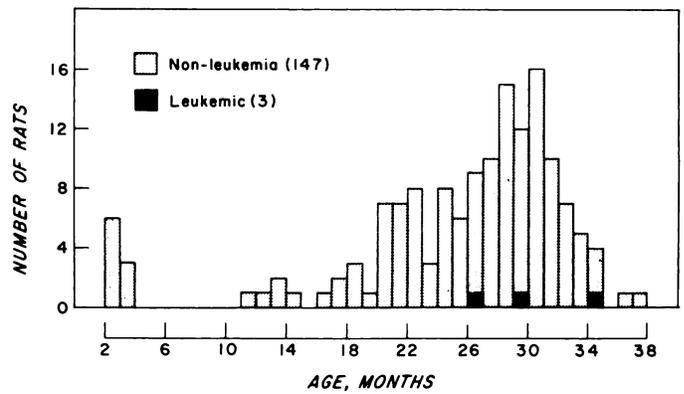


Chart 3. Histogram showing number and age distribution at death of Fischer rats splenectomized at age 1 and 2 months.

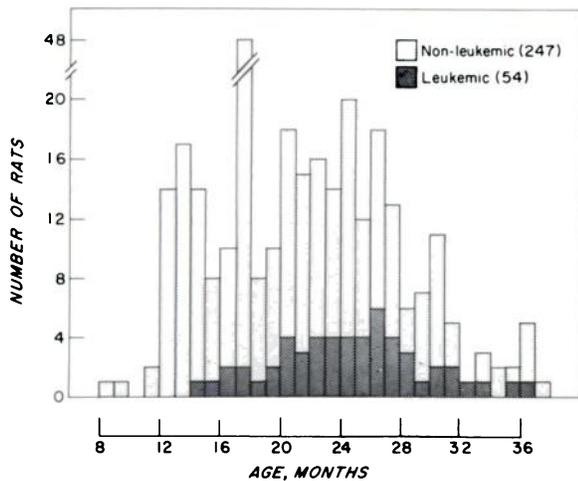


Chart 1. Histogram showing number and age distribution at death of untreated nonleukemic and leukemic W/Fu rats.

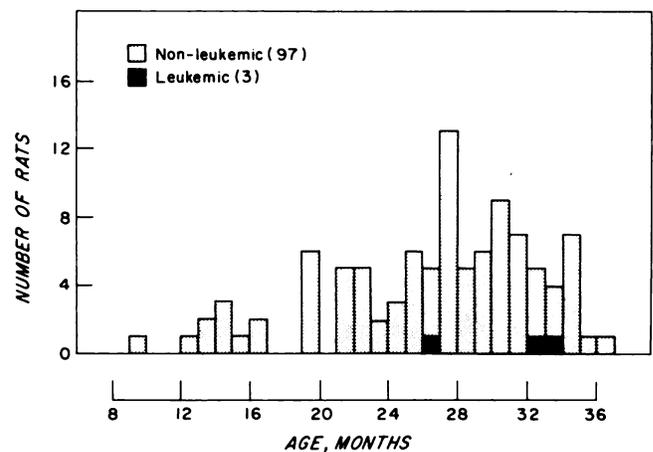


Chart 4. Histogram showing number and age distribution at death of W/Fu rats splenectomized at 2 months.

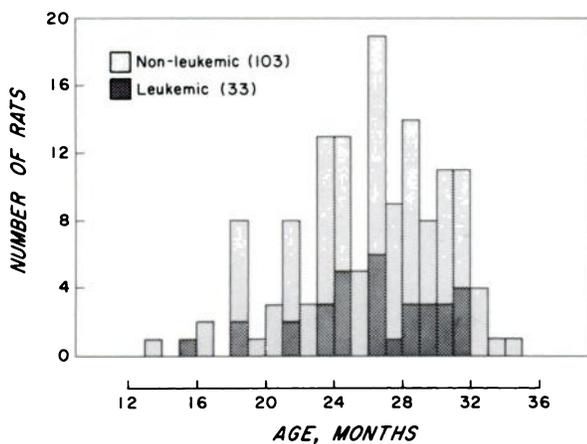


Chart 2. Histogram showing number and age distribution at death of untreated nonleukemic and leukemic Fischer rats.

source of potentially leukemic cells. Whether leukemogenesis is due to a vertically passed viral agent contained in spleen cells or whether there is in the spleen a population of genetically committed leukemic cells remains to be determined.

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