10717 P

# Proliferation of Myeloid and Lymphoid Cells Induced by Extracts of Urine from Leucemic Patients.*

F. R. MILLER, J. T. WEARN AND R. W. HEINLE.

*From the Department of Medicine, Western Reserve University, School of Medicine, and the Lakeside Hospital, Cleveland.*

Leucemias occur spontaneously in many different species of animals. Mammalian leucemia has been transmitted from one animal to other animals by living cell transplants.[1, 2, 3] Avian leucemia has been transmitted to other animals of the same species with cell-free, bacteria-free filtrates.[4, 5] Successful transmission of human leucemia to humans or other animals has never been accomplished.

The experiments reported here were performed to test whether urine from human individuals with leucemia might contain some agent capable of stimulating the reticulo-endothelial system of other animals.

Urines were collected from patients with chronic myeloid leucemia, chronic lymphoid leucemia, subacute monocytic leucemia, Hodgkin's disease, multiple myeloma, carcinoma, and aplastic anemia. Urine was also collected from normal individuals. Extracts of these urines were prepared by adsorption on Kaolin and elution with alcohol after the method of Houssay and Biasotti.[6] Their method was modified only by reducing the pH of the urine to 1.5-3.0 before adsorbing on Kaolin and with the adjustment of the pH of the final aqueous solution to neutral. This solution, after filtration through Berkefeld V or Seitz filters, was given to rats, mice, guinea pigs, and monkeys, but this report deals only with the results in guinea pigs.

Thirty-four guinea pigs received the extract from the urines of patients with chronic myeloid leucemia in doses of from 2-4 cc twice daily. The majority of the animals were ill or died within 6 weeks, although some showed effects of the injections as early as 2 weeks, and others not before 4 months. Usually at about 5 to 6

* This research has been aided, recently, by a grant from the Commonwealth Fund.

1 Gie, Tio Tjwan, *Amsterdam Acad. Proefschr.*, 1927.

2 Richter, M. N., and McDowell, E. C., *J. Exp. Med.*, 1930, **51**, 659.

3 Furth, J., Seibold, H. R., and Rathbone, R. R., *Am. J. Cancer*, 1933, **19**, 521.

4 Ellerman, V., and Bang, O., *Centr. f. Bakt.*, 1908, **46**, 4.

5 Furth, J., *J. Exp. Med.*, 1931, **53**, 243.

6 Houssay, B. A., and Biasotti, A., *Compt. rend. Soc. de biol.*, 1933, **133**, 469.

weeks the animals lost weight, had subcutaneous edema, and marked anemia. The total white blood counts generally were not elevated, but frequently during the latter part of the injection period myelocytes, myeloblasts, and nucleated red cells, as well as unidentified immature cells, appeared in the blood stream. Hyperplasia of the myeloid white cells was invariably present in the bone marrows. Sections of the spleens showed myeloid metaplasia, a destruction of the splenic architecture, and reduction in size and number of the normal splenic follicles. Sections of the livers showed myelopoiesis in the parenchyma and frequently extravascular and periportal infiltration with myeloid cells. The adrenal, lungs, lymph nodes, bladder, body wall, and occasionally the heart muscle showed the same reaction in lesser degree. Only one of the 34 animals showed no reticulo-endothelial change.

The extracts of the urines from all of the patients with other conditions, as well as those from the normal individuals, exhibited no myeloid change in any organ. In this group there were 17 animals which received extracts from normal urine, 4 which received extracts from the urine of patients with chronic lymphoid leucemia, 2 which received that from an individual with multiple myeloma, and one each from the urines of individuals with aplastic anemia, subacute monocytic leucemia, Hodgkin's disease, and carcinoma. The animals which received extracts of urine from patients with chronic lymphoid leucemia and those from multiple myeloma did show hyperplasia of the lymphoid elements. The animal which received the extract from the urine of an individual with subacute monocytic leucemia and that which received the extract from the urine of a patient with aplastic anemia showed hyperplasia which we do not classify. Two blank controls were negative.

*Summary.* Myeloid metaplasia in liver, spleen, adrenal, and other organs, as well as myeloid white cell hyperplasia of the bone marrow, was produced in 33 guinea pigs by injections with extracts of urines obtained from patients with chronic myeloid leucemia. One animal, similarly treated, showed no change. Twenty-eight guinea pigs, injected with extracts of the urine from normal individuals and individuals with diseases other than myeloid leucemia, showed no myeloid change. The animals which received the extracts of urine from patients with chronic lymphoid leucemia and multiple myeloma showed lymphoid hyperplasia. Two animals showed hyperplasia which has not been classified.