

Vit. B₁₂ from the second to fourth weeks of age on a 70% sesame meal diet deficient in Vit. B₁₂ and lysine resulted in a failure of morphological differentiation of testicular tissue accompanied by a decrease in comb growth. Supplementation with Vit. B₁₂ and lysine produced markedly greater testicular growth and differentiation over that in the normal controls.

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Presence of Myelokentric and Lymphokentric Acid in Sera of Patients with Lymphomatoid Diseases. (18288)

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The urine of patients with leukemia and other lymphomatoid diseases has been shown to contain substances(1) that we have named myelokentric and lymphokentric acid(2). These substances seem to play a part in the proliferation and possibly the maturation of myeloid and lymphoid cells. These substances have been found also in the organs(3) of patients with these diseases and in normal beef liver(4).

Heinle and his co-workers(5) have shown that relatively small amounts of material extracted by methods other than ours from similar urinary sources showed considerable potency for proliferation of myeloid cells. From this work we have considered the possibility that small amounts* of plasma or serum from patients with these diseases might contain sufficient conjugated material to produce reactions in the organs of animals. There-

fore, the sera from three types of leukemia, Hodgkin's disease and normal individuals have been given to guinea pigs, and at various intervals after injection the animals were sacrificed and the organs studied.

Material and methods. Under sterile precautions 20 to 40 ml of blood was removed from each subject, placed in a sterile tube, allowed to clot, and later centrifuged for ½ hour at 3000 r.p.m. For injection, 5 ml of the serum was drawn off and introduced into the peritoneal cavity of a guinea pig. Usually two animals were used, one of them being sacrificed after 24 hours, the other after 48 hours; in 2 experiments the interval was 8 hours. Sections were made of liver, spleen, lymph nodes, adrenal, kidney and bone marrow.

Many of the sera from normal individuals were collected at the time of donations of blood for transfusions. To obviate any discrepancy due to the alarm mechanism which might occur incidental to the removal of blood, samples in 3 instances were taken at the start of the donation as well as at the end. Samples of serum were obtained from 9 patients with chronic myeloid leukemia, 6 patients with chronic lymphoid leukemia, 6 patients with monocytic leukemia, 4 patients with Hodgkin's disease and 12 normal individuals. Table I shows the distribution of

1. Miller, F. R. and Turner, D. L., *Am. J. Med. Sc.*, 1943, v206, 146.

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3. Eri, L. A., Turner, D. L., and Miller, F. R., *Blood*, 1946, v1, 379.

4. Turner, D. L. and Miller, F. R., *Proc. Soc. Exp. Biol. and Med.*, 1943, v54, 177.

5. Hirschmann, H., Heinle, R. W., and Wearn, J. T., *Proc. Soc. Exp. Biol. and Med.*, 1945, v58, 5.

* Urine dose = 500 ml to 7.1. Versus serum dose = 5 ml.

TABLE I.

	No. of animals		
	8 hr	24 hr	48 hr
Chronic myeloid	2	13	10
" lymphoid	2	7	6
Monocytic leukemia		6	6
Hodgkin's disease		3	4
Normal individuals		18	17
Total	4	47	43

the animals receiving these sera.

Results. In this report only the changes that were found in the lymph nodes are described, although all the organs that were sectioned were surveyed. The survey was made to determine whether any consistent picture of myeloid, lymphoid or mixed reaction could be found, *i.e.*, reactions that would be similar to those described following the administration of urinary extract(1).

In the organ survey it was found that minimal specific reactions occurred in the organs, other than the lymph nodes, of animals that received serum from patients with each of the 4 diseases.[†] It was also found, however, that in a certain number of the animals that received serum from normal individuals any one of the 3 reactions was elicited with, however, a lack of response in the lymph nodes. The lymph nodes, and these were usually mesenteric or caecal nodes, although some tracheal nodes were examined, seemed to fall into 4 groups depending on which serum was given. A description of these nodes follows.

Lymph nodes. The lymph nodes from the animals that were sacrificed at 8 and 24 hours after receiving the serum from patients with chronic myeloid leukemia revealed similar findings. There was lymphocytic destruction, depletion of the number of lymphocytes, edema of the intercellular spaces, pleomorphism of the cellular structure, a slight infiltration of polymorphonuclear leukocytes, a loss of follicles, and an apparent increase in the underlying connective tissue. A few

scattered eosinophiles were found in the nodes of all animals (Fig. 1, 2).

The nodes from the 10 animals that were sacrificed at 48 hours after injection exhibited a beginning return of normal lymphoid cells, less destruction of lymphocytes, less pleomorphism and less edema. There was more fibrosis than in the previous group. Although a few scattered eosinophiles could be found in nodes from each animal, a definite eosinophilia occurred in the nodes from 2 of them.

The animals that received the serum from patients with chronic lymphoid leukemia were divided into 3 groups: those that were sacrificed at 8 hours, at 24 hours, and 48 hours. The nodes from those sacrificed at 8 hours showed a slight increase in lymphopoiesis and little increase in eosinophiles. The nodes from the 7 animals sacrificed at 24 hours exhibited an increase in size of the lymphocytic collar around the follicles, and an increased number of follicles. The cells tended toward a uniform size and there was a definite spotty increase in the number of eosinophiles. The nodes were frequently compact and rather densely populated with cells in 4 to 6 animals, while in 2 there was some intercellular edema, but in none was there pleomorphism nor a polymorphonuclear infiltration (Fig. 3, 4).

The nodes from the 6 animals sacrificed at 48 hours still exhibited an increase in lymphopoiesis. Intercellular edema occurred in those from 4, an eosinophilia in those from 3, and slight fibrosis in those of 3.

An eosinophilia occurred in the lymph nodes of 11 of the total group of 15 animals.

Nineteen animals were given serum from patients with Hodgkin's disease or monocytic leukemia. Nine of these were sacrificed 24 hours after injection and the other 9 were sacrificed 48 hours after injection. In the nodes of all these animals there was some increase in lymphopoiesis and some pleomorphism and a few polymorphonuclear leukocytes. An increase in elongated fibroblasts was also frequently apparent (Fig. 5, 6). In the nodes from 13 of the animals an increase in eosinophiles was evident, the 6 in which

[†] Sera from patients with monocytic leukemia and Hodgkin's disease gave the same or the mixed reaction.

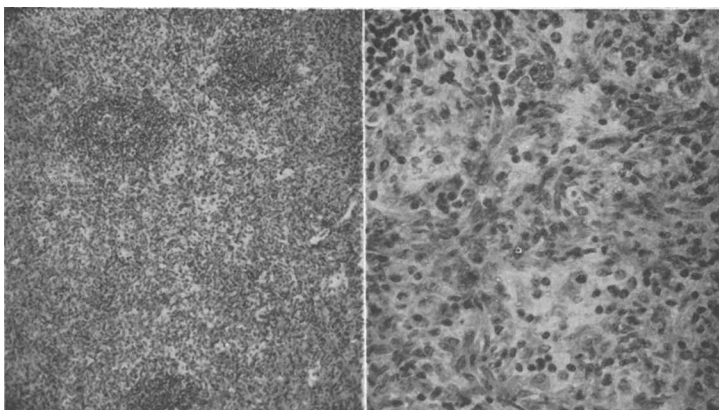


Fig. 1 and 2. $\times 50$ and $\times 200$. Lymph node from guinea pig 24 hr after inj. with 5 cc of serum from a patient with chronic myeloid leukemia.

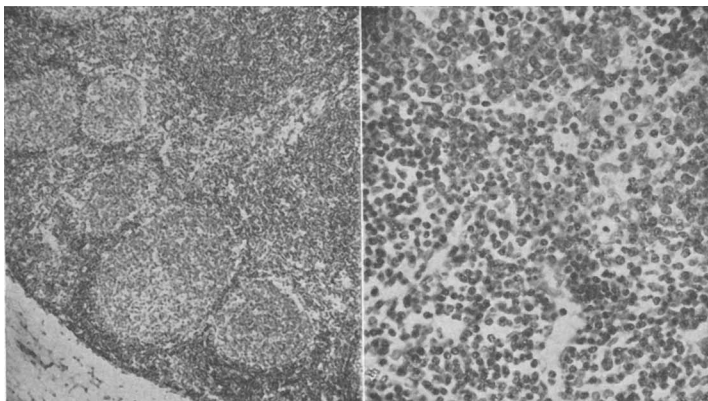


Fig. 3 and 4. $\times 50$ and $\times 200$. Lymph node from guinea pig 24 hr after inj. with 5 cc of serum from a patient with chronic lymphoid leukemia.

this did not occur were animals sacrificed at 48 hours.

Thirty-five animals were given serum from 12 normal individuals. Eighteen of these were sacrificed at 24 hours, and 17 at 48 hours after injection. The nodes from 29 of these animals did not show much change from those of normal animals. In the nodes from 5 animals there was a moderate eosinophilia and in 2 there was some intercellular edema, slight pleomorphism and some increase in lymphopoiesis. All nodes from all animals showed a few scattered eosinophils.

Summary and conclusions. The lymph nodes from animals that received serum from patients with chronic myeloid leukemia have a tendency to the same loss of lymphoid struc-

ture that is seen after the use of cortisone or ACTH; however, an increase in fibrosis and underlying connective tissue is also apparent. In these nodes, too, there is some slight increase in polymorphonuclear neutrophils. The nodes from the 2 groups that received sera from patients with chronic lymphoid leukemia, Hodgkin's disease and monocytic leukemia all showed a tendency to increased lymphoid production, although the third group (Hodgkin's and monocytic leukemia) also showed some increase in fibrosis. In both these groups a definite increase in eosinophiles occurred. Probably the lack of increase in underlying connective tissue in the "lymphoid group" segregates it from the "myeloid and the Hodgkin's monocytic

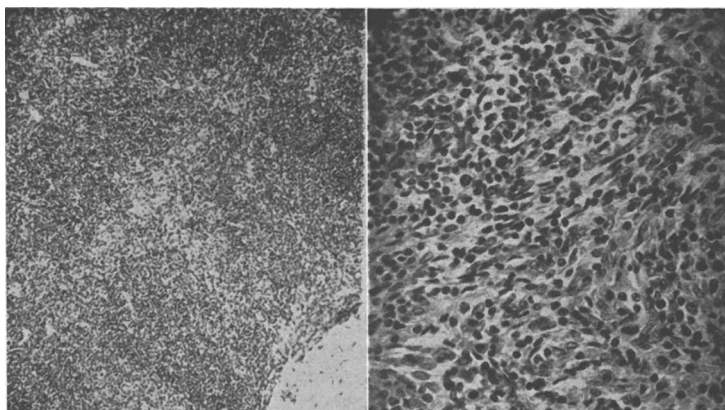


FIG. 5 and 6. $\times 50$ and $\times 200$. Lymph node from guinea pig 24 hr after inj. with 5 cc of serum from a patient with monocytic leukemia.

groups." The nodes from the animals that received sera from normal individuals showed on the whole nothing unusual.

The sera of patients with chronic myeloid leukemia bring about changes similar to those ascribed to cortisone itself or as initiated in action by ACTH in so far as the lymph node change is concerned. Myelokentric acid brings about similar lymph node changes and, as does cortisone, it also brings about increases in erythropoiesis, myelo-leukopoiesis and platelet formation. We do not, however, believe that it is cortisone.

The increased lymphopoiesis in the lymph nodes of animals that received serum from patients with chronic lymphoid leukemia is similar to that which we have described in animals that have received lymphokentric

acid in urinary extracts.

It would seem then that at least 2 and possibly 3 pathologic pictures may be made out in the nodes of these animals. This would seem to indicate that there are substances in the blood of these patients that are probably conjugates of myelokentric and lymphokentric acid. The presence of these may be detected in the sera of patients with lymphomatoid disease by bioassay. It also strengthens our contention that these are humoral hormones.

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Variations in Serum Cholesterol of Normal Rabbits after Injection of Hypercholesterolemic Rabbit Plasma. (18289)

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Investigators have long been interested in producing atherosclerosis by intravenous injection of cholesterol suspensions. Dewey(1), Fitz and Bruger(2), Bevans(3) and Pollak (4) have reported their experience with colloidal solutions of free cholesterol. The

present experiments were carried out to de-

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