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Action of Colchicine on a Malignant Lymphoid Neoplasm in Mice of an Inbred Strain.

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In the normal animal lymphoid tissues have been found to be more susceptible than other tissues to the action of colchicine.[1, 2] Waves of mitoses and pyknoses are found in the thymus, spleen, lymph nodes and Peyer's patches following its administration in proper doses (Dustin's "caryoclasic shock"). The action of colchicine and certain other nuclear poisons is similar to that of X and gamma radiations, which led Dustin to refer to their effect as "radiomimetic". It thus seemed quite logical to test the action of this drug on a lymphoid tumor since (1) normal lymphoid tissue is so extremely sensitive to caryoclasic phenomena and (2) since other investigators were able to obtain regression of other types of tumors using this alkaloid.[3-7]

Mice of the C3H strain were used in this investigation. After a line of leukemia had been carried for 3 transplant generations experiments with colchicine were begun.§ When a piece of leukemic lymphoid tissue was implanted in the right axilla a large local growth formed previous to the appearance of systemic leukemia. The systemic disease did not appear until after 23 days' growth of the transplanted tumor. By 14 days the growth was the size of a kidney

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1 Lits, F. J., *C. R. Soc. Biol.*, 1934, **115**, 1421.

2 Lits, F. J., *Arch. Internat. de Méd. Exp.*, 1936, **11**, 810.

3 Dominici, A., in *Thérapeutique Médicale*, Peau, Syphilis, Cancer, 1932, Paris, Ed. Masson.

4 Amoroso, C., *Nature*, 1935, **135**, 266.

5 Peyron, A., Lafay, B., and Kobozieff, N., *Bull. Assn. Fçaise pour l'Etude du Cancer*, 1936, **25**, 874

6 Peyron, A., Poumeau-Delille, G., and Lafay, B., *Ibid.*, 1937, **26**, 625.

7 Havas, L., *Ibid.*, 1937, **26**, 634.

§ Dr. W. U. Gardner[8] very kindly provided the authors with this material. The spontaneous leukemia arose in an animal which had received 3.9 mg of equilin benzoate in 303 days.

8 Gardner, W. U., *Occasional Publications of the A.A.A.S.*, No. 4, 1937.

bean. If, at this time, 1/40 mg of colchicine in distilled water was administered subcutaneously every third day at a site far removed from the tumor the local growth practically disappeared. Average survival time of controls after transplantation was 31.5 days as compared with 50.5 days survival in treated animals (see Table I—14 test animals and 13 controls).** Life was significantly prolonged in 7 of the 14 treated mice (6 out of 8 where the drug was administered in 0.1 cc rather than 0.5 cc distilled water—see table). In no case was there complete regression of the tumor without recurrence. One treated mouse, however, survived 101 days after transplantation in contrast to the longest survival time of 42 days in the present control group (of 33 mice which have died following implantation of a few milligrams of this tumor, the longest survival time was 43 days).

TABLE I.
Data on Survival Time.
Survival time in days after transplantation in control and colchicine-treated animals.

Controls	Colchicine	Transfer generation	Age of tumor when transplanted
1/40 mg colchicine administered in .5 cc distilled water.			
40	40	T_4*	23
42	101 (k)		
24	21	T_5	22
32	28		
	34		
	34		
1/40 mg colchicine administered in .1 cc distilled water.			
25	57	T_6	22
28	66 (k)		
33	68 (k)		
36			
26	44	T_7	19
30	45		
30	56		
31	56		
32	57		

(k)—killed for histological examination.
*T—transfer generation.

Histological studies revealed that following a third injection almost all the lymphoid cells of the tumor became pyknotic and died, the reticular cells of the lymphosarcomatous growth remaining (19 animals of the 9th transfer generation were used for the histological

** 109 mice have been inoculated with this tumor in 14 transplant generations. There have been "takes" in all cases and a spontaneous regression has never been observed.

observations). Although islets of resistant lymphoid cells were found, regeneration of the tumor apparently began with proliferation of the stroma (reticular) cells. Non-leukemic spleen and lymph nodes of the test animals were histologically normal 72 hours after the third injection of colchicine.

Summarizing, colchicine therapy in a transplanted malignant lymphoid tumor lengthened survival time appreciably in 7 of 14 animals, but did not permanently suppress tumor growth. The reticular stroma cells of the tumor were most resistant to therapy and probably are "malignant" elements in the lymphoid growths of mouse leukemia. "Malignant" lymphocytes proved to be more susceptible to colchicine action than normal splenic and lymph node lymphocytes in the treated tumor-bearing animals. Thymic lymphocytes were, however, killed by colchicine treatment. It is emphasized that colchicine administration is in no sense considered a cure for malignant lymphoid growths, but a drug which may be used to advantage in the experimental histological investigation of such tumors. So far colchicine has been found to hasten death in those animals where lymphoid neoplastic disease was systemic.

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Quantitative Separation and Estimation of Various Porphyrins in Biological Materials.

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We extract the porphyrins from urine, bile and feces by prolonged extraction with acetic acid-ether (Fink and Hoerburger,[1] Fikentscher,[2] Van den Bergh and others,[3] Brugsch[4]). Uroporphyrin is lost but, according to Fischer and Zerweck,[5] this may be neglected except in extremely rare cases. The porphyrins are taken up by 5% HCl from the crude ether extract. Purification involves repetition of the transfer to ether and back to HCl. Phylloerythrin

1 Fink, H., and Hoerburger, W., *Z. physiol. Chem.*, 1931, **202**, 8.

2 Fikentscher, R., *Biochem. Z.*, 1932, **249**, 257.

3 Van den Bergh, A. A. H., Grotepass, W., and Revers, F. E., *Klin. Wschr.*, 1932, **11**, 1534.

4 Brugsch, J. T., *Z. ges. exp. Med.*, 1935, **95**, 471.

5 Fischer, H., and Zerweck, W., *Z. physiol. Chem.*, 1924, **137**, 242.