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The Action of Xanthopterin on Tumor Growth.

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In a recent paper[1] we reported that a "folic acid concentrate" and the crystalline *L. casei* factor which seems to be related to folic acid were found to be strong inhibitors of tumor growth. As a possible relationship of folic acid to Xanthopterin (the pigment of yellow butterfly wings) has been suggested by a number of investigators,[2,3,4,5] it seemed of interest to test the action of synthetic Xanthopterin on tumor growth. Xanthopterin was assayed as described previously by Laszlo and Leuchtenberger.[6] In Table I an experiment is presented in which varying doses of Xanthopterin were studied. It is evident from this table that Xanthopterin is a strong inhibitor of tumor growth. The degree of inhibition depends on the dose injected, and its potency is comparable to that of the *L. casei* factor. Similar results were obtained in 30 experiments in which 214 animals were used.

Leukopterin* (the pigment of the white butterfly) was tested by the same method. It did not cause inhibition of tumor growth even in a dose 100 times larger than that of Xanthopterin. In this connection it might be of interest to quote the observations of Wright and Welch.[5] They reported activity of Xanthopterin and inactivity of Leukopterin in the synthesis of folic acid by rat liver *in vitro*.

In the course of investigations concerned with substances antagonistic to tumor growth inhibitors, as suggested by J. C. Keresztesy, Leukopterin was tested. In Table II one experiment is presented in which the effect of Xanthopterin is compared with that of a combination of Xanthopterin and Leukopterin.

It may be seen from this table that Leukopterin neutralizes the action of Xanthopterin.

In view of the tumor growth inhibitory properties of the *L. casei* factor and of Xanthopterin, experiments are in progress in which mice bearing spontaneous breast adenocarcinomas are treated with these substances. Though no definite conclusions can be drawn so far the changes in these tumors are most striking. After a few intravenous injections some hard tumors are changed into soft bags

TABLE I.
Effect on Tumor Growth of 4 Intravenous Injections of Xanthopterin in Varying Doses Given Over a Period of 48 Hours at 12 Hours Interval.* Seven animals were used in each group.

Group No.	Dose of Xanthopterin, γ	Mean terminal tumor wt, mg	Standard error, mg	Significance ratio
980	0	866	47	—
979	0.031	674	33	3.4
978	0.125	606	27	4.8
977	0.500	513	38	5.9
976	2.000	389	23	9.1

* Female Rockland mice transplanted with Sarcoma 180; start of the experiment 8 days after transplantation; mice kept on normal diet.

1 Leuchtenberger, C., Lewisohn, R., Laszlo, D., and Leuchtenberger, R., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 204.

2 Mitchell, H. K., *Science*, 1943, **97**, 442.

3 Totter, J. R., and Day, P. L., *J. Biol. Chem.*, 1943, **147**, 257.

4 Totter, J. R., Shukers, C. F., Kolson, J., Rims, V., and Day, P. L., *J. Biol. Chem.*, 1944, **152**, 147.

5 Wright, L. D., and Welch, A. D., *Science*, 1943, **98**, 179.

6 Laszlo, D., and Leuchtenberger, C., *Cancer Research*, 1943, **3**, 401.

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TABLE II.
Effect on Tumor Growth of 4 Intravenous Injections of Xanthopterin and of a Mixture of Xanthopterin and Leukopterin Given Over a Period of 48 Hours at 12 Hours Interval.* Seven animals were used in each group.

Group No.	Material injected	Dose, γ	Mean terminal tumor wt, mg	Standard error, mg	Significance ratio
959	Saline	—	577	42	—
956	Xanthopterin	0.5	341	21	to 959: 5.0 to 957: 5.3
957	Xanthopterin + Leukopterin	0.5 1.0	620	48	

* Female Rockland mice transplanted with Sarcoma 180; start of the experiment 10 days after transplantation; mice kept on normal diet.

containing necrotic tissue. Detailed descriptions, both macroscopic and microscopic, will be presented in a subsequent paper. Daily injections of 0.5 γ or 5γ respectively of *L. casei* factor or of 10 γ Xanthopterin were given. The animals were kept on a normal diet.

Summary. Xanthopterin inhibits tumor growth. Leukopterin does not inhibit tumor growth. It neutralizes the effect of Xanthopterin.

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Unidentified Inclusions Within the Erythrocytes in Certain Cases of Febrile Anemia.

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This brief report concerns 3 cases of progressive febrile anemia, 2 ending fatally, which were characterized by the presence within the red cells of unidentified coccoid and bacillary bodies. These were stained dark blue or bluish purple with Wright or Giemsa stains (Fig. 1). From one to 20 or more bodies were present in a single cell, and from 10 to 55% of the cells were affected. They were somewhat pleomorphic, but frequently appeared in the form of diploids, tetrads, or short batonnets, straight or slightly curved. The presence of the structures was often associated with a de-hemoglobinization of the cells; in such cases, they were clustered at the margin.

In unstained preparations, the bodies were colorless, very slightly refractile and possessed of an oscillatory motion within the cell. Treated with HCl and potassium ferrocyanide, they gave a positive iron reaction; the iron staining persisted in acid solutions, but disappeared after exposure to alkali at about pH 10. The morphology of the bodies was not altered by these procedures. They were not blackened by $(NH_4)_2S$, as is hemosiderin, nor by silver nitrate; they gave no histochemical reaction for alkaline phosphatase; the Feulgen reaction was also negative. They were resistant to autolysis, and to tryptic digestion.

By laking the blood with distilled water or saponin, it was possible to obtain a very great concentration of the bodies in the centrifuged sediment (Fig. 2). When a suspension of intact red cells containing the bodies was