

elements of the blood in 21 days. 2. An increase in stippled erythrocytes and eosinophilic polymorphonuclear cells occurs, suggesting mild bone marrow depression. 3. The parenchymatous organs show congestion of the spleen and an increase of eosinophiles in the bone marrow, suggesting again an early bone marrow depression.

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#### Effect of Theelin on Transplantable Mammary Rat Adenofibroma.\*

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Murray,<sup>1</sup> Lacassagne<sup>2</sup> and others have shown in males of certain strains of mice that estrogenic hormone may awaken a dormant malignant potentiality in breast tissue. Lewis and Geschickter<sup>3</sup> reported the presence of measurable amounts of estrogenic and gonadotropic hormones in adenofibromas of the human female breast. Numerous investigators have inquired into this phenomenon in relation to other mammalia and contradictory evidence has been forthcoming. Recently Frank and his coworkers<sup>4</sup> reported observations throwing doubt on the influence of these hormones on breast tissue, for other tissues also contain large amounts of estrogenic hormone normally. Heiman and Krehbiel<sup>5</sup> found measurable amounts of estrin in rat adenofibromas, but Mohs<sup>6</sup> not only failed to find appreciable amounts in such tissue but also observed that estrin administration raised the estrin content in these tumors only if high doses of this hormone were given 2 or 3 days prior to sacrifice.

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<sup>1</sup> Murray, W. S., *J. Cancer Research*, 1928, **12**, 18.

<sup>2</sup> Lacassagne, A., *Compt. rend. Acad. d. sc.*, 1932, **195**, 630.

<sup>3</sup> Lewis, D., and Geschickter, C. F., *J. A. M. A.*, 1934, **103**, 1212.

<sup>4</sup> Frank, R. T., *et al.*, *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1665.

<sup>5</sup> Heiman, J., and Krehbiel, O. F., *Am. J. Cancer*, 1936, **27**, 450.

<sup>6</sup> Mohs, F. E., *Am. J. Cancer*, 1937, **29**, 356.

Since we have access to several strains of transplantable mammary adenofibromas having marked malignant potentialities, as shown by the development of various strains of extremely malignant sarcomas, we have undertaken a series of experiments to study the influence of long-continued injections of theelin on the various strains of our adenofibromas normally containing only very small amounts of measurable estrogenic hormone. In the present experiment male and female white rats from 135 to 150 days of age implanted with a fast-growing adenofibroma of strain 5-B I were injected subcutaneously daily with either 100 or 200 i.u. of aqueous theelin. Thirty-two animals were subdivided into 3 groups. One group, consisting of 6 males and 5 females received 100 i.u. of theelin and a second similar group was given 200 i.u. of theelin over a period of 77 days, while the third group of 5 males and 5 females was used as a control. During the period of injection tumors were measured every other day and at the termination all animals were sacrificed and all tumors were studied microscopically.

Ordinarily the adenofibroma 5-B 1 used in this experiment produces a very glandular tumor. However, in this transplantation the tumors tended toward fibromas with a definite reduction of adenomatous material. Failure of transplant "take" occurred with about equal frequency in each group—2 in the controls and 3 in each of the treated groups. The males grew more glandular tissue than the females in all 3 groups. As compared with male or female animals in the control group, theelin-injected animals showed no increase in gland tissue. Also, the glandular response was not beyond that expected from long-continued injection of an estrogenic hormone. There was no unusual tendency towards sarcomatous degeneration in any of the tumors. No appreciable difference in the organ weights occurred in the different groups except for a slight reduction in adrenal weights in both theelin groups. The estimation of estrin content will be reported elsewhere.

TABLE I.  
Mean Daily Changes in Body Weight (gm./day).  
Group I, Control vs. 100 i.u. theelin; Group II, Control vs. 200 i.u. theelin; Group III, 100 i.u. theelin vs. 200 i.u. theelin; Group IV, Control vs. individuals receiving 100 i.u. plus those receiving 200 i.u. theelin.

Group	Control	100 i.u. theelin	200 i.u. theelin	Diff. (d)	n*	t*	P* for	
							abs. val.	P for of (d) (—d)
I	+.288	+.123		— .165	19	2.227	.040	.020
II	+.288		+.054	— .234	19	2.317	.035	.018
III		+.123	+.054	— .069	20	0.850	.400	.200
IV	+.288		+.090†	— .198	30	2.598	.015	.008

TABLE II.  
Mean Daily Changes in Tumor Weight (gm./day).  
Groups: As in Table I.

Group	Control	100 i.u. theelin	200 i.u. theelin	Diff. (d)	n*	t*	P* for abs. val. of (d)
I	+ .218	+ .029		-.189	14	1.808	.093
II	+ .218		+ .057	-.161	14	2.996	.163
III		+ .029	+ .057	+ .028	14	0.728	.480
IV	+ .218		+ .043†	-.175	22	0.995	.333

\*n = "degrees of freedom."

t = difference of means/standard error of that difference, adjusted for "n."

P = probability of a difference as great or greater than that obtained, occurring by chance alone. See Fisher, R. A., "Statistical Methods for Research Workers," London, Oliver & Boyd, 1934, 5th Ed., Chap. V.

† It is proper to combine these into one group as there is no significant difference between the administration of 100 i.u. and 200 i.u.

*Conclusions.* In spite of long-continued injections of theelin, a rapidly growing mammary adenofibroma of the white rat transplanted into 32 rats lost a large part of its adenomatous content. No unusual growth behavior attributable to the injection of an estrogenic hormone could be demonstrated in the tumor tissue either grossly or microscopically. Theelin decreases body weight, but the size of the dose, in the limits given, is not significant. In other words, the loss in weight is not significantly greater when administering 200 i.u. than it is when administering 100 i.u. However, theelin has no significant effect on the mean daily changes in tumor weight.

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### Filtrability of the Chinese Strain of *Spirochaeta recurrentis*.

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Novy and Knapp<sup>1</sup> first demonstrated that after having gone through Berkefeld filters, the filtrate of blood from animals infected with the American strain of relapsing fever spirochaetes was infectious; these workers concluded that the form present in the filtrate represented an invisible developmental stage. Later Breinl and Kinghorn<sup>2</sup> working with *Sp. duttoni* arrived at the same conclusion. Todd

<sup>1</sup> Novy, F. G., and Knapp, R. F., *J. Infect. Dis.*, 1906, **8**, 291.

<sup>2</sup> Breinl, A., and Kinghorn, A., *Memoir XXI, Liverpool School of Tropical Medicine*, September 1, 1906.