Group II (Progynon-B). The lumina of the alveoli were filled with milk. In marked contrast many mitotic figures were observed in the gland parenchyma of rats in Group I. The lumina of the alveoli usually contained very little milk, and in a few cases they were entirely absent.

Conclusions. The effectiveness of estrogens in inhibiting lactation in the rat can be increased through simultaneous administration of a gonadotropic principle from pregnant women's urine. Many cells in mitoses are observed in the mammary gland parenchyma of rats so treated. It is believed that this is the mechanism of the inhibitory action of these hormones on lactation. That is, one would not expect a proliferating gland to secrete as efficiently as a non-proliferating gland. The administration of an estrogen plus a gonadotropic principle to lactating rats augments the lactogen content of the pituitary gland.

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Influence of Heredity and Environment upon Number of Tumor Nodules Occurring in Lungs of Mice.

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In previous publications it has been shown that the occurrence of lung tumors in mice is influenced by environment and also by heredity[1] and that probably, in the strains studied, a single dominant Mendelian factor is concerned.[2, 3] We emphasize, however, that our conception as to number of genes may be affected by further study of environmental conditions. The present paper deals with the influence of heredity and environment upon degree of susceptibility among mice with tumor.

The measure used, in this instance, to determine degree of susceptibility, is the number of tumor nodules found in each individual. Although the counts covered only those nodules visible on the surface of the lung and obviously may not represent the total number possessed by the mouse, they are sufficiently accurate for our purpose. In Table I, comparisons are made of the number of lung

[1] Lynch, C. J., *J. Exp. Med.*, 1927, **46**, 917; 1931, **54**, 747; *Occas. Publ. Am. Assn. Ad. Sci.*, 1937, **4**, 22.

[2] Bittner, J. J., *Pub. Health Rep.*, 1938, **50**, 2197.

[3] Lynch, C. J., *Third Internat. Canc. Cong.*, in press.

TABLE I.

Mice Belonging to Various Groups Arranged According to the Number of Tumor Nodules Occurring in the Lungs of Each Individual.

Tumor	Group of mice	% tumor	No. of Nodules																					
			0	1	2	3	4	5	6	7	8	9	10	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	91-100	11-100
Spontaneous	Strain 1194	4.4	1676	67	8	2				1				78										0
	" Swiss-8	43.9	384	176	69	27	19	4	1	2	1			299	1									1
Induced	" 1194	20.5	290	66	3	4	1			1				75										0
	" Swiss-8	100.0				2				2		1	1	6	17	16	6	3	2	1				45
	Backcross to 1194	68.3	13	9	3	3	3	1	1	1		1	2	24	4									4
	F_2	91.7	3	1	4	6	2			1	1	2		17	6	4	2	3			1			16
	Backcross to Swiss	100.0			1	1							1	3	8	8	9	4	5	3		2	1	40

nodules occurring in mice from 2 strains living under ordinary laboratory conditions and also in mice from the same strains after treatment with tar. Various generations from a cross between these strains are also compared after tarring. Strain 1194 is a low tumor strain which has been under observation in our laboratory for many years, and this sample, which is characteristic, has only 4.4% lung tumor among mice of all ages. Of 78 individuals with tumor, the very large majority had a single nodule though one mouse had as many as 7. On the other hand, Strain Swiss-8 has a higher percentage of tumor. In the group of 684 mice represented in the table, the tumor incidence was 43.9%. As to number of nodules, the range per individual was somewhat greater than in the first strain. Also the number of individuals with multiple nodules was, in a statistical sense, significantly greater among the Swiss-8 than among the 1194 mice ($\chi^2 = 19.9$ and P is $<.01$). The difference between strains is clear.

It has been shown previously that certain treatment with chemicals increases the percentage of tumor mice though not equally so in all strains[1] and it appears from the present experiment that the number of nodules per individual also may be increased by this means. When Strain 1194 was tarred, the tumor incidence increased from 4.4 to 20.5% even though the treated mice were killed rather early (12-13 months of age). In this strain the number of nodules was scarcely affected; the range in nodule number was about the same as in the non-tarred mice of this strain and about the same percentage of the tumorous animals had a single focus of malignant growth. The effect of tarring upon the Swiss-8 strain was more marked; of 51 animals treated, all had tumor, all had multiple growths and the large majority had more than 10. Evidently the change in external factors caused a striking shift in the frequency of the nodules, possibly by lowering the threshold of susceptibility. While the Swiss-8 strain may not have been genetically uniform at the time this experiment was performed, there can be no doubt that the tar had an effect. The difference between the Swiss-8 and the 1194 strain is more pronounced when the mice are tarred and under this condition the influence of both heredity and environment can be seen.

In an attempt to get further evidence of the genetic effect besides that shown by the contrast between strains, these strains were crossed. None of the first hybrid generation from this cross was treated; however, in similar experiments to be reported later, the F_1 were intermediate as to number of nodules shown. Mice from the hybrid generation were crossed back to the low strain as well as to the high strain and were also inbred to produce an F_2 generation. Representa-

tives from the 3 groups thus obtained were subjected to tarring. The tumor rates may have been somewhat affected by parental variability. When the cross was made to the low tumor strain the range in number of nodules per mouse approached that given by the low tumor parents and the class with a single tumor was the mode. On the other hand, crossing back to the high tumor strain resulted in progeny with a range in number of tumor foci as great—even slightly greater than that of the parental Swiss-8 strain. The F_2 generation, which was intermediate between the backcross groups in respect to percentage of tumor mice, was intermediate also in regard to range and distribution in number of nodules. If a mathematical comparison is made on the basis of the possession of more than 10 nodules, it is found that a significantly greater number of mice with more than 10 occurs among the F_2 than among the mice obtained by backcrossing to the low tumor strain No. 1194 ($\chi^2 = 7.22$ and P is $<.01$), and that a significantly smaller number of such individuals occurs in the F_2 than among the mice from the backcross to the Swiss-8 ($\chi^2 = 18.12$ and P is $<.01$). It is apparent that multiplicity of tumor nodules is influenced by heredity. Previous evidence indicated that probably a single dominant gene is concerned in the inheritance of susceptibility to lung tumor. While heterozygosity of this gene as well as uncontrollable extrinsic variables may affect, to some extent, the degree of susceptibility, it is possible that additional genes, as well as certain known environmental conditions, may influence the number of tumor nodules shown by each mouse.

Summary. Evidence is presented showing that degree of susceptibility to lung tumor in mice, as measured by the number of nodules occurring in the individual, is affected by both heredity and environment. The number of genes concerned has not been determined.