this eosinophilic material is also found in the form of large homogeneous clumps, which are occasionally enclosed in a vacuole. Accumulations of eosinophilic material bearing a great resemblance to the intracellular eosinophilic masses may at times also be found extracellularly.

The cytoplasmic changes described above occur simultaneously with the nuclear alterations previously noted by us in sarcoma cells maintained in pure culture. Both are accompanied by great and sometimes extreme hypertrophy of the cells involved.

Our observations indicate that the peculiar nuclear and cytoplasmic alterations which we have described, and which have also been pointed out in part by earlier investigators (Borrel, Fischer, Roskin, Zweibaum), represent different aspects of a slowly progressive and decidedly pathological process. Although the changes in the sarcoma cells are extremely varied and complex their combination forms a definite syndrome of serious cell disease which, in conditions of life *in vitro*, inevitably overtakes cells bearing the causative agent of Rous sarcoma, and leads ultimately to the death of the sarcoma cell colonies.

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Presence in Various Grains of Factors Inhibiting Tumor Growth.

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The following report deals with the results of experiments on the influence of various grains on tumor growth. These studies were stimulated by experiments of Lewisohn and coworkers.[1] They observed that the therapeutic results of intravenous therapy of yeast extracts on spontaneous mammary carcinomas in mice could be improved by feeding polished rice instead of a normal diet. The question was raised, whether this improvement was due to a lack of substances in the polished rice diet essential for tumor growth, or whether the polished rice contains an additional tumor inhibitor. To study this problem in detail, we employed a rapid test for tumor growth inhibitors, developed in this laboratory by Laszlo and Leuchtenberger.[2]

Method. In the rapid test, treated groups of transplanted tumor mice (Sa.180) are compared with untreated controls as to the size and weight of their tumors. At the start of the experiment, 7-10 days after transplantation, groups of 7 mice are formed, each bearing a transplanted Sa.180 of the same size from the same transplant. If these matched groups are injected intravenously twice daily with saline solution for 2 consecutive days, the tumor-sizes and tumor-weights of treated animals and controls will agree after 48 hours. If one or more of these groups are injected intravenously twice daily on 2 consecutive days with the standard preparation (yeast extract as previously described) the tumor growth in these groups is inhibited. The extent of this inhibition is such that after 48 hours the differences of mean terminal size and mean terminal weight in treated and untreated groups permit the detection of tumor growth inhibitors even in a small number of animals.

Results. In a series of experiments it was found that at least four intravenous injections of 0.1 cc (corresponding to 5.25 mg solids) of the standard are necessary for an inhibitory effect, which is statistically significant, if mice are fed a normal diet. If mice are fed a polished rice diet, 4 injections of 1.75 mg solids of the same standard are sufficient for a similar inhibition of tumor growth. Control groups

1 Lewisohn, R., Leuchtenberger, C., Leuchtenberger, R., Laszlo, D., and Dische, Z., *Cancer Research*, 1942, **2**, 818.

2 Laszlo, D., and Leuchtenberger, C., to be published in *Cancer Research*, 1943.

TABLE I.

Effect of a Standard Preparation on Tumor Growth in Mice on Normal Diet and on Polished Rice Diet.

Female Rockland mice transplanted with Sarcoma 180 on June 6, 1942, passage MP24. Four intravenous injections (2 on June 15 and 2 on June 16).

			June 15		June 17		June 17	
No. of animals	Diet	Dose of standard in mg	Mean initial size	Standard error	Mean terminal size	Standard error	Mean terminal size	Standard error
7	Mouse pellets	5.25	.159 in²	.011 in²	.121 in²	.017 in²	220 mg	45 mg
7	" "	1.75	.169	.012	.214	.024	489	69
7	" "	0 (Inj. saline sol.)	.173	.013	.229	.029	524	111
7	Polished rice	1.75	.169	.014	.149	.022	169	30
7	" "	0 (Inj. saline sol.)	.163	.015	.229	.023	499	68

with saline injections kept on polished rice diet do not differ materially in their tumor growth from control groups kept on normal diet. Table I illustrates one such experiment.

Similar results were obtained in a set of experiments which are presented in Table II (1-5).

To study whether these results were caused by the deficiency in the polished rice diet, the following experiments were carried out (Table II):

(a) Mice were fed synthetic diets with* or without† the addition of vitamins of the B complex and 4 injections of 1.7 mg of the standard were given. The results did not differ from those obtained in animals injected with the same dose and kept on normal diet (Table II, 23-26).

(b) Mice were fed polished rice with 3% casein. The results were similar to those obtained with polished rice alone (Table II, 10).

(c) Mice were fed polished rice and the vitamins of the B complex. The feeding of these vitamins did not change the results materially (Table II, 11).

(d) Mice were fed brown rice instead of polished rice and injected intravenously with 1.7 mg of the standard. Inhibition of tumor growth in the mice fed brown rice was similar to the growth inhibition in animals fed polished rice (Table II, 7).

(e) Mice were fed rice bran diet and injected intravenously with 1.75 mg of the standard. The tumors appeared to grow like those in mice on normal diet. Autoclaving of the rice bran for 4 hours at 120°C seems to stimulate tumor growth (Table II, 8 and 9).

(f) Mice were fed polished rice previously autoclaved for four hours at 120°C and injected intravenously with 1.7 mg of the standard. The inhibitory effect of the polished rice was lost (Table II, 6).

From these observations it seems evident that the increased inhibitory effect, resulting from the combined polished rice diet and intravenous injection of the standard, is not due to dietary deficiency. Nor is the effect apparently caused by caloric restriction as determination of food consumption and body weight in experiments with other deficient diets indicate. Neither loss of body weight nor decreased food intake explain this effect. However, these experiments suggest the presence of a tumor growth-inhibiting factor in the rice. Therefore, the extraction of a tumor growth inhibitor from the rice was attempted. A watery extract was prepared which, when injected intravenously in a dose of 0.1 cc corresponding to 2.4 mg solids, inhibits tumor growth to a similar extent as 5.25 mg of the standard, both groups being fed on normal

* Synthetic diet with the addition of vitamins: I. Sucrose, 75%; casein, 18%; salts, 5%; cod liver oil, 1%; corn oil, 1%; thiamin, 200 γ; riboflavin, 500 γ; nicotinamid, 1 mg; alanin, 2 mg; cholin, 1.7 mg; pantothenic acid, 1 mg; pyridoxine, 200 γ.

† Synthetic diets without the addition of vitamins: II. Casein, 3.9%; starch, 87%; cod liver oil, 3%; salts (modified Osborne-Mendel), 6%. III. Casein, 3.9%; starch, 65%; crisco, 22%; cod liver oil, 3%; salts (modified Osborne-Mendel), 6%.

TABLE II.
Effect of a Standard Preparation on Tumor Growth in Mice Fed Different Diets.

Serial No.	No. of animals	No. of exp.	Dose of standard, mg	Diet	Mean terminal tumor wt, mg	Standard error
				Normal		
1	41	6	5.25	Mouse pellets	254.8	17.7
2	28	4	1.75	" "	523.4	43.8
3	89	13	0	" "	548.8	23.0
				Rice		
4	141	21	1.75	Polished rice	220.8	9.5
5	122	18	0	" "	558.8	19.4
6	20	3	1.75	Autocl. polished rice	477.0	38.3
7	20	3	1.75	Brown rice	258.0	30.4
8	21	3	1.75	Rice bran	458.7	47.9
9	7	1	1.75	Autocl. rice bran	682.9	123.4
10	7	1	1.75	Polished rice + 3% casein	221.4	63.9
11	7	1	1.75	Polished rice + Vit. B complex	284.3	84.8
				Barley		
12	35	5	1.75	Pearled barley	262.1	24.1
13	25	4	0	" "	412.8	42.2
14	14	2	1.75	Autocl. pearled barley	327.1	33.0
15	14	2	1.75	Malted barley	472.1	46.5
16	7	1	1.75	Pearled barley + Vit. B complex	328.6	70.2
				Misc.		
17	7	1	1.75	Wheat flour	382.9	69.1
18	7	1	1.75	Wheat germ	491.4	64.5
19	7	1	1.75	Oats	387.1	60.0
20	7	1	1.75	Corn meal	395.7	50.3
21	6	1	1.75	Soya bean flour	228.3	46.7
22	6	1	0	" " "	395.0	52.1
				Synthetic		
23	7	1	1.75	(a) Synthetic diet I	484.3	53.7
24	7	1	1.75	(b) " " I	475.7	73.6
25	7	1	1.75	" " II†	555.7	83.4
26	7	1	1.75	" " III†	486.0	25.9

TABLE III.
Effect on Tumor Growth of 4 Intravenous Injections of Various Extracts Given Over a Period of 48 Hours

No. of animals in group*	Type of extract	Dose, mg	Mean initial size, in²	Standard error	Mean terminal size, in²	Standard error	Mean terminal wt, mg	Standard error
7	Standard preparation	5.25	.171	.009	.167	.013	283	51
7	Polished rice	2.40	.179	.011	.171	.012	264	39
7	Pearled barley	3.60	.167	.010	.147	.014	200	38
7	" "	1.20	.171	.010	.191	.021	310	60
7	Malted "	7.50	.180	.004	.270	.008	686	39
7	Saline solution	0	.164	.007	.250	.011	627	75

* The animals were kept on a mouse pellet diet.

diet. Table III illustrates one such experiment. Whether this extractable tumor inhibitor is identical with the previously mentioned feeding factor, cannot be answered yet.

Similar feeding experiments were carried out with pearled barley, malted barley, wheat flour, wheat germ, oats, cornmeal and soya beans (see Table II). An increased inhibitory effect was obtained by feeding the animals pearled barley and soya beans (Table II, 12, 13, 14, 21, 22) while the effect of wheat flour, oats and cornmeal was less evident (Table II, 17, 19 and 20). No increased inhibiting effect was obtained by feeding malted barley and

wheat germ (Table II, 15 and 18). Thus far, extracts were prepared only from pearled barley and malted barley. Intravenous injections of pearled barley of 0.1 cc corresponding to 1.2 mg solids showed an inhibitory effect similar to 5.25 mg of the standard when groups of animals were kept on normal diets. Extracts from malted barley were ineffective (Table III). At present no conclusions can be drawn as to the quantities of tumor growth inhibitors in the different grains. Experiments for the quantitative determination and chemical characterization of these factors are in progress.

Summary. Tumor growth-inhibiting substances are demonstrated in various grains with the aid of a rapid test on Sarcoma 180. They are effective by feeding in combination with injections of a standard solution of yeast extracts. Extracts of these grains are effective upon intravenous injection.

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Treatment of Spontaneous Breast Cancers in Mice with Pearled Barley.*

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We have presented in previous papers[1,2,3,4] our results with intravenous injections of yeast extract in the treatment of spontaneous breast adenocarcinomas in mice. We reported complete disappearance of these tumors in 30% of the animals, if the tumors were not of excessive size. In our last publication[4] we reported that by combining the injections of yeast extract with the feeding of polished rice we were able to double the percentage of complete regressions and to get these results not only in small tumors, but in tumors of considerable size.

We mentioned in this paper that since the preparation of beer had been changed, due to the exigencies of the war, successful results could be obtained only with a yeast extract prepared from bock beer, as bock beer was still prepared according to the old technic. Bock beer is prepared only once a year.

We were planning to prepare a large quantity of this extract when we were informed that the breweries had decided to discontinue the manufacture of bock beer for the duration of the war. Thus we were forced to abandon the use of yeast extract and to search for other sources of tumor growth-inhibiting substances.

In the preceding paper[5] we demonstrated on the growth-rate of a transplanted tumor (Sarcoma 180) an increased inhibitory effect, resulting from the combination of a polished rice diet and intravenous injections of yeast extract. From observations with other diets it was evident that this effect is not due to a deficiency in the diet. Furthermore it was possible to extract a factor from the rice which inhibited tumor growth when injected intravenously. As feeding experiments and injections of extract of pearled barley gave a similar inhibition of tumor growth in the rapid test, we tested the influence of pearled barley on spontaneous tumors.

In this preliminary report we shall present results obtained by treating mice with intravenous injections of pearled barley extract and a diet of pearled barley or polished rice.

The pearled barley extract is prepared in

1 Lewisohn, R., Leuchtenberger, C., Leuchtenberger, R., and Laszlo, D., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 558.

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3 Lewisohn, R., Leuchtenberger, C., Leuchtenberger, R., Laszlo, D., and Bloch, K., *Cancer Research*, 1941, **1**, 799.

4 Lewisohn, R., Leuchtenberger, C., Leuchtenberger, R., Laszlo, D., and Dische, Z., *Cancer Research*, 1942, **2**, 218.

5 Lewisohn, R., Laszlo, D., Leuchtenberger, C., Leuchtenberger, R., and Dische, Z., PROC. SOC. EXP. BIOL. AND MED., 1943, **52**, 269.