Table 1. Lymphomas in mice inoculated when newborn with filtrates from radiation-induced lymphoid tumors or from irradiated thymus glands.

Source of filtrate	Net No. of mice	Lymphomas		Latency (day)	
		No.	Percent	Median	Range
Experimental animals					
X-ray-induced lymphoma	59	10	17	582	253–688
Lymphoma C43	26	5	19	449	340–551
Thymus glands obtained:					
2 days postirradiation	27	0	0		
8 days postirradiation	21	0	0		
32 days postirradiation	21	0	0		
64 days postirradiation	39	3	8		370, 405,* 618
128 days postirradiation	20	3	15		333, 473, 580
Filtrate-induced lymphoma† (first passage)	6	2	33		83, 176‡
Filtrate-induced lymphoma† (second passage)	13	9	69	202	91–336
Controls					
Hemangioma	15	0	0		
Reticuloendothelial tumor	10	0	0		
Strain AK lymphoma	24	0	0		
Saline or no treatment	74	1	1§	565	

* Lymphoid tumor used for first passage.
† Assayed in newborn reciprocal F_1 (C57BL/Ka × BALB/c) hybrid mice.
‡ Lymphoid tumor used for second passage.
§ Statistical analysis: filtrates from x-ray-induced lymphoma and lymphoma C43 versus controls: χ^2 (corrected) = 17.760; $P < .001$.

pearance of leukemogenic activity. Microscopically identifiable lymphomas *in situ* first appear at about 30 to 50 days after irradiation (*8*). During the first 32 days after x-irradiation the filtrates were devoid of leukemogenic activity. Activity was evident in thymi harvested at 64 days and was perhaps somewhat greater by 128 days. The latency for lymphomas arising in mice injected with the 64- and 128-day filtrates was of the same order as that following injection of filtrates from frankly disseminated tumors.

Serial cell-free passage of a filtrate-induced lymphoma in newborn F_1 hybrid mice yielded lymphomas in two of six (33 percent) and in nine of 13 (69 percent) in the first two passages, with latency of 3 to 11 months. On transplantation, these tumors behaved as though they were of hybrid origin; this excludes the possibility that they were produced by contamination of the filtrate with intact tumor cells. Preliminary results of a subsequent cell-free passage indicate persistent activity of the agent.

It appears that cell-free filtrates from x-ray induced lymphoid tumors of C57BL mice can elicit the disease in compatible hosts. Similar results have recently been reported by Gross (*9*) for strain C3H. The active principle has been shown to have the following properties: (i) It is latent in untreated C57BL mice. (ii) Appropriate x-irradiation of the host "activates" it, and it can be recovered from at least some of the resulting lymphoid tumors. (iii) It passes bacterial filters. (iv) It exhibits specificity in that it causes only lymphoid tumors on injection into nonirradiated newborn isologous and compatible F_1 hybrid hosts. (v) Its potency is increased on serial passage, as was also noted by Gross (*9*). These characteristics appear to exclude all agents other than viruses and subcellular genetic determinants.

In many of its properties, the x-ray-activated leukemogenic agent bears, at first glance, a striking similarity to the temperate phage-lysogenic bacterial system (*10*). It does not, however, destroy its host cells on activation; instead, it causes them to proliferate more rapidly than normal. Moreover, the activity of "infectious" preparations is not enhanced (indeed, it was diminished) by x-irradiation of the host. Despite such differences, bacterial lysogenesis remains a useful model on which to base further investigations.

The demonstration of a leukemogenic filtrable agent in the cells of radiation-induced lymphoid tumors provides the first evidence directly linking the external carcinogens to viruses or virus-like agents. It thus lends new emphasis to the long-held view that all neoplasms result from such agents. Nonetheless, this thesis will require step-by-step experimental documentation for a variety of neoplasms and external carcinogens.

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5. Physical factors of irradiation were as follows: 120 kv (peak); 7.5 ma; 0.25 mm Cu + 1.0 mm Al added filter; 30 cm target-mouse distance; output, 25.5 r/min; HVL, 0.36 mm Cu.
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Biophysical Approach toward Tumor Regression in Mice

Abstract. An external electrical source of low magnitude was used in a series of experiments to alter inherent tumor potentials in mice. While no significant increase of tumor growth was noted in the acceleration group, total tumor regressions were obtained in the inhibition group. Preliminary studies with leukemia did not yield significant results.

It has been shown in the human being that a growing fetus or a growing uterine tumor will cause the uterus to be electronegative with respect to the outer abdominal surface (*1*). In the guinea pig and mouse, the tumor is also electronegative (*2*). This supports the many findings that a growing region is electronegative with respect to a slower growing or nongrowing region in the same organism, whether plant or animal (*3, 4*).

In plants, Lund has demonstrated growth acceleration and deceleration by an external potential source (*4*). The studies described here were based on the hypothesis that the growth rate of malignant tumor tissue would respond similarly to an external electrical source (*5*).

A rapidly growing type of tumor was chosen for initial experiments, and various control measures recommended by

the National Cancer Institute were followed. Swiss albino mice equated for sex, age, and body weight were given trocar implants of sarcoma-180, and fur was clipped from the tumor area. Copper or zinc electrodes were covered with sponge rubber, saturated with saline solution, and placed upon the unbroken skin over the tumor area with the cathode at the tumor site for inhibition. In studies of the acceleration of tumor growth the polarity was reversed. Low values of current were used to prevent cautery. The second electrode consisted of a rest or support, made from a saline-solution-saturated sponge to which the animal was secured, the contact being over a large, unclipped ventral area.

In experiment 1, 30 female mice were divided randomly into three equal control, acceleration, and inhibition groups. Electrode leads for the control group were separated to prevent even contact potential from entering as a variable since it could exceed the inherent tumor potential.

Current was applied to test groups for a period of 5 minutes four times daily for 7 days. All mice were sacrificed and photographed, and the tumors were removed and weighed with an accurate laboratory balance. The results appear in Table 1.

Pure direct current was chosen for all but the first experiment. A restraining device was built to handle ten animals simultaneously. The animals were secured on individual insulated rods attached to a polystyrene plate. Each rest was covered by copper and by sponge rubber for electrolyte retention. Over each mouse was placed a plastic saddle containing a rectangular copper electrode covered with sponge rubber saturated in saline solution. Each circuit was separate, with current controlled by a series rheostat.

In the second experiment, only control and inhibition animals were used. They were sacrificed after 7 days, the tumors were removed, and weight and volume determinations were made. The results are also shown in Table 1.

In the third study an acceleration group was added. One tumor in the inhibition group reached a peak in size and then began to decrease as treatment progressed. When it was removed it had the appearance of a thrombus, while the other tumors were shiny, red, and turgescent. On the fourth day of treatment a small white line appeared on the tumor; on the fifth day the line was larger and dark in color. Within the next 48 hours, invagination of the darkened area of the tumor began. Because of this effect, another experiment was conducted, and in order to attempt complete regression the animals were not sacrificed.

Table 1. Summary of data on tumor inhibition and acceleration.

Item	Experiment 1	Experiment 2	Experiment 3
Location of implant	Axilla	Scapula	Thoracicolumbar
Electrode size	Round, 1 in.	½ by ¾ in.	1 by 1½ in.
Current	2 ma at 6 v, pulsating d-c	2 ma	2½ ma
Prior growth of tumor	24 hr	78 hr	48 hr
Total time of treatment	⅓ hr	15½ hr	33 hr
Mean weight of tumors in controls	1.7 g	1.5 g	0.66 g
Standard deviation	0.6	0.5	0.11
Mean weight of inhibited tumors	1.6 g	1.0 g	0.41 g
Standard deviation	0.5	0.4	0.18
Difference probability of inhibition (t-test)	< 90 percent	97 percent	95 percent (vol.)
Mean weight of accelerated tumors	1.9 g		0.58 g
Standard deviation	0.5		0.14 wt.
Difference probability of acceleration (t-test)	< 90 percent		< 90 percent
Percentage acceleration	10		12
Percentage inhibition	6	33	38

Twenty females were given intrascapular implants. The mice were treated for an hour and allowed to rest an hour. Treatment averaged 4.8 hours per day. The mean weight of both control and test groups was 21 g at trocar implant. Treatment began 24 hours after trocar with a current of 3 ma at 3 v.

After 15 days of treatment the tumors were measured with calipers. The mean tumor volume of treated animals was 42 percent of that of the control animals, which was 5.33 cm^3.

By the 21st day all control animals had died and a 60 percent total regression of the test tumors had occurred. (*Total regression* means that the tumor had decreased progressively in volume, hardened, and dropped off, leaving a new skin surface at the former tumor site.)

A confirmation study was made with 18 test and 18 control animals 6 weeks old, each weighing about 25 g. A 10-day tumor growth period was allowed.

Test animals were subjected to 3 ma at 6 volts for 3 hours a day with 1 hour rest between test periods. Control animals followed the same regimen except that no current flow was permitted.

Each electrode lead was connected to a "scrambler box" so that the technician could not distinguish between control and test animals. Electrode leads to the control animals "floated" within the "scrambler box" to avoid contact potential effects. Current flow through each test animal was regulated separately by the experimenter. Animals were housed individually in a plastic cage containing wood shavings. Current density time was set for 0.016 ma hr/mm^2 of electrode surface area.

As treatment began, the mean volume of both test and control tumors was 3.1 cm^3. At 17 days, the mean control tumor volume had increased to 5.7 cm^3 and test tumor volume had increased to 4.3 cm^3. At 24 days, the mean volume of the control tumors was almost 7 times the mean volume of the test tumors. The seven surviving test animals had complete tumor regression; they have survived for more than a year since trocar and are healthy, active, and free of tumors. On these animals, fur again covered the tumor site by the 50th day. Two of the controls survived 31 days.

In this confirmatory test, not tabulated, a probability of difference of 90.5 percent was found between control and test groups. Regression of tumors in the test animals is considered to be highly significant.

No differences were observed between copper and zinc electrodes. When KCl instead of NaCl was used as the electrolyte all animals died quickly.

In preliminary studies of leukemia induced by intraperitoneal L1210 tumor tissue implant, no appreciable effects were observed, although a 15 percent increase in longevity appeared to occur in the test group.

From our results with nearly 500 mice, it appears that continuation of the studies with other types of tumors is desirable (*6*).

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X-ray Dosimetry and Contact Microradiography with Color Film

Abstract. The effect of x-rays at various voltages and intensities, with monochromatic and polychromatic beams, on Ektachrome daylight and artificial-light film was investigated. The colors were rated according to the Munsell color system and ranged over all the spectrum except red. The color in terms of hue, value, saturation, and chroma was a function of wavelength as well as intensity, and thus the method may be useful in dosimetry as well as in radiography. Microradiographs of metals and wood were remarkable in showing detail not obtainable with conventional black-and-white photographic emulsions.

For some time prior to recent reports of the use of color film to distinguish between radioactive isotopes (*1*) and for registration of electron micrographs (*2*) we have been interested in investigating the possibility of increasing the information provided by contact microradiographs registered on color film beyond that derived with the conventional fine-grained, black-and-white photographic emulsions. Also, in the course of our investigation there appeared a paper by Blum (*3*), describing two types of sensitive coatings which permit registration in arbitrary colors of the action of x- or γ-rays of different wavelengths or of ionizing particles of different energies.

It is the purpose of this report to summarize briefly our experience with Kodak Ektachrome daylight and artificial-light film which we could process.

The action of x-ray beams of varied spectral quality or wavelength distribution (in some instances essentially monochromatic) generated at 40 kv by cobalt, chromium, copper, and molybdenum target tubes on the film alone was studied. Copper and molybdenum radiation at 30, 20, 10, 7, and 5 kv, and at 35 and 30 kv, respectively, was also investigated.

The colors produced were classified visually according to the Munsell color system. Colors ranging from blue, blue-green, green, yellow, yellow-red, and purple-blue to gray were obtained. Red, however, was not obtainable.

The reproducibility of the colors under similar exposure conditions was shown—that is, the reciprocity law holds for color film. However, the method of film storage before exposure, as well as change in x-ray tubes having the same target, seems to have affected the colors somewhat. The artificial-light film produced more saturated colors than the daylight film. For the same value of *E*, the same voltage yielded the same color, while a different voltage yielded a different color. The hue varied more from one target to another at the same voltage and *E* value in daylight film. The hue remained the same after exposure to radiation from any given target for one kind of film. It was easier to overexpose daylight film than artificial. The color property of value decreased with decreasing *E*. There were greater shifts in value and chroma with decreasing *E*. Sometimes even a change of hue was evidenced. Herein lies the key to the use of color film in the evaluation of x-ray dosage.

With a newly designed camera, x-ray beams from copper and molybdenum targets were transmitted through various metal and wood specimens in contact with color film, and the resulting shadow images were examined for color and resolution of the fine structure of the specimen.

Artificial-light film brought out the phase structure of metals at several of the higher voltages, especially with the copper radiation, with remarkable clarity and with differentiation of composition far beyond that in black-white images. Softer radiation was needed to bring out the structure in the wood specimens. Specimens containing elements of large atomic number seemed to render the film more sensitive in resolving structure when higher voltages were used.

Green and blue-green images were obtained for metal specimens on daylight film, while blue was obtained for metal and wood specimens on artificial-light film.

The processing time is the same as that required in the conventional method of microradiography on black-and-white film, although more manipulation is necessary. Because of the rather large grain size, extensive enlargement of the color microradiographs is not feasible. However, the use of these transparencies as slides is very convenient.

Because of the complex nature of the film and the fact that the formulation is highly confidential and not disclosed by the manufacturer, such problems as the inability to obtain red coloration must be answered with conjecture. Thus, it is possible that the radiation may have destroyed the dye or its carrier. Further, it is also possible that variations from one emulsion lot to another may have been responsible for certain variations in color which were unexplainable. The balancing necessary because of the greater saturation of the yellow dye which is used may also be a contributing factor.

Besides producing encouraging results, indicating interesting and valuable applications in radiography and dosimetry, and even for Laue diffraction patterns made with polychromatic x-radiation, this investigation has opened new areas of research in the field of radiation chemistry and may perhaps contribute to the development of new color-film formulations more specifically adapted to radiation in the x- and γ-ray ranges of the electromagnetic spectrum.

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Chromosomal Translocation in Domestic Fowl Induced by X-rays

Abstract. The cytological appearance and behavior of an x-ray-induced reciprocal translocation between the first and second chromsome of the domestic fowl is described, and its relevance to the further definition of linkage studies in the fowl is observed.

Although there are possibly better organisms among the vertebrates for cytological and genetical investigations than the domestic fowl, economic considerations have led to its frequent utilization, especially for genetic studies, and a large amount of breeding data has been accumulated. Five autosomal groups and one sex-linkage group, with a substantial number of genes in each group are known (*1*). The cytology of fowl, however, has been said to be less well known than that of other vertebrates (*2*), and the chromosome complement has been variously estimated to be between 40 and 80, with the mode near the latter. If these estimates were correct, the prospects for any cytological correlation of genetic data would be indeed dim. But recent studies utilizing a smear tech-