high in linoleic acid-containing fats (*4*) without tocopherol supplementation and also fortify the concept that tocopherol functions as a biological antioxidant, which is apparently required only where strongly peroxidizable lipids are present. Since such lipids are normal constituents of tissue, one would expect to find that tocopherol is required in amounts in some way related to the amounts of such lipids present.

Of some interest is the observation in a current experiment in which an attempt to reduce the high linoleic-acid content of erythrocytes in patients who had been on a corn oil diet is being made by substituting coconut oil for the corn oil. After 1 month on coconut oil (60 gm per day), there has been little change in the relative amounts of linoleic acid in the erythrocytes of these patients—amounts which remain much higher than those found in nonexperimental subjects. Apparently (although final conclusions must await the lapse of more time to permit a complete turnover of the erythrocytes), the ability of tissue to hold onto linoleic acid tenaciously, if other sources of energy are available, conforms with the observation (*4*) that while 2-percent corn oil diets, from which tocopherol has been removed, seldom produced encephalomalacia in chicks, 2-percent corn oil plus 7-percent coconut oil which had been similarly treated produced the same high incidence of encephalomalacia (over 70 percent) that 4-percent corn oil did. One should also be aware that linoleic acid is a variable component of lard (varying from 2 to 12 percent, depending upon what the hog ate), and studies of tocopherol or cholesterol metabolism in which lard is used (*1*) should take the linoleic-acid content of the lard into account.

It is of interest to note that the same lipid mixtures which increase the tocopherol requirement and promote encephalomalacia in the chick (*4*) also reduce the plasma cholesterol levels in the rat (*12*) and in man (*13*).

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Experimental Evidence in Support of the Dormant Tumor Cell

Abstract. When rats were injected intraportally with as few as 50 Walker-256 carcinosarcoma cells and then examined 5 months later for hepatic tumor growth, none was evident. If, however, 3 months after injection the rats were subjected to repeated laparotomy and liver examination at 7-day intervals, 100 percent had a tumor within a few weeks.

When specific numbers of viable tumor cells are injected into animals known to be receptive to the growth of such experimental neoplasms, a certain number of "takes" may be expected to occur within a given time. It has been suggested that animals demonstrating no such tumor growth have been able in some fashion to destroy the cells injected. That such cells might not be destroyed but will continue to exist indefinitely in a dormant state has been suggested by experimental and clinical evidence (*1, 2*). Few factual data, however, are available (*3*). Dormancy implies "malignant cells which, although remaining alive in the tissues for relatively long periods, show no evidence of multiplication during this time, yet retain all their former and vigorous capacity to multiply" (*1*).

Recently, while investigating factors which might influence the take and growth of artificially induced hepatic metastases (*4, 5*), we observed that rats injected intraportally with small numbers of Walker-256 carcinosarcoma tumor cells failed to show evidence of tumor growth for inordinately long periods of time. The rats might well have been considered free of tumor. If, however, they were subsequently subjected to repeated surgical trauma in the form of laparotomy with liver manipulation, growth of dormant tumor cells occurred, so that 100 percent of the rats demonstrated hepatic neoplasms.

All animals were adult female Sprague Dawley rats weighing 150 to 175 gm at the time of injection. They were allowed to eat *ad libitum* on a stock diet of Chow checkers and water. The preparation of tumor cell suspensions and the technique of intraportal injection have previously been described in detail (*4*). An aliquot of a filtered saline plasma tumor brei was used for cell counting in a fashion similar to that used for leucocyte counting. Proper dilutions of tumor cell suspensions were made so that each 0.5 ml of the suspension to be injected contained either 250 (experiment 1) or 50 tumor cells (experiment 2). The animals were lightly anesthetized with ether, celiotomy was performed, and the animals were injected intraportally via a large mesenteric vein with 0.5 ml of the saline plasma solution containing tumor cells. To insure maximum viability of the tumor cells, no suspension was used longer than 1.5 hours after its preparation. Approximately 30 rats could be injected during this time. After varying periods of time, exploration for tumor was carried out by an aseptic technique. Animals were considered to have a tumor only after gross examination and later confirmation by microscope. All rats grossly free of tumor were reexamined at weekly intervals until growth was evident, or until they died.

In experiment 1, 122 rats were injected with 250 tumor cells each. Groups of 30 were first examined at 2, 3, and 4 weeks after injection, and 32 were inspected at 8 weeks. The results of this experiment are shown in Fig. 1. At first inspection there was no remarkable difference in the number of positives, whether the animals were looked at as soon as 2 or as long as 8 weeks, there being 20, 20, 27 and 16 percent with demonstrated neoplasms. But on subsequent examinations an increasing number became positive, so that after four laparotomies the 114 rats that survived the multiple surgical procedures all had tumors in their livers. In this experiment the finding of major significance was that all animals first examined at 2, 3, or 4 weeks and surviving multiple laparotomy were positive by 8 weeks, whereas only 16 percent of those opened for the first time at 8 weeks showed tumors.

When it was evident that animals showing no tumor for as long as 8 weeks after injection (84 percent) could be triggered into tumor growth by laparotomy and liver manipulation, experiment 2 was performed.

In experiment 2, 50 rats were injected intraportally with 50 tumor cells; 17 were explored for the first time at 12 weeks, 16 at 13 weeks and 17 at 21 weeks. No tumor was present in any of the animals at the time of first examination (Fig. 2) but, with repeated laparotomy between the 12th and 20th

weeks, all surviving animals had liver neoplasm.

These results would indicate that, when as few as 50 tumor cells are injected intraportally and no growth is observed in the liver for at least as long as 3 months, it cannot be assumed that (i) the animal has been able to "cope" with these few cells, (ii) an "insufficient" number for growths has been inoculated, (iii) the cells did not "lodge" in the liver, or (iv) the cells were not viable. It would seem that they did remain in the liver in a viable but dormant state until triggered into growth by some factor or factors still to be elucidated but in all probability associated with surgical trauma with its attendant metabolic alterations. The mechanism involved in under study. It is suggested that cancer cells, alive to begin with, may be enduringly capable of growth if conditions are favorable (*6*).

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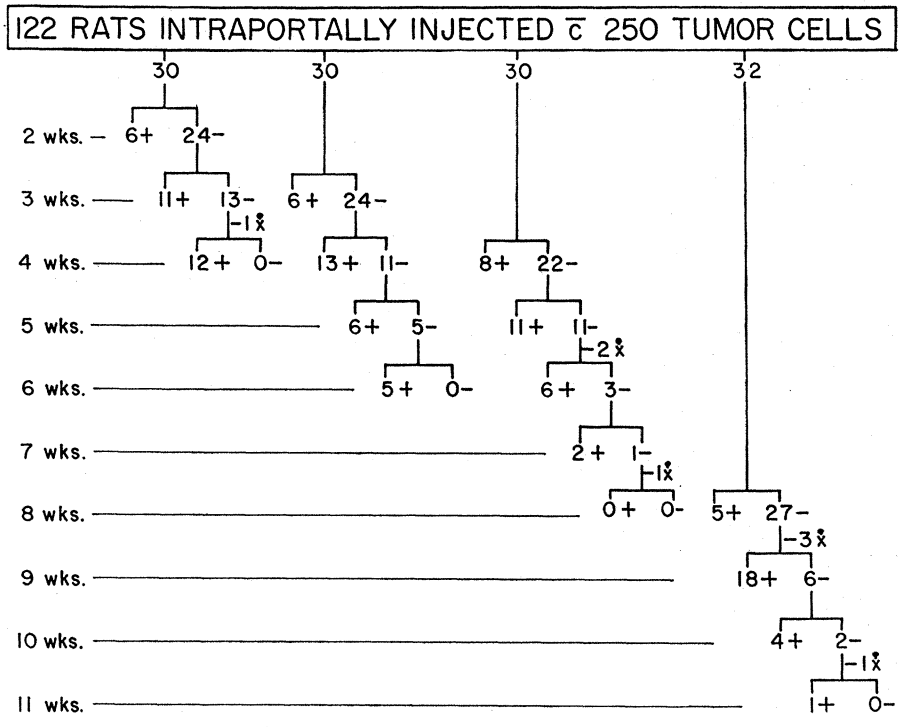

Fig. 1. Effect of repeated laparotomy upon the incidence of hepatic tumor growth following intraportal injection of 250 tumor cells: +, rats demonstrating liver tumor; —, rats free of hepatic tumor; *ẋ*, nonsurvivors.

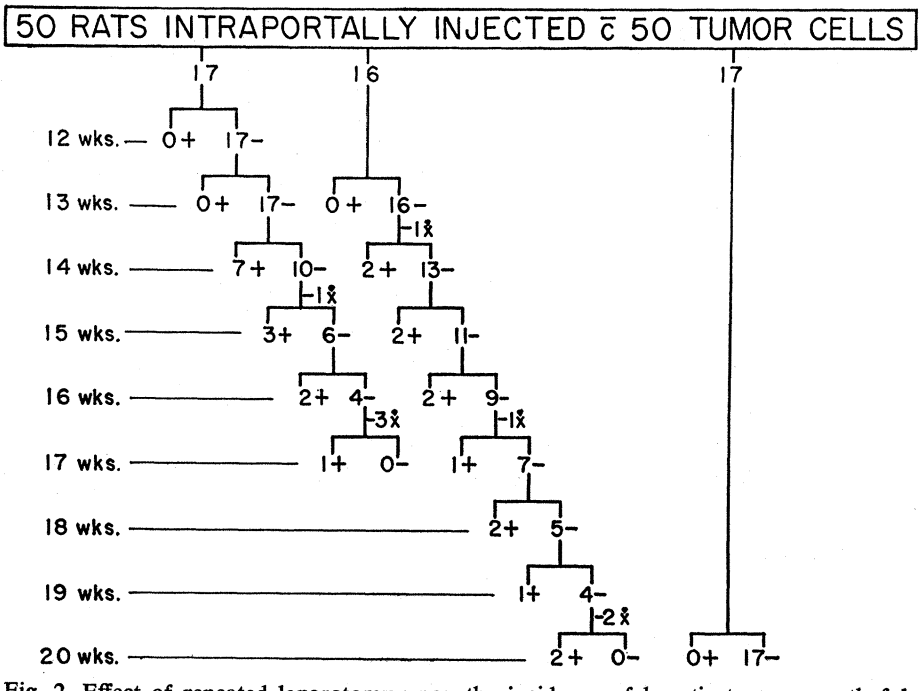

Fig. 2. Effect of repeated laparotomy upon the incidence of hepatic tumor growth following intraportal injection of 50 tumor cells: +, rats demonstrating liver tumor; —, rats free of hepatic tumor; *ẋ*, nonsurvivors.

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* Senior research fellow, U.S. Public Health Service.

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Fusion of Complex Flicker

Abstract. Brown and Forsyth have recently performed a flicker-fusion experiment showing clearly that there is more to flicker than meets the eye. This report presents an analysis of their results which indicates the likelihood that at fusion threshold all but one of the Fourier components of their presentation are imperceptible.

Brown and Forsyth have reported on a very interesting flicker-fusion experiment (*1*). They adopted a presentation extremely well suited to probing the visual processes taking place within a single cycle of flicker. A pulse $(A/2)$ msec long was followed by $(A/2)$ msec of darkness. Succeeding this was another pulse $(B/2)$ msec long, followed by $(B/2)$ msec of darkness. This sequence was continuously repeated. Those values of A and B which gave flicker fusion were then plotted, B against A (Fig. 2 of their report).

This report proposes an explanation of Brown and Forsyth's results and derives some implications from them. The explanation is based on a consideration of the Fourier components of their pulse sequence and on the explicit assumption that the subject discerns any one component at an amplitude which is independent of the presence of other components below threshold amplitude.

This treatment of stimulus components is suggested strongly by the results of de Lange (*2*) and of others cited by him. He presented a spot of constant average luminance modulated in various complex waveforms. For