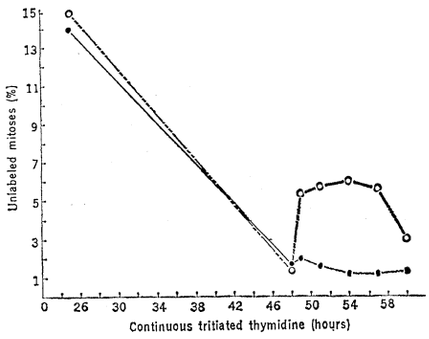

Fig. 2. Percentage of unlabeled mitoses during continuous labeling with ^{3}H-TdR, in controls (solid circles) and following administration of antiserum to mouse lymphocytes (open circles) after the 48-hour sample.

at 54 hours, 6.0 percent ($P < .01$); at 57 hours, 5.7 percent ($P < .01$); and at 60 hours, 3.0 percent were unlabeled ($P < .25$). One of the six tumors treated with ALS showed no response; the means above, however, include all six animals. In the later time periods, anaphases and telophases appeared following release of inhibition by colchicine in both groups.

At 48 hours the percentage of unlabeled interphase cells averaged 22.0 percent. Subsequently, the percentage of unlabeled interphase cells did not differ significantly in the two groups. The mitotic index increased in both groups after colchicine was given at 48 hours. The increase in the mitotic index was slightly, but insignificantly, greater in the group treated with ALS. Cytophotometry of unlabeled interphase tumor nuclei, contrasting the 48- and 54-hour samples in each animal, showed a modest but insignificant depletion of 4C, or G_2, nuclei in the 54-hour smears of the tumors treated with ALS.

The peripheral white blood cell count of mice with a 7-day-old ELD ascites tumor averaged 19,600 cells per cubic millimeter. Four hours after administration of ALS, the peripheral white blood cell count averaged 14,000 per cubic millimeter. A lymphopenia was observed in the intraperitoneal fluid after injection of ALS.

With immunosuppression, some unlabeled tumor cells were released promptly into mitosis, entering the cycling pool. Cytophotometry showed that there were many more unlabeled G_2 cells than could be stimulated into mitosis during the experiment. Our previous studies showed a similar mitogenic effect by hydrocortisone at 48 hours and at 96 hours of continuous labeling (*8*) and by azathioprine at 48 hours labeling. The presence or absence of colchicine made no difference. There was no mitogenic effect from distilled water or isotonic saline.

We conclude that some noncycling tumor cells were probably restrained by immune inhibition. The mitogenic response to ALS occurred within 4 hours after injection, persisted for about 6 hours, and then gradually subsided. Since unlabeled mitoses appeared promptly after treatment with ALS, despite continuing administration of ^{3}H-TdR, and since some unlabeled dividing tumor cells escaped the colchicine block to finish mitosis, we conclude further that immune restraint was probably exerted on metabolically competent, DNA-replicated tumor cells in the G_2 period of interphase. Immune inhibition is therefore one of the parameters controlling tumor growth in this experimental system (*9*). These results have a bearing on the concept of the dormant tumor cell.

Immunological control mechanisms have been demonstrated in experimental tumors by a variety of methods (*10*). Allogeneic and isogeneic lymphocytes have depressed tumor growth, possibly by inhibition of DNA synthesis (*11*). Antilymphocytic serum has increased the growth rate of tumors in mice (*12*) but had an unpredictable effect in another study (*13*).

The effect of ALS is apparently mediated by host lymphocytes (*14*). Action of sensitized lymphocytes is directed toward alteration of antigens bound to the surface of the tumor cell (*15*). Our evidence then suggests that administration of ALS, acting via immunologically competent host lymphocytes, resulted in a cell surface event that initiated mitosis in noncycling, G_2 population, ascites tumor cells.

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RNA Competition in RNA-DNA Hybridization Systems

It is interesting that results of Riggsby and Merriam (*1*) are explained by the findings of Britten and Kohne in the same issue of *Science* (*2*). Riggsby and Merriam found that in mammalian systems there is competition between RNA species in RNA-DNA hybridization systems only if the ratio of RNA to DNA is relatively high. The observations by Britten and Kohne that there are many hundreds of thousands of repeated sequences in DNA of higher animals readily explain why a high RNA/DNA ratio is needed. If the RNA/DNA ratio is low there will still be many of the redundant DNA sites to be covered by the RNA. In bacteria there is no redundancy of DNA sequences, hence this phenomenon is not observed.

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