# Inhibition of Walker Tumor by Autolyzed Lymphosarcoma Cells.* (23535)

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The concomitant growth of 2 different tumors transplanted in the same host has been observed either to inhibit or to promote the development of the involved tumors. Bruwer *et al.*(1) were the first to report that a growing Murphy Rat Lymphosarcoma (MRLS) could inhibit the growth of a Walker carcinoma transplanted in the same site. We later observed the same phenomenon and wanted to verify whether the inhibition was due merely to competition of the two growing tumors for an essential factor or whether the mechanism was more likely to be a direct action of the lymphomatous cells on the Walker neoplasm.

To study the effect of non-viable lymphosarcoma, we used a 3-day-old suspension of MRLS cells in saline, for we knew that this partly autolyzed suspension does not take when injected. The Walker tumor was transplanted in an air-pouch as this method is ideal for testing local actions.

*Materials and methods.* Sixty-five female Sprague-Dawley rats of the same age, weighing approximately 150-170 g, were distributed into groups each having a mean bodyweight of 160 g. The animals were fed exclusively Purina Fox Chow and received tap water to drink. The Walker neoplasm was transplanted by injecting 0.5 ml of a suspension containing 0.2 g of crushed tumor tissue per ml of a 1% saline solution. The autolyzed suspension of MRLS is prepared in the same way, but left 3 days in a closed, sterile container, at room temperature, before it is injected. An air-pouch is made by injecting 25 ml of air into the subcutaneous tissue situated between the shoulder blades of a rat. When a tumor suspension is introduced into the cavity of the air-bubble thus formed, a tumor-pouch is produced(2). Our present study consisted of 3 experiments. In the first, we used 25 rats divided into 2 groups. All animals received a Walker tumor transplant in an air-pouch. Group 1, composed of 10 rats, was given no other treatment and served as control. Group 2 consisted of 15 rats which received, immediately after the tumor suspension, an injection of 0.5 ml of autolyzed MRLS in the air-pouch. Our second experiment was an exact repetition of the first, except that two groups of 10 rats each were used. In the third experiment, 2 groups of 10 rats each were again used. An air-pouch was made on the back of all the animals. The experimental group received 1 ml of autolyzed MRLS in the cavity of the pouch, while the controls had no injection. After 10 days, both groups were given 1.5 ml of Walker tumor suspension. The air-pouches in the control group had to be partly reinsufflated to make them equal in volume to the MRLS injected pouches.

*Results.* In the first of the experiments with concomitant injection of Walker carcinoma and autolyzed MRLS, none of the treated animals showed any apparent tumor development on the 17th day after transplantations while all the control rats had died, bearing large Walker tumors. One of the treated animals was then killed and the site of transplantation compared with that of the last control to die (Fig. 1). Only necrotic tissue could be found in the MRLS treated rat. On the 24th day, tumor nodules began to appear at the periphery of the pouch in 4 of the remaining 14 rats. The tumor grew to a large size around the MRLS injected area and killed the 4 animals on the 43rd and 44th days. The remaining 10 rats were then killed and autopsied. No tumor could be found. The pouch had perforated and the necrotic tissue had been eliminated. Only scar tissue remained in the inter-scapular region.

Repetition of the same experiment gave the following results: Of the 10 controls, all de-

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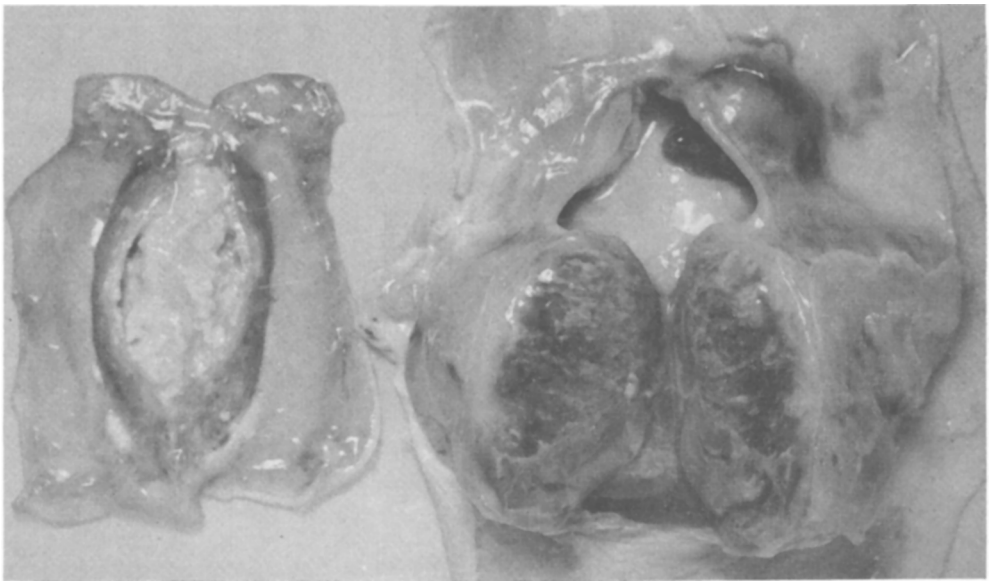

(a) (b)

FIG. 1. (a) Necrotic tissue in a 17-day-old pouch injected with both Walker tumor and autolyzed MRLS. The bearer was killed for photographic purposes. (b) Pouch of the same age containing Walker tumor alone. The bearer was the last of its group to die.

veloped large tumors and died within 15 days. None of the MRLS treated animals showed any sign of tumor until the 20th day, when nodules began to be visible around the pouch. These tumors developed and finally killed the bearers.

In the third experiment, the Walker tumor injected in the pouch prepared with autolyzed MRLS did not grow and was eliminated through perforations in the outer wall of the pouch in 7 of the 10 animals. In the remaining 3, late tumor nodules started to grow 3 weeks after transplantation, while all controls had died with large tumors before the end of the 2nd week.

*Conclusions.* 1. The inhibition of Walker tumors by MRLS tissue does not depend upon concomitant growth of the 2 tumors. Autolyzed, non-growing MRLS is also effective in preventing or retarding Walker tumor development. It seems that, when the inflammation caused in the air-pouch by the autolyzed suspension is sufficient to perforate the wall of the pouch and eliminate its content, no tumor will later develop. On the other hand, if no perforation occurs, the carcinoma eventually grows but is considerably retarded. The animals injected with MRLS survive sometimes as much as 2½ times (experiment 1: 43/17 days) as long as the untreated tumor bearers. Undoubtedly this is not the result of any type of inflammation, for we have studied the action on tumor growth of many irritants and autolyzed tissues, and none had an effect comparable to that of autolyzed MRLS(3). 2. The termination of the inhibitory phase seems to depend on the age of the Walker transplant (about 3 weeks) and not on the duration of the inflammation caused by autolyzed MRLS. Indeed, the tumor development is prevented for the same length of time, either by a 10-day-old MRLS-pouch or by a newly formed MRLS inflammation.

*Summary.* Autolyzed, non-viable lymphosarcoma tissue, when injected, either before or simultaneously, in the same site as Walker tumor, can inhibit or retard the growth of the latter.

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