STUDIES IN BIOLOGICAL RESISTANCES TO MALIGNANT TUMORS

IV. THE EFFECT OF MULTIPLE INJECTIONS OF IRRADIATED SARCOMA CELLS UPON THE GROWTH OF ESTABLISHED HOMOLOGOUS TUMOR GRAFTS

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Our failure to produce recognizable immunity responses in rats following a single injection of Roentgen irradiated tumor cells (1) prompted the attempt to establish some degree of protection in

![Chart V](image-url)
these animals by the use of multiple injections of the inactivated material. To this end we have used 3 injections of tumor cells which had been exposed to the "Rad" (2) dosage of Roentgen rays in treating rats with established homologous tumor grafts. The injections of 0.15 cc. each were made at intervals of a week. Aside from this change in the number of injections for immunization, the conditions of the experiment as outlined in our previous report have remained unchanged (1).

Charts V and VI record the results of an experiment of this type (Experiment 9).

In this experiment 78 rats with actively growing tumors were used. The tumor grafts were planted on December 20th, 1923, and three weeks later, on January 11, 1924, 56 rats received subcutaneous injections of the irradiated tumor cells. The second and third injections were made on January 18th and
January 25th, respectively. In this experiment 22 rats were allowed to go untreated as controls. The tumors in each of these 22 untreated rats showed regular progressive increases in size until all finally succumbed from the effects of the new growth. Of the treated rats, one showed the complete disappearance of the tumor four weeks after receiving the last injection, and another showed the same seven weeks after the last injection. With these exceptions the tumor progressed regularly in the same manner as did the tumors in the untreated animals.

In experiment 10 (Charts VII and VIII) 33 controls and 67 treated animals were used. Every animal whether of the treated or the control groups showed progressive increases in the size of the tumors from week to week (Chart IX), and all finally died as a result of the tumor. The curves depicting weights of animals, sizes of tumors and lengths of life in both the control and treated animals for each of these experiments are parallel.
DISCUSSION

Three injections of irradiated tumor cells at weekly intervals have failed to protect rats against established tumor grafts of the Rat Sarcoma No. 10 of the Crocker Institute. Neither have we observed a stimulating effect upon the tumor growth as a result of the injections. Chambers and Scott (3) have emphasized the possibility of a biphasic action in antigens of this type, namely a stimulating and an inhibiting action, with the result that either of these effects may be observed in experiments of this type. They claim partial but not consistent success in separating tumor antigens into fractions which show a preponderance of either the one or the other effect when subsequently injected into animals.
Chart IX. Showing the progressive increases in size of the tumors from week to week among treated and untreated rats in a typical experiment (Exp. X).
This conception finds analogy in the stimulating effects of certain materials added to tissue cultures in vitro. Much more work must be done before conclusions can be drawn to support this hypothesis.

As the study of experimental cancer has brought out numerous conditions which will inhibit or prevent the growth of a subsequently inoculated tumor, we feel that a method claiming to increase biological resistance should be efficacious also against established tumors. It is also necessary that it should be tested on a large series of animals, adequately controlled, as well as with as many experimental tumors as possible.

We believe that the differences in results obtained by us and the English investigators may be due perhaps to the frequent remissions that are known to occur with Jensen's rat sarcoma; perhaps to the conditions of our experiments which may have been too heavily "loaded" to permit the demonstration of an existent though weak increase in resistance; or perhaps to a combination of these factors.

CONCLUSIONS

The growth of established tumor grafts of Rat Sarcoma No. 10 was not affected by three injections at weekly intervals of homologous tumor cells devitalized by Roentgen irradiation under the conditions of our experiments.

The hypothetical biphasic action of antigens of this type requires further investigation in that it might have a bearing on the interpretation of failure to establish some degree of immunity in animals following the injection of devitalized tumor cells.

REFERENCES