

CLASSICS OF BIOLOGY AND MEDICINE

Interpretation of Some Results from Radiotherapy and an Attempt to Determine a Rational Treatment Technique^a

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We wish to discuss: (1) the strange selective action of X rays on epithelial tumors; (2) tumors produced by X rays.

Firstly, all physicians have observed with the same interest mixed with surprise that X radiation can kill the cells of a neoplasm while leaving the neighboring healthy tissues or even the tissues invaded by the tumor intact. But experiments on animals have shown that radiation has a selective action among healthy tissues. For example, in our experiments on the testicle of rat, we have been able to destroy the germinal cells whereas the interstitial tissue and the sertoli syncytium were unimpaired. As a result of these experiments, it has been possible to formulate the following law: X rays are more effective on cells which have a greater reproductive activity; the effectiveness is greater on those cells which have a long lineage, on those cells the morphology and the function of which are least definitively fixed. From this law it is easy to understand that roentgen radiation destroys tumors without destroying healthy tissues.

It was quite puzzling when many and incontestible observations demonstrated that these same roentgen rays capable of destroying malignant tumors in patients

were also capable, at times, of producing in the epithelial tissues of the radiotherapist, previously perfectly healthy, negligently exposed in the field of radiation, the appearance of tumors identical to the ones they can destroy. There is no longer any doubt about this point; X rays have produced in radiologists epithelial tumors in the skin of the hands which are invasive and metastasize to the lymph nodes. How can we interpret these apparently paradoxical results? Again, the animal experiments allow us to find a very plausible explanation for these facts. Regaud and Blanc have recently shown that the sperm of rats exhibit giant cells [formes monstrueuses] after exposure to X rays. We also have found teratocytes in our histologic preparations. These authors state clearly that these giant cells are due to atypical mitoses of the spermatocytes. On our part, we have also observed other testicular lesions which cannot be explained except by action of radiation on the overactive spermatogonia. It follows that the roentgenization, when it is not intense enough to kill cells, can still influence their further evolution. Is not an atypical evolution, in the present status of our

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knowledge, the main characteristic of epitheliomas and cancerous cells?

From the point of view of the practice of radiotherapy, one must learn from these facts that one must avoid the production of atypical mitoses by radiotherapeutic treatments. It seems pretty clear that the practice of delivering small and repeated doses, in contradistinction to the technique of few and heavy doses, is more apt to produce these nondestructive irritations with resulting giant cells and probably malignant transformations which have been observed. Therefore, one should prefer the method of massive doses. The ideal technique, given a complex tissue made up of two or more elements of which the element one wishes to destroy by radiation is characterized by a greater mitotic activity, would be to make this complex tissue absorb, at one time, the maximal dose of radiation compatible with the preservation of the other elements one wishes to preserve. This will be so much easier to achieve, and the curative effect much clearer, if the reproductive activities of the cells to be destroyed and of the tissues to be preserved are quite different. Radiation therapy seems to be contraindicated in those circumstances in which the histolog-

ical characteristics of the tissues to be destroyed and of the tissues to be preserved are equal with respect to reproductive activity. As a matter of fact, in this case there will be no selectivity of the X rays and there is no dose which would be adequate.

When the two elements, one of which is to be destroyed by radiation therapy, have slight reproductive differences, it is very difficult to devise a technique and to determine the doses which should be used. It is in this case that monster cells and atypical mitoses are most likely to be produced after the application of the X rays. One can see from this discussion how much the histological makeup of the tumors is important to the understanding of radiotherapy.

Assuming all this information is available, there are still many more facts to be known before one can really determine radiation therapy absolutely scientifically. One must not forget that an X ray beam, even with the best determined spectrum, is very heterogenous and that the specificity of responses of various cells to this complex radiation is still to be determined; this is the aim of our current research.