

THE RATIONALE OF ROENTGEN- AND RADIUM-THERAPY.

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THE time has perhaps arrived when we may endeavour, with some prospect of success, to reconstruct the rationale of Roentgen- and Radium-therapy, or at all events, to collect the materials for such a reconstruction. We have already at our disposal a vast amount of material accumulated during many years of empirical treatment, but our data, both physiological and pathological, are so bewildering that it is almost hopeless to attempt to marshal them in any due sequence or order.

We are dealing with an agent which appears to blow both hot and cold. The X rays are said to cure cancer, but they also cause cancer. They stimulate epithelial growth, and destroy embryonal tissue; they increase metabolism and raise the resistance of the organism; and, on the other hand, they attack the leucocytes and arrest growth and development. X rays of exactly the same quality in slightly different doses will cause irritation with increase of physiological activity, paralysis and inhibition with subsequent restitution of function, or total destruction of tissue and death.

It is high time that we had some working hypothesis to account for all this, even if only to serve as a finger-post for further research. For we are in presence of a new conception in medicine—not the chemical reactions of material remedies with which we are more or less familiar, but the impact of ethereal waves on living tissue.

These ethereal waves, of various lengths and frequencies, are the real therapeutic agents; not alone, be it said, the waves as they leave the Roentgen bulb or radium capsule, but the secondary rays excited in the irradiated tissues themselves. This is true both in radium- and Roentgen-therapy, for a radium capsule is but a portable Roentgen bulb, and an X-ray target is an applicator artificially radio-active.

It would be a matter of convenience if we had a word to include both Roentgen and radium treatment. I would suggest the term “gamma-therapy”—*i.e.*, treatment by gamma rays. Gamma-therapy will then include, not a single invariable modality, but maybe a variety of undulations as numerous as the remedies of pharmacological medicine.

The radio-therapist has been reproached with using one and the same remedial agent—the X rays—as a sort of panacea for a large number of different diseases, varying both in causation and character. Our critics, however, are forgetful of the fact that the term X rays covers a great variety of gamma radiations, and that a Roentgen irradiation varies, not only with the quality and quantity of the rays, but also with the nature and thickness of the filter, and with the density and chemical composition of the irradiated tissue.

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Unfortunately, the X rays have been hitherto regarded as a more or less homogeneous and constant application, whereas Roentgen rays of different hardness are as different in their therapeutic action as alkaloids from different plants. Each quality of rays has its own selective, physiological, and pathological action, and each has its appropriate dose. No. 5 Benoist is one remedy, No. 7 Benoist is another remedy, while No. 7 Benoist filtered through aluminium differs in quality and potency from No. 7 Benoist filtered through silver. Roentgen rays of different wave-lengths may possess effects as different as those of morphia and strychnine.

Hence the first desideratum for accuracy of treatment is the definition of the quality of the X rays. The ideal prescription would give the quality of each component of the beam in terms of its wave-length and intensity. This is at present impossible, and we must still content ourselves with relative measurements. Some recent experiments at the Cavendish Laboratory have shown that the penetration, or hardness, of a beam of X rays may be best measured by the velocity of the exciting cathode rays as they strike the anticathode. This velocity might therefore be used in our prescriptions as a definition of the quality.

A more practical method, however, would be to define the beam of rays by the nature of the secondary rays which it is capable of exciting, since each metal emits secondary rays of a definite character, and emits no secondary rays unless bombarded by rays harder than those of its own peculiar radiation. Hence we may speak of a "copper" or a "silver" X-ray beam, meaning thereby a beam of rays just hard enough to excite secondary rays in a copper or a silver plate. Either of these methods would give us some real measurement of the maximum hardness of the X rays which we are using, and would be infinitely more precise than the radio-chromometric methods at present in use.

There are three conceptions which may assist us in building up an hypothesis to account for the therapeutic action of the gamma radiations. One is the "Radio-vaccination theory," which I brought forward recently in the discussion on vaccination at the Royal Society of Medicine. This is a vitalistic theory.

The second, the "Mechanical theory," is founded on Leduc's observations of the formation of poles of diffusion and centres of osmotic force by dissociation or ionisation of the larger molecules.

The third, which I may call the "Cannibal theory," is founded on the interesting researches of Mr. H. C. Ross—viz., the stimulation of growth and mitosis as a result of the death of neighbouring cells.

The first hypothesis, that of radio-vaccination, has gradually grown up to account for a number of phenomena otherwise inexplicable. The first of these was the fact that a number of skin diseases of totally different origin and nature seemed to improve under exceedingly small doses of X rays. Psoriasis, lupus, eczema, were all apparently benefited. An acne which had resisted treatment for years would disappear under the rays just as if treated

by injections of vaccines. What more natural than to suppose that the patient himself had furnished the necessary vaccine, under the stimulus of the Roentgen irradiation. The hypothesis received still further confirmation when cases of lupus were reported in which irradiation in one region—for instance, the leg—was followed by improvement in another region, such as the face. The same thing was observed in other diseases. Acne of the face was apparently cured by X rays applied to the similar lesions on the back or shoulders. High-frequency effluves applied to a crop of boils would apparently render the patient immune to further inoculation; lupus erythematosus of one region was influenced by X-ray treatment of another part, and even widespread carcinoma of the breast was improved by irradiation of a portion only of the affected area.

Further corroboration was afforded by the observation that in certain cases of lupus, and even of cancer, irradiation of the affected glands was followed by an improvement of the lesion itself.

Even the ordinary process of Roentgen epilation appears to be a biological, rather than a merely destructive, phenomenon. At all events, it is at least in part a vital reaction, a phagocytosis, since it has been found that the process of epilation is more rapid in the diseased areas, and is delayed by the application of disinfectants and the consequent depression of the processes of vital reaction and repair.

But the strongest evidence of the vaccinal action of X-ray treatment is derived from a consideration of the various modes of attack on rodent ulcer. In the whole purview of medicine there is nothing more impressive, or more certain, than the cure of a small rodent ulcer by electrical methods. But the cure may be affected in many ways—by Roentgen rays, by radium, by ultra-violet light, by high-frequency effluves, or by zinc ions. What is the common factor in all these cures?—cures, I say, for the process is not one of destruction, but of repair. It is not merely a bactericidal action, nor is it merely a selective action on the tissues. It is a biological recoil, the resentment of the cells of the organism to the insult of the ethereal vibration. The habitual defence of the living cells to such an insult is exactly the same as that to a bacterial invasion—viz., the production of antitoxins and other antibodies. It is, in fact, a true vaccination.

One of the greatest arguments in favour of the vaccinal hypothesis is the occurrence of a latent period after a Roentgen or radium irradiation, a latency which precedes the reaction. This ominous pause is, to my mind, most eloquent. It proves that all the resources of the organism are being called upon to resent the insult. The reaction is not merely a physical or chemical one, but a true vital or biological reaction, in which the energy of the recoil may overstep the energy of attack. Let me explain. If I strike an inanimate object—the table, for example—it returns the blow immediately, and strikes my knuckles with the exact force I expended. But if I strike my neighbour, he would probably return the blow with interest, an interest which would be rather increased than lessened by a brief period of latency. Similarly, the

pause after Roentgen irradiation is proportional to the degree of the insult, and is a participation of the whole organism to resist the electrical or ethereal invasion.

In opposition to this vitalistic theory we have the physical theory as propounded by its great exponent, Professor Stéphane Leduc. This explains the processes of mitosis and cell division as conditioned merely by the physical laws of osmosis and diffusion. In this view the destruction and the stimulation, the cure and the production of a cancer cell, may equally be explained by alterations in surface tension and diffusion. We may suppose that the gamma rays break up the larger molecules of the tissues into smaller groups, or ions, thus producing local foci of increased concentration, and centres of osmotic force.

The most fertile hypothesis, however, is, in my opinion, the third one, which I may call the "cannibal hypothesis." The theory is founded on the researches of Mr. H. C. Ross on the induced division of leucocytes and the genesis of tumours, a report of which, written by Sir Ronald Ross, appears in the ARCHIVES OF THE ROENTGEN RAY for April, 1912. It must, however, be understood that I alone am responsible for importing his idea into the realm of radiotherapy. Briefly, the hypothesis is that both physiologically and pathologically cell proliferation is primarily due to cell death. Cell death is the originating cause both of cell growth and of tissue repair. In cancer, cell death causes the growth of the tumour—a sort of hypertrophied and badly-nourished scab or scar. In fertilisation, cell death—possibly the death of part of the spermatozoon—is the *causa causans* of the division and segmentation of the ovum. Similarly, in Roentgen and radium irradiation, cell death is the basis of all therapeutic action.

The researches at the Lister Institute have shown conclusively that the division of the leucocytes of human blood in vitro may be set agoing by the addition of creatin, xanthine, and other chemical products of cell destruction. The ova of *Ascaris megalocephala* may be caused to divide by the same means, and in animals tumours may be produced by the injection of chemicals containing the amidine group.

It will readily be seen how well this hypothesis fits in with the phenomena of Roentgen and radium irradiation. It has always been difficult to picture to oneself a process which in certain doses shall destroy a cancerous tissue, and in other doses and other circumstances shall stimulate a malignant growth, and X rays are undoubtedly capable of doing the one and the other. The new hypothesis, however, supplies us with a simple explanation. The gamma rays bombard the irradiated tissue. As a consequence, we shall find here and there, scattered at more or less regular intervals through the irradiated tissue, a dead cell or leucocyte which has been struck by the radiating hail of projectiles. These corpses will be found at different depths, sparsely scattered throughout the whole extent of the irradiated tissue. The products of their decomposition will attract and stimulate the multiplication of the cannibal wandering phagocytes, and at the same time set free a supply

of energy for the aboriginal cells of the tissue. The whole neighbourhood is stimulated, and strange cells are attracted from afar to the fratricidal feast. This will account alike for the absorption of an adenoma under the action of the X rays, or the disappearance of a lupus under radium irradiation. If, however, the destruction be too extensive, other chemical substances may be produced, and the cells of the irradiated area themselves will be stimulated to abnormal growth, as is sometimes the unfortunate result of excessive irradiation in an X-ray burn or lupus scar.

Not only so, but the so-called *auxetics*, the products of decomposition of the slain cells, will be carried by the circulation along the blood and lymph channels to a distance, and will there stimulate the mitosis of similar cells in other parts of the body. This may indeed be the real *modus operandi* of "radio-vaccination"—the cure of a lupus, or the like, in one region by the irradiation of another distant area.

The new theory asserts that cancer is due to the combination of two factors, the ordinary stimulants of cell proliferation, plus substances called "augmentors," which are produced in chronically injured tissues by the action of saprophytic bacteria. The X rays cause a limited and scattered cell death, which in turn stimulates chronic cell proliferation. Later on pathogenetic bacteria invade the site, producing augmentors, such as choline and cadaverine. It is the combination of such augmentors with auxetics, such as creatine, that gives rise to malignant proliferation and infiltration.

It is interesting to note that here, as elsewhere in Nature, every increase of life is associated with death. It would appear as if the progeny must draw its energy as well as its material from the parent stock, as if the chemical energy which we designate by the vague form "vital" were in some mysterious manner passed on from the old and dying to the young and growing cell. How, otherwise, can we account for the fact that products of death and disintegration are the chosen stimuli of life, and that even histological cells, like men, must rise "on stepping stones of their dead selves to higher things"?

In conclusion, let me express my belief that the various modalities of radio-activity will play a most important rôle in the medicine of the future, as they have doubtless done in the evolution of the past, and even in the mechanism of Life itself. If, as has been suggested, radio-activity furnishes that minimal impulse required to liberate the dormant energy of the seed and soil, what wonder that those ethereal undulations which are at the basis of growth and development should become the chosen agents for modifying physiological and pathological processes.
