

## SELENIDE TREATMENT OF CANCER

## A CRITICAL REVIEW

In a recent paper<sup>1</sup> Dr. A. T. Todd gives an account of the modifications introduced into the method of colloid treatment of cancer, begun in Bristol eight years ago, with colloidal lead selenide. The changes are, briefly, the elimination of lead entirely, except for the local application to ulcerated growths of lead amalgam ointment, and the substitution of two new colloids—a sulphur selenium colloid "SSe," and a radio-active selenium colloid "R.A.S." In the latter, selenium is combined with feebly radio-active radium residues, radium G and higher disintegration products.

The treatment begins with intravenous injection of SSe, followed two days later by  $1\frac{1}{2}$  Holzknrecht units of deep  $\alpha$  rays. The reaction which follows each of these procedures—mild exacerbations of symptoms—is carefully noted, and the repetition of both at weekly intervals aims at maintaining this degree of reaction, the dose of colloid and of  $\alpha$  rays being adjusted accordingly. This first course lasts eight weeks—that is, till 12 H of  $\alpha$  rays have been applied. Alternation then begins, and for three weeks a weekly dose of R.A.S. is administered, again aiming at a moderate but definite reaction. SSe and R.A.S. are then given on alternate weeks for a period of six months. In a case progressing satisfactorily injections then cease for eight to ten weeks, after which a further course of alternating SSe and R.A.S. is maintained for three months more. When progress has continued for nine months treatment is stopped, and the patient attends for observation only for a further period of six months. He is then discharged, being warned to return if any suspicious symptoms occur.

## Theoretical Conceptions

It will be obvious from this summary that even in favourable cases treatment is tedious; in unfavourable cases it may last longer, and is continued till the patient is moribund, for even in desperate cases improvement may ultimately set in. In discussing the reasons for the modifications embodied in his new methods Dr. Todd draws attention to the exacerbation of the disease which followed the attempt to combine  $\alpha$ - or radium-radiation in therapeutic doses with the earlier colloidal lead selenide (D4S) treatment. Excessive doses of the colloid gave the same result in animal experiments. This effect Dr. Todd believes to be due to the presence of the radiation-sensitive selenium, converting a relatively small into a relatively large dose of radiation, as it is well known that excessive radiation of an insensitive new growth may lead to aggravation of symptoms and more rapid progress. It is possible, as he maintains, that these effects are in both cases due to damage of a defensive mechanism.

In an interesting digression Dr. Todd expounds his conviction that the new growths are the result of an infective virus, and that his treatment is successful because it is adapted to this conception of the disease. The reviewer does not believe that this is necessarily true. Even in the filterable tumours of the fowl, in which the evidence for the participation of a causative virus is strongest, the virus is so firmly combined with the cell structures that even the strongest viricidal antisera (active against filtrates) are incapable of rupturing the combination and of robbing living cell-suspensions of their property of giving rise to new growths. Still less is this possible in a growing tumour, and for pathological and therapeutic purposes the cell, with its contained infecting agent, forms an indissoluble pathogenic entity. If an analogous cell-

virus complex subsists in the neoplasms of mammals the unification is even more complete, and the therapeutic problem is essentially the problem of the destruction or encapsulation of the parenchyma cells of the new growth. This encapsulation is essentially a non-specific overgrowth of the stroma, and it may be brought about in a variety of ways. It is still impossible to predict the outcome of treatment by these procedures because rather narrow limits are set to the amount of stimulation the stroma or "junction tissue" can tolerate, and because of the second incalculable variable—the inherent malignancy or virulence. This varies from one neoplasm to another, but is relatively constant in any one tumour. The upper threshold of effective stimulation of the "junction tissue" cannot be passed without disaster. Hence it comes about that only by the therapeutic test can the cancer cases be distributed into the classes in which the treatment is more or less successful or fails.

## Results of Treatment

After discussing the prognosis, both from the purely clinical side and from the outcome of certain laboratory tests, Dr. Todd gives the results of the treatment of two series of cases. Series I, May, 1931, to September, 1932, comprises ninety-five unselected cases, untreatable by surgeon and radiologist. In this series, of those patients who had completed an adequate course twenty-nine have died and fifteen are alive and well. Three patients apparently cured died from other causes. In series II, sixty-two cases, unselected as to clinical and pathological state, twelve patients who had received adequate treatment have died and three have been discharged as apparently cured. In assessing the significance of the duration of freedom from symptoms it should be remembered that the apparently cured have been under observation for six months without treatment before discharge. From the data supplied it is not possible to ascertain the survival times after "toilet" operation, and many will regret this omission. Dr. Todd informs me this interval has never been less than six months before discharge: usually "toilet" operation, or, for example, colostomy, is done at the beginning of the treatment.

## Summary

To sum up, approximately 20 per cent. of unselected patients with cancer, rejected by surgeon and radiologist, have been restored to health. Of the remainder a considerable fraction have shown temporary improvement. Is this method of combined colloid and radiation therapy which Dr. Todd has developed with a patience, ingenuity, and sustained enthusiasm that all must recognize, capable of still further improvement? Or does it effect an unconscious, unforeseeable selection of a group of patients who, left untreated, would die, but having the germs of a defensive mechanism and a not too high degree of malignancy of their neoplasms, can have the scale turned in their favour? Only by a wider test of the method by others, and by its application as a preventive of recurrence after operation as Dr. Todd suggests, can this fundamental dubiety be satisfactorily resolved.

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The twenty-second annual report, in the *Journal of the American Medical Association* of May 19th, on the ninety-three cities of the United States with a population of more than 100,000 shows that for the first time since the summaries were undertaken no city registered a typhoid mortality rate higher than 10 per 100,000. Sixteen cities had no typhoid deaths at all—an unprecedented record. The improvement is probably somewhat greater than the figures indicate, since the estimate of the 1932 population is made without allowing for possible increase.

<sup>1</sup> *Brit. Journ. Surg.*, 1934, xxi, 619.