

the relationship has been deliberate. In the first place, it is due to an effort to elucidate those forms of cancer with which irritation is most constantly associated, without considering other forms in which the particular irritants concerned do not play a part. In the second place, it is due to the fact, already frequently emphasized, that these irritants have nothing in common beyond their association with cancer. The varied investigations of the past nine years have added a knowledge of new forms of irritation. It has become more and more evident that irritation effective in one case may be, and often is, quite ineffective in another.

The experimental aspect of the comparative investigation of cancer has met with much adverse criticism, largely because of the necessity for reproducing experimentally all the natural lesions of the disease, and then utilizing this procedure to devise methods to prevent them, as well as from the necessity for cultivating the cancer-cell in order that a constant supply may be available for a variety of purposes. This supply can most satisfactorily be maintained by growth in living animals, the application to tumour-cells of Ross Harrison's method of cultivating normal tissues in coagulated plasma by Burrows and Carrel being still impracticable as a routine method of continuous propagation.

Ever since the beginning of these investigations it has been maintained that the mere cultivation of cancer had important, if only indirect, bearings upon its nature and genesis. Thirty-five of the tumour-strains have now been growing for over three years—*i.e.*, for longer than a mouse lives—while fifty other strains have been grown for extended periods. The one feature all these tumour-strains have in common is the power of continuous growth which they possess, in spite of the most divergent structure, and of extremes in the rate of growth varying from an almost explosive rapidity to one much inferior to that of embryonic tissue, as determined by weighing experiments.

It can be shown that there is a constancy in the behaviour of a tumour-strain and a variability which is individual. The variations which occur are similar to those which distinguish the eighty-five strains from one another. They are not mainly induced by the environment, but rise spontaneously; otherwise all strains would approach a common type, which they do not. The demonstration of the occurrence of these variations under artificial conditions permits of the inference that they could also occur under natural conditions, and yields objective evidence of the validity of the conclusion that the cancer-cell is a biological modification of the normal cell endowed with many inherent properties of the latter. The objection at once suggests itself that these variations during prolonged propagation are secondary, and do not necessarily indicate corresponding primary changes as responsible for genesis; but this objection cannot be maintained against the facts that the potentiality for variation has been demonstrated, as has also the tenacity with which the several varieties are adhered to.

It has been ascertained that every fresh transplantation effects a disturbance of the cancer-cells. They are thrown into a state equivalent to regeneration from which they tend to recover, as analogous as possible to reactive proliferation when naturally occurring. Hence the features observed under artificial propagation throw suggestive light upon the nature of cancer and its genesis in those cases in which a prolonged phase of reactive proliferation has intervened between the first response to irritants and the development of cancer.

#### *Immunity and Therapeutic Investigations.*

Apart from the investigations in which the reactions of immunity have been employed to elucidate the nature of cancer, numerous experiments bearing upon the possibilities of treatment have continued to be made. The onset, rise, fall, and disappearance of immunity as induced by the inoculation of normal and cancerous tissue have been accurately defined in parallel experiments. The distinctions and similarities in the immunizing powers of different tumours, especially of sarcoma as distinct from carcinoma, have been extensively studied. The dissemination of cancer has been studied experimentally both by injecting cancer-cells directly into the blood-stream and by implanting them in internal organs. It has been found possible to produce the lesions of dissemination in these ways both in the absence and in the presence of a primary growth, and, what is more important also, to prevent them. Since every procedure found efficacious to modify in any degree the growth of transplanted cancer has been tested on mice naturally affected with the disease it is needless to enter into details, more especially since problems difficult of solution in the mouse, because of its small size and the short duration of its life, can now be studied under the more favourable circumstances obtaining in the rabbit.

As pointed out in previous reports, nothing but harm can result from the premature application to the treatment of the human subject of methods still found to modify the growth of propagated cancer in animals. In order to emphasize still more strongly this warning, it may be stated that the methods which induce an active immunity to propagated cancer have been tested on thirty-three mice with natural cancer, and have given no evidence of powers either to hinder growth and dissemination, or to prevent recurrence of spontaneous cancer after surgical removal. These methods have also been found to be of no avail in preventing the successful inoculation of an animal with its own tumour; and they have their practical application at present only in the elucidation of the properties of cancer-cells.

The successful treatment of animals bearing propagated cancer, by means employed to induce passive immunity, has been described by other investigators. Some of these methods have been tested in the laboratory, but have not yielded positive results. It becomes increasingly evident that the therapeutical treatment of cancer is not to be sought for along these lines.

A considerable number of cases of natural healing of spontaneous malignant new growths have now been observed in mice affected with spontaneous cancer. The changes leading to natural cure appear to depend, as in propagated cancer, on an altered condition of the cell and its contents, rather than on an alteration in the general condition or constitution of the affected animal. Means must be devised for elucidating the nature of the change in the cell before curative measures can be discovered.