THE PART PLAYED BY INJURY AND REPAIR IN THE DEVELOPMENT OF CANCER;

WITH REMARKS ON THE GROWTH OF EXPERIMENTAL CANCERS.*

BY

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CAN we demonstrate experimentally the reason for the very localized starting-point of a tumour, although a great number of epithelial cells had been in contact during days and weeks with the cancer-producing agent (tar in the case of the experimental tar cancer)?

Mice were tarred in the usual manner till some of the animals showed early papillomata. Under the microscope these tumours proved to be very localized epithelial hypertrophies. We know that in this stage of the experiment the skin of the mouse tends to form numerous tumours in a very short time when tarring is continued, but that if tarring is stopped at this stage only a very small number of tumours will appear. The tarring was stopped at this stage of the experiment and a few days afterwards incisions were made in the skin, care being taken to make them in places where no papillomata had appeared. These wounds very soon assumed an oval shape and healed in the normal time. There was first a layer of fibrin and dead cells, and under this material we very soon found the first symptoms of healing in the form of new epithelial cells. In the majority of cases we observed in the wounds—healed or partly so—new tumour processes. In some instances there were only two or three tumours in one scar, in others there were many more. I never observed that the whole scar was involved in the tumour process. Sometimes the tumour growths were so numerous that the scar could be localized with the greatest ease. I have said that the tumours appeared in some cases after the scar had healed and the new epithelial cells—that is to say cells never themselves in contact with the tar—produced in these experiments primary growths. We know there is a relation between tar and tumour formation; we now learn from these experiments that the liability to tumour formation can be transferred to daughter and grand-daughter cells without the cells showing any change microscopically, nor in the biological sense. These tumours which we produced just at the place where we expected to see them were very malignant, and sometimes in a very short time the whole scar and the surrounding tissue were replaced by a typical cancer growth. We have thus an opportunity of getting a clearer insight into the local origin of tumours in a skin area where all the cells had been in contact with the cancer-producing material. Every now and then the animals get little wounds. These wounds may be so small that they escape attention. They heal as a rule very quickly, and we may suppose that some of them will produce a tumour in the same way as was shown in our experiments. In a very short time these tumours may be larger than the little (often almost invisible) scars from which they started. These experiments may have a general significance for the local beginning of a tumour.

Some other experiments throw a light on the old question of the manner of extension of a tumour. When we study the first beginning of a tumour we find a local hypertrophic growth. Somewhat later the surrounding cells hypertrophy also, and so on, until there exists on the skin a hypertrophic proliferation generally in the form of a papilloma. The way in which such a papilloma grows seems to indicate an influence of the central parts of the papilloma on the surrounding cells of the living organism, with the result that the latter also hypertrophy. At a later stage the central parts of the papilloma are changed into cancer cells, and we noticed that the cancer cells influenced the surrounding hypertrophic cells exactly in the same way as the hypertrophic cells had before influenced the surrounding normal cells.

These observations on the growth of young tumours, as was demonstrated in 1924 at the cancer congress in Strasbourg, bear out the old view of Virchow. It must be of

great value to show in another way the influence of tumour cells upon the surrounding living cells of the organism.

In the first part of this paper I demonstrated that young (regenerating) epithelial cells, in certain circumstances, are very susceptible to tumour formation. On the strength of that observation I made the following experiment: Mice were tarred on the epilated skin until there appeared a few little papillomata, then we stopped applying the tar. A few days afterwards we made two little scarifications, one which was in contact with the tumour, the other at some distance for the purpose of control. We marked the position of these wounds by rubbing in Chinese ink, and after two or three days they were healed. Only a small black line under the new epithelium showed the place where the fine small scalpel had cut through the upper part of the skin. The little healing wound, which either touched the tumour or very nearly did so, showed some interesting changes. The whole mass of new epithelial cells in this wound changed into hypertrophic growth. We never saw in scars that were not in contact with a tumour changes of the same extent. There must be an influence of the tumour cells on the cells of the scar. We know that these cells were very liable to become neoplastic, and therefore it was possible to show this influence clearly. Just as we have seen in a papilloma, the surrounding cells were predisposed to hypertrophic, and afterwards real, tumour growth.

Summary.

1. Injury may have a direct influence on tumour genesis in an extensive area of epithelial cells that are susceptible to tumour formation.

2. Former experiments have made it probable that in the earliest stages of tumour formation the peripheral cells may have an influence on their immediate neighbourhood. When we effect contact between the youngest tumour cells and cells which we know are very susceptible to develop a tumour, then we can clearly see the direct influence of the tumour cells on the other cells of the organism.

It will be the purpose of cancer study to obtain a better insight into these intercellular activities.

SEQUELAE OF ENCEPHALITIS LETHARGICA:

NOTES ON 128 CASES.

BY

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DURING the spring and summer of 1924 there were under my care in Belvidere Fever Hospital, Glasgow, 143 patients suffering from encephalitis lethargica. Of 132 patients who were discharged from hospital, 128 were examined twice within a year at roughly six-monthly intervals.

The Degree of Impairment.

During the acute attack the cases were divided on a clinical basis according to the outstanding clinical feature—namely, lethargic, choreiform, myoclonic, psychotic, hyperalgesic, ophthalmoplegic. They were also classified according as the attacks were mild or severe, and these classifications were used to ascertain what correlation, if any, existed between the degree of impairment and the type and severity of the original attack. The results of examination a year after the attack are embodied in the following table.

Group.	Type of Attack.		
	Mild.	Severe.	Total.
I. Cases with no impairment	37	12	49
II. Cases with slight impairment (working or attending school, but with difficulty)	28	13	41
III. Cases with marked impairment (unfit for work or school)	7	21	28
IV. Cases with very marked impairment...	—	10	10

* Read before the Royal Society of Medicine, Pathological Section, March 14th.