

The Viability of Human Carcinoma in Animals.

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The object of the present research is to determine the cell changes occurring in portions of human carcinoma implanted into animals, and more particularly to ascertain if such implanted tissues are capable of surviving for a time, and if so, the manner in which they succumb.

Implantation of human carcinoma into animals has been made by numerous observers, and the failure of such implantations to produce tumours is now an ascertained fact. Among the earliest experiments are those of Ballance and Shattock,* the objective of which was to determine if human carcinoma was transferable from man to animals; in these observations the immediate effect of implantation upon the cells of the growth was not determined. Von Langenbeck,† Jürgens,‡ Dagonet and Maclaure,‡ and Gaylord§ produced in animals, by inoculation of carcinoma, tumours which, however, differed in structure from the original. Lewin|| succeeded in obtaining inoculable granulomata in dogs by implantation of a human ovarian carcinoma, and also in rats by inoculation of a carcinoma of the cervix of the human uterus; this author made numerous attempts to obtain inoculable tissues by implantation of human carcinoma, but only the above two were successful.

The effect of implantation of mouse carcinoma and sarcoma into rats has been studied by Ehrlich,¶ who found that during the first 8—10 days after inoculation the rate of growth was scarcely less than before implantation;

* "A Note on an Experimental Investigation into the Pathology of Cancer," 'Roy. Soc. Proc.,' 1890, vol. 48, p. 392; 'Brit. Med. Journ.,' 1891, 1, p. 565.

† Quoted by Lewin, *loc. cit.*

‡ "Versuche über die Übertragbarkeit des menschlichen Carcinoms auf die Ratte," 'Archives de Médecine Expérimentale,' 1904, No. 5, September.

§ "Über die Bedeutung der Plimmerscher (bezw. Sjöbringschen) Körperchen und die durch menschliches Material erzeugtes Krebswucherung bei Tieren," 'Zeitschr. f. Krebsforschung,' 1903, vol. 1, p. 93.

|| "Über Versuche, durch Übertragung von menschlichen Krebsmaterial verimpfbare Geschwülste bei Tieren zu erzeugen."

¶ 'Beiträge zur experimentellen Pathologie und Chemotherapie,' Leipzig, 1909, p. 135.

at the end of this period, however, growth ceased and gradual absorption occurred.

The method adopted in this research was that of implanting subcutaneously, with aseptic precautions, several selected portions of a malignant growth, freshly excised (pieces being put aside for microscopical observation), and following up the changes taking place in the cells of the growth by reference to sections of the implanted masses, removed for examination at different periods. The time elapsing between separation from the human body and the completion of implantation varied between 20 and 25 minutes. Implantation was effected by puncturing the skin with a straight cataract knife, and introducing on the point of the knife a piece of tissue having the form of a cube of $1-1\frac{1}{2}$ mm. The portions of tumour implanted were removed at intervals of 1—13 days.

The number of tumours used for implantation was 41; 10 tumours were, however, employed in connection with unsuccessful implantations, so that only 31 need be referred to here. Of these, 19 were epithelioma (17 primary growths, 2 secondarily infected glands), 10 were scirrhus of the breast (9 primary growths, 1 secondarily infected gland), 1 was spheroidal-celled carcinoma, and 1 rodent ulcer. Implantation was made upon the monkey (20 tumours), rabbit (4 tumours), pigeon and guinea-pig (each 2 tumours), cat, rat, and mouse (each 1 tumour).

The usual causes of unsuccessful experiments were suppuration and failure to recover the pieces of tumour implanted. Suppuration was not met with so frequently as was expected, even in the case of growths ulcerated on the surface; when present, sometimes every piece of a tumour used for implantation became the seat of suppuration, in other cases suppuration occurred at some of the sites of implantation, while at others no inflammatory reaction occurred. A more serious difficulty was failure to recover the portion of tumour implanted. In a small number of cases this arose from the piece of tissue lying near the opening in the skin by which it was introduced, and in consequence desiccation ensuing. In other cases the piece of tumour implanted appeared to have moved from its original position and could not be traced. Not unfrequently the portion of growth implanted seemed to have undergone very rapid absorption, with the result that either the piece of tumour implanted could not be traced or no unmistakable growth of the original mass could be recognised in what is regarded as the remains of the implanted mass; difficulties of this kind were common from the fifth day after implantation onwards, and thus tend to limit the number of observations possible at later periods.

The result of implantation is summarised in the table. The usual course

of events occurring after implantation was as follows :—In naked eye aspect the tumour, which was usually easily recognisable, being moist and greyish in aspect and lying loosely among the tissues of the host, did not appear much changed during the first two days. After this period it became dry and increasingly adherent to the surrounding tissues, from which it was less readily distinguished after the fifth day. On microscopic examination the central portions of the growth were found to have undergone necrosis during the first two to three days, presumably in part, at any rate, owing to defective supply of oxygen. Some of the cells at the periphery of the implanted mass, on the other hand, at first remained unchanged in appearance and exhibited more or less evidence of proliferation, generally presenting for the first two to four days mitoses, though fewer in number than was exhibited by the growth before implantation. After the fifth day all the cells of the implanted tumour had become altered and ceased to exhibit mitoses; their nuclear chromatin no longer presented the usual arrangement, but had become collected into irregular masses or fragments. Accompanying the necrotic changes occurring in the portions of tissue implanted, leucocytes, mostly polynuclear, made their appearance in large numbers, being replaced subsequently by mononuclear cells before which the remains of the implanted tissue disappeared. The disappearance of a piece of tumour of the form of a millimetre cube appeared to be completed after the second week of implantation.

In the summary given in the table the proportion of observations in which living cells and mitoses were noted during the first five days after implantation is given in a percentage form. It will be seen that inhibition of the function of cell division is early marked, while cell death occurs (at the periphery of the implanted mass) more slowly. If the experiments made upon the monkey alone are considered, the percentages obtained are more regular, being respectively: 67 and 25 on the first day; 69 and 8 on the second day; 67 and 0 on the third day; 37 and 12 on the fourth day; 20 and 20 on the fifth day. The experiments made with animals other than the monkey are too few in number to yield percentage values, but the circumstances that mitoses were not met with after implantation suggests that human carcinoma is less viable in these animals than in the monkey.

The result of implanting human carcinoma upon animals, it will be observed, is similar to that of implanting mouse carcinoma upon rats already referred to. In both cases a limited degree of inoculability is observable, some of the implanted cells continuing for a time to live and to divide, but whereas in the latter case the rate of proliferation is at first little affected and regression does not begin till the eighth to the tenth day, in the present experiments the

cells of the implanted portions of tumour ceased to proliferate at an earlier period, and were no longer living after the expiration of five days.

In conclusion I must express my indebtedness to Dr. Wakelin Barratt for the assistance he has given throughout the course of this work.

Summary.

1. Portions of human carcinoma implanted into animals were observed during the first five days to retain their vitality and to exhibit mitoses after implantation.

2. After the expiration of this period no evidence of vitality was observed.

3. Mitosis was markedly inhibited within 24 hours of implantation, whilst the life of the implanted cells was abolished less rapidly.

On Ceratopora, the Type of a New Family of Alcyonaria.

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[PLATE 6.]

In the introduction to the British Museum Catalogue of the Jurassic Bryozoa (1896), Gregory remarks that, "to the palæontologist, who cannot check his conclusions by the evidence of vascular anatomy or embryology, these tube-dwelling animals are a vexation and a puzzle." This passage has reference to the difficulties that the palæontologist meets in determining the proper systematic position of many fossils that are known to us only by the tubular skeletons that they have left deposited in the rocks. Simple or colonial tubular skeletons, or more correctly shells, may be formed for the protection of recent sedentary animals belonging to the Protozoa, Cœlenterata, Annelida, Polyzoa, and Mollusca, and in many cases the only trustworthy guide to their systematic position is to be found in the study of the soft structures that formed the shell, the shell itself affording no distinctive characters.

In some cases the presence of septa, and in others of tabulæ, may indicate affinities; but even these characters may be misleading and give rise to erroneous conclusions. The presence of septa—now called pseudosepta—