

**Address.****THE HISTOLOGICAL CLASSIFICATION OF TUMORS.\* †**

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NORMAL cells and tissues are classified according to striking morphological characters which distinguish different kinds of cells from one another. These characters, aside from size and shape of cells and nucleus, may lie within the cell (eosinophilic granules, axis cylinder processes) or be extracellular substances produced by the cells (collagen fibrils, osteoid substance). They represent the differentiation which the cells undergo in order to perform their different functions.

Tumor cells tend to differentiate like normal cells; hence tumors are usually classified histologically like normal tissues, that is, according to the microscopic structure of their cells and intercellular substances. In tumors which grow slowly, the differentiation of the cells is usually well marked; in those which grow rapidly, it may be slight or wanting. It is important, therefore, to study embryological as well as normal tissues so as to have a clear knowledge of how muscle and other cells look in the early stages of differentiation. A knowledge of embryology is also useful in explaining the location of certain tumors (a glioma over the coccyx) and the nature of such a tumor as the chordoma which arises from remains of the notochord, a fetal tissue.

In classifying tumors, it is important to ascertain what is the one essential cell in each type of simple tumor and to name the tumor accordingly, leaving out of consideration the blood vessels and connective tissue of the stroma. They are furnished by the tissues in the midst of which the tumor develops because there is a physiological demand made for them by the tumor cells. All tumors composed of one type of cell, at whatever rate of speed they are multiplying, should be considered under one heading, not separated into slowly and rapidly growing groups and described separately. Such a separation is artificial and misleading.

The essentials for the exact diagnosis of tumors, especially those which are growing rapidly, are perfectly fresh tissues obtained at the operating table if possible, immediate fixation in proper solutions which will preserve faithfully all the morphological characters on which an exact diagnosis depends, and special staining methods to render prominent the characteristic structures.

A limited number of characteristic cells will be described and some of the varieties of tumors composed of them will be demonstrated photomicrographically.

The ordinary connective tissue cell or fibroblast is an elongated, flattened cell with a flat, oval nucleus. It is characterized by the produc-

tion of two kinds of fibrils (fibroglia and collagen fibrils) which can be stained in sharp contrast to each other. The fibroglia fibrils are in intimate contact with the cytoplasm of the cell; the collagen fibrils are entirely free from it; they both run parallel with the long axis of the cell. Cells of this type produce a series of tumors ranging from the dense fibroma to the soft rapidly-growing fibrosarcoma (so-called spindle cell sarcoma). Even in the most rapidly-growing tumors of this series both kinds of fibrils are produced, although they may be very delicate and few in number. Occasionally some of the cells contain multiple mitoses and others large lobulated or multiple nuclei with numerous centrosomes.

The myxoma and myxosarcoma differ from the tumors of this group only in having a certain amount of fluid, containing more or less mucin, between the collagen fibrils. They should not, therefore, be classed as a separate type of tumor.

The smooth muscle cell is a long spindle-shaped cell with a rod-shaped nucleus. It is characterized by a number of fine striations running longitudinally in the cuticle of its cytoplasm. Towards the tapering ends of the cell these striations, termed myoglia fibrils, coalesce more or less intimately to form what appear to be coarse fibrils. Slowly and rapidly-growing tumors composed of this type of cell (leiomyomata) occur most commonly in the uterus but may arise in other parts of the body. In one rapidly-growing malignant leiomyoma, in parts where the cells were proliferating most rapidly, they ceased forming fibrils and became more or less spherical in shape.

The neuroglia cell varies considerably in shape and size. It may be round or spindle shaped or of intermediate form. It is characterized by the production of fibrils of one kind only, the neuroglia fibrils, which run parallel with the spindle-shaped cell and in all directions around the spherical cells. These fibrils touch the cytoplasm of the cell to which they belong in some part of their course. From this type of cell quite a variety of gliomata arise, some of which grow slowly while others multiply rapidly and may invade the pia of brain or cord and grow along it. One glioma occurring over the coccyx and giving rise to metastases in both groins evidently arose from remains of the neural canal.

The endothelial cell is characterized by no production of fibrils, hence it stands out in marked contrast to the cells already described. It gives rise to two types of tumors, the hemangioendothelioma and the lymphangioendothelioma. The first type occurs in two varieties, the capillary and the cavernous.

The capillary hemangioendothelioma occurs in the form of small blood vessels which invade fat, muscle and nerve tissues, and occasionally grow within veins and arteries. The endothelial cells sometimes form several layers around the lumina of the vessels, giving the appearance of a perithelial growth, and rarely papillary masses of endothelial cells may project into the lumen of a vessel and more or less occlude it. If through

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† Synopsis of lecture which was illustrated by one hundred and twenty-seven lantern slides.

rupture or pressure the lumina of the vessels become obliterated, the endothelial cells grow in masses and whirls. After a time collagen fibrils extend in between the endothelial cells from the connective tissue cells of the stroma and transform the tumor into what looks like a fibrosarcoma, but fibroglia fibrils are lacking.

In four cases of gradually extending cavernous hemangioendothelioma the tumors were found to consist of endothelial cells, supported by thin layers of connective tissue cells and fibrils, growing within and along blood vessels. In places they distend or burst through the vessel walls so as to form tumor nodules composed of large blood spaces separated by thin septa of connective tissue covered on both sides with endothelial cells.

A neuroma of adrenal origin with widely distributed metastases was characterized by masses of delicate fibrils which reacted to a variety of stains like nerve fibrils.

The neuromata of the eye have been shown by Verhoeff to consist of nerve cells which tend to differentiate like the cells of the retina. The rosettes occurring in these tumors often show very definite rods and cones projecting through an external limiting membrane just as the normal rods and cones do.

In the rhabdomyoma the cells tend, by differentiation of the cytoplasm, to produce the sarcous elements of the normal fetal striated muscle cells.

In the chordoma occurring at the base of the skull the curious vacuolated cells of the notochord are faithfully reproduced.

Epithelial cells occur in great variety; so also do the epithelial tumors of which the cells tend to differentiate like the normal cells. It is advisable, therefore, to study by themselves each type of normal epithelial cell and the group of tumors with cells differentiating like it. Only the names of a few can be mentioned here: The adenomata of the mammary and coil glands with the layer of smooth muscle cells surrounding the epithelial cells; the various types of carcinoma of the breast; the characteristic benign and malignant epithelial tumors of adrenal cell origin; the chorio-epithelioma derived from fetal epithelium covering the chorionic villi; the ciliated epithelial tumors derived from remains of the Wolffian duct, and the adamantinoma derived from remains of the enamel organ.

The vague terms "spindle and round cell sarcoma" and "perithelial angiosarcoma" should be avoided so far as possible. A spindle cell sarcoma may be composed of connective tissue, smooth muscle, endothelial or neuroglia cells. A round cell sarcoma may in reality be a lymphoma, osteosarcoma, malignant leiomyoma or neuroma. A true perithelial angiosarcoma does not occur. The tumors which most frequently show such an appearance are the melanotic sarcoma and the neuroma of the eye; rarely even a carcinoma of the breast may exhibit this type of growth which is purely nutritional in origin. The cells at a distance from the blood vessels undergo necrosis and absorption, leaving the vessels isolated with a sheath of tumor cells around them.

## Original Articles.

### INJECTIONS OF SEA WATER IN SKIN DISEASES.

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IN October, 1908, Dr. Robert Simon,<sup>1</sup> of Paris, presented before the Boston Society of Medical Sciences a series of beautiful lantern slides illustrating the marvelous therapeutic results which he had obtained in the treatment of numerous dermatoses by the injection of isotonic sea water.

To repeat these experiments was my immediate wish, but the procuring and preparing of this new therapeutic agent offered certain difficulties in ways and means, but owing to the great kindness of Dr. T. J. Leary, Professor of Pathology in Tufts Medical School, who delivered the tubes of water ready for use, and the generosity of Dr. F. A. Washburn, Jr., Superintendent of the Massachusetts General Hospital, who made this kindness possible, the difficulties were overcome, and in January, 1909, Dr. E. Lawrence Oliver, Assistant to the Skin Department, began the present series of injections which were continued and concluded by Dr. Jaynes, House Officer, and to all of these gentlemen I now return my sincere thanks.

Sea water, according to A. G. Mayer,<sup>2</sup> contains the chlorides of sodium, magnesium, calcium and potassium, and the sulphate of magnesium. These salts have different and opposite effects, i. e., sodium chloride is a stimulant to nerves and muscles, while the magnesium, calcium and potassium salts are inhibitory in their actions, and Mayer describes these opposing forces in the case of one of the medusæ whose pulsations are produced by the electrical (?) energy generated, as in a battery, by the action of these various salts.

With this acknowledged phenomenon as a basis for the possible therapeutic power of sea water the following experiments were undertaken. The water was obtained from the ocean about thirty miles south of Woods Hole, Massachusetts, and from a depth of thirty feet, thus insuring a pure, uncontaminated supply. This water was placed in sterile jars and brought to Boston where it was purified by passing through a Chamberland filter and rendered isotonic with blood serum by the addition of sterile tap water in the proportion of ten parts of the former to twenty-three of the latter. This product was placed in sterile glass ampullæ holding 200 ccm. One end of these receptacles was bent in the form of a hook and the other drawn out into a straight line and both extremities were sealed.

The injections were made three times a week deep into the buttocks of the patient who lay on his side and allowed the fluid to run into the tissues by the force of gravity, the ampulla being suspended about three feet above the body and the water passing through a sterile rubber tube and long irido-platinum needle. The rapidity of the injections varied a great deal in the different patients, some requiring at least a half hour to take in 150 ccm. The pain and discomfort attend-