ESTRATTO

DAGLI

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DEI PATOLOGI

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1912
On the classification of blastomatous tumors.

Plates III, IV.

In 1902 I published in the Journal of Pathology a paper upon the Classification of Tumors, based upon the histogenesis of various tissues. That classification has been very generally accepted by English and American pathologists; I have, however, seen little or no reference to it in the writings of continental European pathologists, and, as in the years that have passed since this publication, I have increasingly found that it is helpful in a comprehension of the different orders of neoplasms and their relationships, it has seemed to me that it might be serviceable to seize this opportunity to bring that classification before my European Colleagues in as brief, and, I trust, as clear a form as possible.

Just as the form and structure of the individual of any species is the outcome of the phylogeny of that species, or, in other words, is the resultant of the particular conditions to which that individual and its progenitors have been exposed in the course of countless generations, so the component cells of the individual and the special characters of the same are the resultant of the forces which have acted upon those tissues. A given cell of the embryo in a given relationship to the rest of the embryo has thus inherent tendencies to give origin to cells of a particular order. Conversely, with a full knowledge of the embryogeny of the different tissues it is possible to determine the origin of any particular order of differentiated cell. Thus the whole microscopical study of tumors and their histological diagnosis must be based upon histogenesis.

If we make a broad survey of the tissues of the body, they group themselves into two contrasted orders for which, owing to the confusion of our present terminology it has been necessary to coin particular terms. These are the lepidic (λεπίς, a rind or membrane) and the hylic tissues (χυλός, crude matter or pulp) respectively. But for the confusion that at present exists, the former might be spoken of as the «epithelial tissues», but when from old association so many are apt to regard the epithelial tissues as only of epiblastic or hypoblastic origin, and to make a contrast between «epithelial» and «endothelial», it

1 — J. G. ADAMI.
becomes necessary to employ some word which will not lead to this confusion.

A lepidic tissue, therefore, is one in which the characteristic elements are accumulations of cells characterized by an absence of definite stroma between the members of the cell groups, characterized also by the fact that the blood vessels do not penetrate the groups, although stroma, containing blood vessels, is present below or between the cell accumulations, being separated from them by a basement membrane. In the other, or hylic order, we deal with tissues characterized by the fact that the individual cells forming the dominant features are separated by a definite stroma in which there may, or may not, be blood and lymph vessels (vide Pl. III). Cells lying in a stroma are the characteristic elements of a hylic tissue, cells lying upon a stroma, of a lepidic tissue. In both orders of tissue, both elements are present. Thus, for example, the vessels in the stroma of a hylic tissue are lined by lepidic elements. It is the dominating element that determines with which tissue we have to deal. In his well known classification WALDEYER, undoubtedly, had a glimmering of the importance of a recognition of these two orders, but the embryological knowledge of his day did not permit him to go far enough. As in his day, so now it is all important to recognize the three primary embryonic cell layers, but it is essential to recognize in addition that there is not the distinction that he would make between the tissues originating from the two primitive germ layers, the epiblast and the hypoblast, and the third layer, the mesoblast. It is all important to recognize that each of these three layers gives origin to both lepidic and hylic tissues, and that as the tumors of lepidic origin take on the carcinomatous character, those of hylic origin, when atypical, assume sarcomatous characters. Carcinomatous and sarcomatous growths may originate from any one of the three original germ layers. It will be seen upon consideration that these terms carcinoma and sarcoma can only be used in a histological sense: any attempt to attach an embryological significance to them leads to hopeless confusion. The accompanying diagram (vide Pl. IV), illustrates this point. For example, from the epiblast there originates the neuroblast, the nerve tissues of the brain and spinal cord, the arrangement of whose cells is typically hylic. The only persistent lepidic elements of the nervous system are the epithelial lining of the spinal canal and the ependyma of the brain cavities. From the hypoblast also originates the notochord, which is of hylic arrangement, while, as regards the mesoblast, that subsequently becomes differentiated into the lepidic Mesothelium lining the body cavity and the Mesenchyme which retains the hylic type. In its turn the Mesothelium gives origin to certain glandular organs like the cortex of the adrenal and kidney, the testes and ovaries, which are of glandular, lepidic type, and, on the other hand, to the skeletal
muscles of hylic type. Whether we regard the endothelium of the vessels and lymphatics as of mesothelial origin or as a later differentiation from the mesenchyme, this is of lepidic type and mesoblastic origin. We may thus classify the tissues as follows:

**TABLE 1.**

**Lepidic tissues.**

*The specific cells are in layers or groups lying upon a stroma; separated from that stroma by a basement membrane. Vessels run in the stroma but not between specific cells.*

1. **Epiblastic.**


2. **Hypoblastic.**

   Epithelium of digestive tract and associated glands (tonsils, thymus, thyroid, liver, pancreas, etc.), epithelium of trachea and lungs. Epithelium of bladder, female urethra, prostatic portion of male urethra.

3. **Mesothelial.**

   Lining cells of serous cavities, cortex of adrenals, of kidney, Graafian follicles, tubules of testis, epithelium and glands of Fallopian tubes, uterus, vagina, vasa deferentia, vesiculae seminales, etc.

4. **Endothelial.**

   Endothelium of blood vessels and lymphatics.

**Hylic or primitive pulp tissues.**

*The specific cells lie in a stroma, which is penetrated by vessels.*

1. **Epiblastic.**

   Nerve cells, neuroglia, cells of sheath of Schwann.

2. **Hypoblastic.**

   Notochord.

3. **Mesenchymatous.**

   Fibrous connective tissues, fat cells, cartilage, bone, bone marrow, spleen, lymphoid tissue, involuntary muscle, blood vessels, blood corpuscles.

4. **Mesothelial.**

   Striated muscle (including cardiac muscle), interstitial cells of ovary and testis.

If we now accept, as I trust all must accept, that the blastomatous tumors retain, more or less perfectly or imperfectly, properties of the tissues from which they originate, we then are able to classify blastomas into the two great groups of lepidomas and hylomas, redividing these again into typical and atypical members of each order.
TABLE II.

Lepidomata or "Rind ,, tumors.

<table>
<thead>
<tr>
<th></th>
<th>TYPICAL</th>
<th>ATYPICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Of epiblastic</strong></td>
<td>Cutaneous Papilloma</td>
<td>Squamous Epithelioma.</td>
</tr>
<tr>
<td><strong>origin</strong></td>
<td>Adenoma of sweat, sebaceous a. salivary glands.</td>
<td>Adenocarcinoma and carcinoma of same.</td>
</tr>
<tr>
<td><strong>Of hypoblastic</strong></td>
<td>Adenoma and Papilloma of digestive and respiratory tracts, thyroid, pancreas, bladder, etc.</td>
<td>Adenocarcinoma and carcinoma of same.</td>
</tr>
<tr>
<td><strong>origin</strong></td>
<td>Adenoma of kidney, testicle, ovary, urogenital ducts, uterus, prostate, serous membranes.</td>
<td>Carcinoma and sarco-carcinoma (mesothelioma) of same.</td>
</tr>
<tr>
<td><strong>Of mesothelial</strong></td>
<td>Adenoma of kidney, testicle, ovary, urogenital ducts, uterus, prostate, serous membranes.</td>
<td>Haemangioendothelioma.</td>
</tr>
<tr>
<td><strong>origin</strong></td>
<td>Haemangiomata.</td>
<td></td>
</tr>
<tr>
<td></td>
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</tbody>
</table>

Hylomata or "Pulp ,, tumors.

<table>
<thead>
<tr>
<th></th>
<th>TYPICAL</th>
<th>ATYPICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Of epiblastic</strong></td>
<td>Neurona, glioma, neurinoma (neurofibroma).</td>
<td>Glio-sarcoma, neurino-sarcoma, etc.</td>
</tr>
<tr>
<td><strong>origin</strong></td>
<td>Chordoma.</td>
<td>Chordo-sarcoma.</td>
</tr>
<tr>
<td><strong>Of hypoblastic</strong></td>
<td>Fibroma, myxoma, lipoma, chondroma, osteoma, leiomyoma, lymphoma, myeloma, etc.</td>
<td>Fibro-sarcoma, myxo-sarcoma, etc., spindle celled, large and small round celled sarcoma.</td>
</tr>
<tr>
<td><strong>origin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Of mesenchymatous</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>origin</strong></td>
<td>Rhabdomyoma.</td>
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The typical members of the two orders present no difficulties. Regarding the atypical certain general principles have to be laid down.

1. Conditions of earliest and oldest acquirement are those which are most obstinately retained and are latest lost. We should expect to find, and, as a matter of fact we find that, just as in the development of tissues cell differentiation manifests itself at a period much later than the assumption of the lepidic arrangement, so in the undifferentiation or anaplasia characteristic of tumor growth, the cells pass back to a stage at which, from their individual properties, it is impossible
to recognize their parentage, long before they lose their lepidic arrangement. In other words, the lepidic arrangement is so tenaciously retained that in the majority of atypical tumors it is its presence or absence rather than the properties of the individual cells that gives us the clue to the original tumor.

II. In embryogeny the development of the membrane-like, or lepidic, arrangement is always a progressive and not a regressive phenomenon; there has always been a preceding hylic stage, without differentiation between the lining layer and the underlying cells. In the regressive process of anaplasia, or lessened differentiation, a tissue which has been hylic cannot assume the lepidic type. On the other hand, with extreme anaplasia, cells which have had the lepidic arrangement may revert to the earlier hylic disposition. A tumor formed of cells of one order which in certain areas exhibits the sarcomatous arrangement, in others the carcinomatous, and in yet others, transitional stages from the lepidic to the hylic arrangement must therefore be regarded as originating from a lepidic or lining membrane tissue; it cannot have originated from a hylic tissue.

At most, as demonstrated by certain of Ehrlich and Apolant's transplantation experiments, we must admit that the cells of certain tumors may retain certain properties in a latent stage through numerous transplantations, that an obvious carcinoma simplex with solid cell masses may on transplantation give origin to an adenocarcinoma of more nearly typical glandular arrangement. This however, is at most a progressive change from one grade of lepidoma to another; it is not a transition from hyloma to lepidoma. I have come across abundant instances in which a tumor surely of epithelial or lepidic origin, in regions of rapid growth, furthest removed from the focus of origin, has approximated more and more nearly to the hylic arrangement; I have not come across a single instance in which I must accept the reverse process, of assumption of lepidic or lining membrane characteristics by tumors of hylic origin. The nearest approach to such conversion has been in some gliomas, in which cavities, the result of necrosis and autolysis, become lined by more flattened or cubical cells, evidently of glial origin. But here there is no basement membrane developed, no line of demarcation between these surface cells and those immediately underlying them; it is not the production of a differentiated cell layer, but a modification in the form of the more superficial cells, due to position.

III. If in embryogeny lepidic tissues of epiblastic and hypoblastic origin are as a group of earliest development, those of mesothelial origin are of later origin, and those of endothelial type of yet later origin, then (in accordance with the principle that properties of oldest acquirement are those most tenaciously retained), we should expect to find, and as a matter of fact we do find, that, as a group, tumors of tissues
of epiblastic and hypoblastic origin retain their lepidic characters most tenaciously, while those of endothelial origin most frequently show reversion or regression to the more primitive hylic arrangement. It is, in fact, only the more slowly growing endotheliomas that present indications of a lepidic arrangement, and even these frequently exhibit areas that are purely sarcomatous. Tumors of definitely mesothelial origin occupy an intermediate position. Tissues of this provenance may afford typical adenomas, or adenocarcinomatous growths, but where more atypical, careful study frequently reveals areas exhibiting transition from the (lepidic) carcinomatous to the (hylic) sarcomatous arrangement, the condition of Carcinoma sarcomatodes. This can be well seen among the tumors of the adrenal and renal cortex, the « hypernephromas » and the « nephromas » (1), but is to be seen also in some ovarian and testicular tumors, and we have seen areas in prostatic cancers also passing on to a sarcomatous arrangement. If the lining membranes of the body cavities be regarded as mesothelial, rather than endothelial, then the tumors arising from these manifest very strikingly this same transitional or regressive tendency. I thus am inclined to group the tumors originating from mesothelial and endothelial tissues as Transitional lepidomas.

IV. But doing this it must be remembered that apart from embryological considerations the structure of a tumor may also be regarded as the expressions of the grade of anaplasia attained by the formative cells. In the case of tissues of epiblastic and hypoblastic origin, extreme anaplasia may also be associated with a regression to the more primitive hylic arrangement. This, for example, is seen in certain epiblastic tumors of that type to which Krompecher has given the unfortunate name of Basal-celled carcinomas. But this is the exception, not the rule. The vast majority of tumors from epiblastic lining membranes retain with great tenacity the lepidic arrangement.

On the other hand, there are mesothelial lining membranes which affords tumors that rarely show transition to the hylic or sarcomatous type: for example, those of the uterine mucosa. These show almost as marked a tendency to remain adeno-carcinomatous as do the rectal tumors of hypoblastic origin. It may be that the generally accepted embryogeny of the uterine mucosa is incorrect. This I am not inclined to urge because, as already stated, in the homologous prostate certain carcinomas do show a liability towards a more sarcomatous appearance. Making this admission, I do not believe that the recognition that the

different tissues of mesothelial origin show a distinct variation in the extent to which their tumors are liable to revert to more primitive hylic arrangement is an admission of erroneous hypothesis, or that the general principles here laid down are incorrect. Rather I would recall the astronomical example of the « lunar theory ». For long years astronomers, that is, employed this theory to calculate mathematically the position of the moon in relation to the sun at a given date, but always there was a correction to be made, indicating that the sun’s course in space is modified by some unknown, or, more accurately, undetermined factor. So here I would urge that the broad lines of this hypothesis are correct, and the hypothesis itself most serviceable, even if we have still to determine the factor or factors which in one or other organ influence the extent to which anaplasia may proceed.

In conclusion, let me say that I am strongly opposed to alterations in terminology, and that although I introduced these terms lepidoma and hyloma close upon ten years ago, I have never once personally employed them for diagnostic purposes. It is wholly adequate for the clinician, so far, to describe a tumor as a carcinoma, a sarcoma, an endothelioma, or a mesothelioma of one or other organ. Possibly the time is at hand when the terms here suggested, or corresponding terms possessing a precise meaning, will be found desirable. We cannot but recognize that our present terminology is entirely unsatisfactory to us as pathologists, as students of science anxious to employ words which have an exact meaning. When it requires careful reading to determine whether the word Krebs in German, or Cancer in English refers only to carcinomas or to malignant tumors in general: when in French works the term Épitéliome applies to any form of carcinoma and is used for malignant epithelial growths, in contradistinction to Adenome, which refers to benign epithelial growth, although in English and German it applies to the one form of squamous-celled carcinoma only: when in Italian, if I am not mistaken, it may mean the one or the other according to the affiliations of the user; then the time has arrived to introduce a new and appropriate terminology by international consent, regarding which there shall be no ambiguity. These are very far from being the only instances of uncertain and careless usage of terms in connection with neoplasia: instances abound on every side. It is a matter of profound satisfaction that the International Association for Cancer Research has appointed an influential Committee to study and make recommendations upon this subject of nomenclature. I trust that this, the first International Congress of Pathologists, will signalize its entry into existence by aiding and abetting this movement for the employment of terms, which, precisely defined, shall by international consent receive universal acceptation and application.
Lepidic Tissues.

1.

Hylic Tissues.

4.

J. G. Adami. On the Classification of blastomatous Tumors.
Scheme of Tissue Relationships.

G. Adami. *On the Classification of blastomatous Tumors.*