GENETIC INTERPRETATIONS IN THE DOMAIN OF ANATOMY.*

PRESIDENTIAL ADDRESS BEFORE THE ASSOCIATION OF AMERICAN
ANATOMISTS.

BY

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The science of anatomy, although one of the oldest of all sciences, was long neglected in America, and taught only in a routine fashion by professors who had little or no thought for the promotion of the science or any aim higher than teaching a certain number of established facts in gross anatomy to the maximum possible number of students. Within the last generation the few pioneers of anatomy have been succeeded by teachers, many of whom share the highest ideals of anatomical science, and have contributed important discoveries by which it has been really advanced. Our Society is at once the symbol and the outcome of these comparatively new conditions in America, and we have as our duty not only actively to encourage research, to spread anatomical knowledge, and to earn appreciation of anatomy as a living science, but also to exert a missionary influence by which the dignity and vitality of our science shall be brought to recognition at all our universities.

* The following recent or new technical terms are used in the course of the address and are recommended for adoption.

Cytogenic glands, false glands which produce cells, as for example, the lymph and genital glands.

Cytomorphosis, to designate comprehensively all the structural modifications which cells or successive generations of cells may undergo from the earliest undifferentiated stage to their final destruction.

False glands, all glands, which develop without ducts.

Lymphæum, a more or less definitely circumscribed area consisting of cellular reticulum, the meshes of which are charged with leucocytes and are in direct communication with lymph-vessels or more rarely with blood-vessels. It is a site for the multiplication of leucocytes.

Mesepatium, the membrane (French, *méso*) extending from the stomach and duodenum to the median line of the ventral abdominal wall, and in which the liver develops. It comprises a *dorsal* mesepatium (lesser omentum) and *ventral* mesepatium (falciform or suspensory ligament).

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It is sometimes said, and perhaps more often thought, that anatomy is a completed science. This assertion is based upon the thoroughness and exhaustive character of the descriptions to be found in our text-books of the anatomical conditions in the human adult; yet even as regards the organization of the adult we have still much to learn, especially concerning the microscopic structure with which we are still very imperfectly acquainted.

But anatomy is not alone a descriptive science. It is also comparative and genetic. In both these directions its development is very far from complete, and a vast amount of original research must still be completed before comparative anatomy and embryology shall have approached anywhere near even the present perfection of descriptive human anatomy.

To embryological research must be attributed a large part of the extraordinary progress which anatomy has made during the last twenty-five years. By embryology we have gained a far deeper understanding of all anatomical forms, we have acquired new interpretations for pathological facts, and we have secured for the first time some clear insight into the essential structure of the brain. I need not do more than allude to these achievements, since they are familiar to us all, and have most profoundly affected our anatomical conceptions. Our point of view has changed, and we interpret the anatomy of the adult in terms of the genesis of the organs and tissues during their embryonic development.

Perhaps no man has contributed so much towards this result as the great Leipzig anatomist, Wilhelm His, whose death this year we have to lament. He was a great master. He had full command over the problems of anatomy and contributed in the richest measure to their solution. His influence in America has been especially strong and widespread, and has certainly had much to do in bringing about the progress of anatomy in this country, which we are seeking to maintain, and if possible, increase. In what I have to say to you on this occasion, you will perceive

Phrenic area, the area on the superior or cephalad surface of the liver, by which the liver is attached permanently to the diaphragm. It includes the whole of the territory of the coronary and triangular "ligaments," so-called in current text-books.

Sinusoid, an irregular blood space, produced by the subdivision of a larger blood-vessel by the ingrowth of the parenchyma of an adjacent organ.

Structural unit, the territory of an organ supplied by a single terminal branch of an afferent vessel (artery or vein); the volume of such a unit is often only 10-20 cubic millimeters.

Trophoderm, the special layer of cells formed on the exterior of the young mammalian blastocyst, and serving to secure the implantation of the ovum in the uterus.

the influence of His clearly, and I cannot let the opportunity pass of expressing publicly my gratitude and admiration for the greatest anatomist of his time.

Although embryology has already contributed in so ample measure to the promotion of our science, we are still far from having accepted all the enlightenment which she offers us. With your permission I will try to present to you certain embryological aspects of anatomy, the character of which I have sought to indicate in the title of this address, by the words "genetic interpretations."

First of all, let us consider the subject of cytomorphosis. This word I proposed in 1901¹ "to designate comprehensively all the structural modifications which cells or successive generations of cells may undergo from the earliest undifferentiated stage to their final destruction." As stated on that occasion it is convenient, though somewhat arbitrary, to distinguish four fundamental successive stages of cytomorphosis. These stages are (1) the undifferentiated stage: (2) the stage of progressive differentiation, which itself often comprises many successive stages; (3) the regressive stage or that during which degeneration or necrobiosis occurs; and (4) the stage of the removal of the dead material. The general data on which the conception of cytomorphosis is based have been briefly put together also in my text-book of embryology, and it seems therefore superfluous to dwell upon them at length in addressing you.

I cannot of course claim any greater originality in the establishment of the conception of cytomorphosis than is implied by the definite formulation of the ideas upon which it is based. These ideas have been gradually gathered as the fruit of numerous investigations in histogenesis. The mentioned investigations have made us all familiar with the conception of undifferentiated embryonic cells, with the gradual progress of differentiation in the cells during the embryonic, foetal, and even post-natal periods; and have also made us acquainted with various examples of degeneration and atrophy occurring in the course of development, both before and after birth. Up to the time when I proposed the term there had been, so far as I know, no attempt to survey all this array of facts from a single unifying point of view. But such a point of view is, I believe, well calculated to render our notions more precise as to many processes of development, and to afford us at the same time the practical benefit of being able to present the facts of histogenesis in our teaching in a way, which is very advantageous, because it facilitates in the student's mind the establishment of a real insight into the general course of development by emphasizing principles of very wide application. To me, at least, it seems that the conception of cytomorphosis should be made the

foundation of all our instruction in anatomy, and that its importance should be constantly emphasized in our class-rooms and that when good illustrations of cytomorphosis are encountered by the student, his attention should be especially directed to them, so that he may become familiar with the conception. Let me mention a few illustrations which I have found serviceable in teaching.

But first I must call your attention to an aspect of cytomorphosis, which has not hitherto, so far as my knowledge goes, been sufficiently emphasized. We may distinguish two fundamental phases. During the first, cell division occurs, during the second, cell division does not occur. During the first phase we may find a progressive alteration, which gradually takes place in successive generations of cells, but apparently the amount of differentiation which can occur while cells retain the power of active division is comparatively slight. During the second phase, since the cell no longer divides, the alteration takes place in the single cell, and the alteration, which occurs under these conditions, is typically great and may be best designated by the term final differentiation, differentiation being here held in our minds clearly distinct from degeneration. By final differentiation we mean the establishment of that special organization of a cell, which brings to perfection the specialized physiological function for which the cell is destined. Thus the alteration of a mesenchymal cell into a muscle fibre is its final differentiation, and establishes the physiological perfection of that cell as a contractile element. Beyond the final differentiation of the cell comes the series of degenerative changes. A comprehensive study of cell degeneration is yet to be made, nevertheless we can already say that, although cell degeneration is chiefly characteristic of the second phase of cytomorphosis, which is also characterized by the cessation of cell division, yet the degeneration may be initiated before the power of cell division is lost and the degenerative change in the cells may go on while they are still proliferating; but typically it seems rather that degeneration belongs to the second phase of cytomorphosis, and this seems to be alike true for necrosis and atrophy, that is to say, simple cell death, and for necrobiosis, that is to say, cell death preceded by structural changes, which we know commonly under the name of hypertrophic degeneration.

Let us pass on now to a few illustrations of cytomorphosis:

The first to which I would direct your attention is afforded by the formation of the "*trophoderm*." This is a new term which I have recently brought forward to designate the special layer of cells formed apparently from the ectoderm (or according to Assheton's theory, from

the entoderm) which serves to secure the implantation of the mammalian ovum in the walls of the uterus. In my "Text-Book of Embryology" I have figured these cells from the human ovum and applied to them the term trophoblast, but as Professor Hubrecht, who introduced this last term into science, has objected to this application of it, it has been necessary to introduce a new term, hence the designation trophoderm. It corresponds in large part, perhaps wholly, to that which Duval designated as the ectoplacenta. It is the first tissue in the mammals to be distinctly differentiated. The cells by their large size, distinct boundaries, and characteristic nuclei, are readily distinguished from any other cells existing in the embryo at the time the trophoderm is differentiated. Very soon after the development of the trophodermic cells, a large part of them begin to complete their cytomorphosis by undergoing degeneration and resorption. By their disappearance, as I have elsewhere pointed out, the intervillous spaces arise. The trophoderm therefore is not only the earliest tissue to be specialized in the development of mammals, but also the earliest tissue to absolutely complete its cytomorphosis.

Another striking illustration of the cytomorphic cycle with its phases of differentiation, degeneration, and disappearance of cells is offered to us by the blood corpuscles. The first blood corpuscles are cells with a minimum amount of protoplasm. The cells then proceed to grow, and as they grow, differentiate themselves in part at least, into red blood globules. In mammals there follows the stage, degenerative in character, by which the nucleus of these red blood corpuscles disappears. The manner of its disappearance is, to be sure, still perhaps a matter of debate, but for us for the moment is of minor importance. After the degeneration or disappearance of the nucleus, the blood corpuscles are destroyed and, having completed their cytomorphosis, are replaced by fresh ones.

A third admirable illustration is offered us by cartilage, and a fourth by bone. In cartilage we see at first a differentiation of simple mesenchymal cells which then enlarge, becoming the characteristic cartilage cells. When ossification of the cartilage occurs we can easily follow the hypertrophic degeneration of these same cartilage cells, which has been so much studied that good accounts of the enlargement and breaking down of these cells preliminary to the ingrowth of the osteogenetic tissue can be found in all the better text-books of histology; but I regret to say I do not recall any text-book either of anatomy, histology, or embryology, which points out the fact that this succession of changes in cartilage cells is a typical and almost perfect illustration of cytomorphosis. Almost the same can be said of bone, for in the formation of this tissue also we have first, the differentiation of the mesenchymal cells into osteoblasts, which

are always of larger dimensions than the cells from which they arise; and after these osteoblasts have become bone cells they cease their development and apparently degenerate. I have to say *apparently*, because, so far as I know, the fate of the bone corpuscle has not been ascertained with certainty. We risk but little, however, in asserting that the bone cells also offer an instance of a normal, complete cytomorphosis.

As a fifth and last illustration, let us choose the epidermis, in which we have a distinct type of differentiation. In the basal layer are the cells, which divide and produce, according to our present notions, all of the cells of the epidermis. When the basal layer cells divide, however, some of them only, pass immediately through further cytomorphic changes in order to make first, the cells of the mucous layer, and later, by undergoing cornification, to constitute the horny layer. Others of the basal cells remain members of the basal layer and continue to proliferate. We thus see the progeny of the original basal cells divided into two classes: the cells of one class pass on in their development, the others retain their ancestral type. In the epidermal cells we observe as in other instances of cytomorphosis, first the enlargement and differentiation of the cells, here occurring in the mucous layer, and later their degeneration or cornification followed by their necrosis and destruction.

It would be easy to multiply these illustrations. All of you could supply more. That which I would urge upon your consideration is the value of the cytomorphic interpretation in explaining the origin and differentiation of tissues in the light of the broadest principle of cellular development which we have up to the present time been able to establish.

I will now ask you to consider certain possible genetic classifications. The most fundamental and important of these seems to me to be that of tissues and of organs according to the germ layers from which they arise. This classification was made the basis of his entire course of lectures upon animal morphology by Professor Carl Semper, the Würzburg zoologist, under whom I had the pleasure of studying in 1875-76. It is not merely very practical and advantageous alike to teacher and pupil, but is also the only thoroughly scientific classification of structures and organs which we can adopt. No other classification should, in my judgment, be seriously considered. So firmly do I hold this conviction that I greatly deplore the fact that our text-books of histology are not written upon an embryological basis, the lack of which deprives them of much of the scientific character and value they ought to have.

As our knowledge of the development from the germ layers has grown, we have learned with ever-increasing certainty that each germ layer has its specific rôle to play. Each germ layer produces its own specific

set of tissues, which are not duplicated by the tissues of any other germ layer. I have already pointed out on another occasion that the importance of the germ layers is as absolute and unvarying in the domain of pathology as in normal differentiation; I need not dwell on that aspect of the question now, but will only repeat the declaration of my belief that the entire teaching of the pathologist as well as of the histologist and anatomist should be based on the doctrine of the germ layers and their specific rôles in histogenesis.

Almost any group of tissues would offer a favorable opportunity for the discussion of genetic classification. We may select those which are differentiated from the embryonic mesenchyma and which are commonly grouped in the adult under the names of the **connective and supporting** tissues. It is almost superfluous, so much is the genetic point of view neglected, to call your attention to the fact that in our current text-books of histology there is often little or nothing which would enable the student to grasp the relations of these tissues to one another or to understand their genetic relationships. It is true that our knowledge in spite of the great advances of recent years is still too incomplete to justify our asserting that the classification which we can now make is final. Nevertheless we can already perhaps attain approximate finality. A very great step in advance was made when the character of the cellular reticulum was established and it was shown that this tissue is different from ordinary connective tissue. It has two principal characteristics: first, the matrix or intercellular substance is nearly or absolutely fluid, so that leucocytes can wander freely in the intercellular spaces of the reticulum; second, the network of original protoplasmic filaments has become directly converted into a network preserving more or less the original form, but consisting not of protoplasm, but of a new chemical substance, reticulin. Where cellular reticulum is developed, as for instance in the so-called adenoid tissue, there may be formed from the cells a minimum amount of connective tissue fibrils and of elastic substance, but if we may judge from our present knowledge the cells, which have produced reticulin, preserve but a very small capacity for the production of other elements of connective tissue. Hence, it seems to me that we may well put cellular reticulum in a class by itself, quite apart from the true connective tissues in which the intercellular substance is not mainly fluid and in which there is an abundant development of fibrillar or elastic substance, or of both, and in which, further, reticulin is nearly if not wholly absent. We shall thus come to place all the connective tissues, properly so-called, in a second genetic group. When we follow in the embryo the history of young connective tissue, we learn that it undergoes two principal kinds of modifica-

tions, those affecting the matrix, and those affecting the cells. On these differences the classification in the following table is based.

We also know that connective tissue can be directly transformed into cartilage, which, therefore, unquestionably belongs in the same second genetic group as the true connective tissues. As regards bone, I find it somewhat difficult to reach a decision, but incline to the conclusion that bone should be regarded as distinct from the true connective tissue, thus making a third genetic division of the tissues derived from the primitive mesenchyma. This conclusion appeals to me partly as a protest against the absurd, though long established and honored, custom of separating cartilage from connective tissue, and putting cartilage and bone together in a common group under the head of supporting tissues. The following table presents the proposed classification in a form which you can easily follow:

TABLE I.—THE MESENCHYMAL TISSUES.

MESENCHYMA.	Cellular reticulum	Matrix specialized.	Mucous tissue
	Embryonic connective tissue		Adult connective tissue
	Bone	Cells specialized ...	Cartilage
			Fat cells
			Pigment cells
			Smooth muscles
			Basement membranes
			Pseudo-endothelium
			Genital interstitial cells, etc.

Let me refer briefly to a third and more special example of the genetic classification of tissues, namely, that of the blood-vessels. As you probably all know, recent embryological investigations have compelled us to recognize not only the three familiar and long-known classes of blood-vessels, arteries, veins, and capillaries, but also a fourth class, that of the sinusoids. Capillaries arise as small vascular sprouts from pre-existing vessels, and these sprouts grow in the mesenchyma. A sinusoid, on the contrary, has an entirely different developmental history, for it is produced by the subdivision of a pre-existing and relatively large vessel. The subdivision is accomplished by the proliferating tubules (or trabeculæ) of an organ, which encounter a large vessel and invade its lumen, pushing the endothelium before them.⁴ The endothelium of the vessel, on the other hand, expands and spreads over the tubules (or trabeculæ). By the convolutions and anastomoses thus produced, a large vessel is subdivided into small ones. It follows that a sinusoidal circulation is purely venous or purely arterial. It may suffice, upon this occasion, to point out again that the structure of many important organs, as for

example, the liver and Wolffian body, cannot be understood or even described correctly without taking into consideration the sinusoidal character of their circulation. In this case also, the adoption of the genetic interpretation is much needed. We shall apply presently the concept "sinusoid" to aid us in the interpretation of glands.

We may pass now from a consideration of tissues to that of organs, and begin with the glands. The classification, which at the present time prevails widely, is one based upon certain incidental peculiarities in the shape of the secretory portion of the glands, so that they are put into two main divisions: the tubular and alveolar; then under each of these we have three main parallel groups:

- the simple tubular or alveolar glands;
- the simple branched tubular or alveolar glands;
- the compound branched tubular or alveolar glands.

But in this classification there is no place for such a gland as the liver and the thyroid. In text-books of histology, we find the liver tucked in under the tubular glands and designated as a reticulated tubular gland, and the thyroid placed as a follicular gland under the head of the alveolar. But in another way the system also fails, for there are tubulo-alveolar glands which again must be classified as simple, simple branched, or compound branched. Essentially this classification is adopted by the authors of the manuals of histology which I have examined. To classify glands thus, seems to me about on a par with classifying organs by their being solid or hollow, a principle, which would put the spinal cord in the same class with the intestine, and nerves in the same class with the tendons. The peculiarities of shape of the secretory portions of glands are entirely secondary, and do not indicate anything fundamental in regard to the structure of the gland itself. We cannot call a system good which, if applied in accordance with its own definitions, would put some of the mucous glands of the stomach in one division, others in another division, because, although these glands are alike in their histological structure, some of them are branched and some are not. Must we not condemn a view, which excludes the ovary from the glands and makes the testis a compound tubular gland, although ovary and testis are strictly homologous organs, even in the details of their structure? These are only samples of the innumerable difficulties which the system encounters, because it is essentially pedantic, admirable as an orderly arrangement of names, but impossible as a presentation of anatomical facts.

It appears to me not difficult to make an entirely new classification of

glands, which shall be based upon their genesis and upon the morphological distinctions, which exist between them. To begin with, we may put the unicellular glands, of which the goblet-cells serve as the most familiar type known in man, in the Class A, v. p. 256; next we may have the true multicellular glands of the epithelial type, which always develop with ducts by which their secretion is discharged; these form Class B; while a third class would include the false glands which never develop with ducts, which produce either merely an internal secretion so-called, or are adapted to the development of cells of special kinds, as, for example, the lymph- and genital-glands; such structures constitute Class C.

We must first attempt a classification more in detail of the true epithelial glands (Class B). In my opinion we can best make two fundamental divisions. The glands of the first division have often been called single or simple follicular glands; I propose for them the term "*simple glands*." The glands in question are always small and have one or several centers of growth according as they are simple tubes or slightly branching. Those of each kind are always very numerous and they occur more or less near together over considerable areas. There are two types of these known. The first are simple invaginated areas with scattered unicellular glands, as for instance the glands of the large intestine, the so-called Lieberkühn's follicles; they might be called simple follicles. Glands of the second type are invaginated areas with specialization of the cells, as, for example, the sweat, gastric, and sebaceous glands; they might be called glandular follicles. In the accompanying table the principal glands of this division are enumerated.

The glands of the second division are of greater bulk and are often referred to as organic or branching glands. I propose to name them "*compound glands*." They are provided with a single main duct, which is more or less freely branched, each branch connecting finally with the secretory portion proper of the organ, which portion may itself also be branched or not. Each gland falling in this division is a more or less complete organ by itself, receiving its special blood supply, and its special innervation—is, in short, a clearly marked physiological entity. Such a gland differs profoundly in its plan of organization from the glands of our first division. Of the second division there are clearly three main types to be distinguished. In the first type the branches of the glands are found to be supported by mesenchyma or its derivative, connective tissue, which is more or less abundant between the ducts and secretory elements of the organ, and in the mesenchyma there is a capillary circulation, which is often brought, however, into intimate proximity with the epithelial elements of the organ. These organs are further character-

ized by the fact that their branches remain distinct. In the second type, on the other hand, the branches unite together and form an anastomosing gland structure, and when this anastomosing condition is found it is associated, not with the development of connective tissue and capillaries, between the epithelial elements of the organ, but, on the contrary, with the presence of a sinusoidal circulation. The branching glands with capillary circulation are numerous, and they may arise, as is noted in the table, from either the ectoderm, the entoderm, or the mesothelium. Glands of the second type, anastomosing and furnished with sinusoids, are few in number. The liver is, of course, the most typical and the most important. With the liver we ought perhaps to associate the parathyroid, for the recent and still unpublished investigations of Dr. John Warren show that when this gland is highly developed it is of an anastomosing type, and make it probable that its blood supply is sinusoidal.

There remains still a third type, which is necessary, because the ducts become obliterated in a certain number of true epithelial glands, which develop primarily with ducts. There results in each case a group of hollow epithelial follicles, which are characteristic. For this type I propose the name, "*ductless epithelial glands*." The thyroid gland and the hypophysis are probably the best-known illustrations of this group of glands. Although the morphology of the pineal gland (epiphysis) is obscure, the organ seems at present to belong to our third type.

Our third Class, C, comprises the false glands, which never develop with ducts. So far as I am aware this statement may be made absolute for all glands of this class. It is true beyond any possible question for most of the glands, which are here to be considered, but it is perhaps as well to note that possibly some of the glands of the first division may be found in some vertebrates to have been primitively provided with ducts. This seems to me possible, but not probable. The first division of the false glands are the epithelioid. They are perhaps exclusively, so far as the essential gland elements are concerned, of entodermal origin, and it has become probable that their circulation is typically sinusoidal. In the present state of our knowledge it would be venturesome to make positive assertions on these two points. In the epithelioid glands we have groups of cells of epithelial origin separated, in the adult at least, from the layer which produced them, and brought into intimate relation with blood-vessels. A second division comprises the mesenchymal ductless glands, which are similar to the epithelioid glands in their general appearance, but their specific elements are derived from the middle germ layer. As an illustration of the ductless false gland of the first division, I may mention the parathyroid; of the second division, the suprarenal cortex. As

to the position of the thymus, I feel quite uncertain and hardly dare to say whether it should be placed among the epithelioid glands or among the cell-producing glands. Similarly, how to place the interstitial cells of the genital glands in our system is not yet quite clear to me. The third division is that of the cytogenic glands, and of these we may readily distinguish three important types: the first, those in which lymph cells arise; second, those which produce red blood corpuscles; and third, those which yield the genital elements. The glands of the first type may be called lymphæal structures. "Lymphæal" is a new term derived from "Lymphæum," itself a new technical expression, which I have used for several years in my lectures on histology and have found advantageous. A lymphæum may be defined as follows: it is a site for the multiplication of leucocytes and is a more or less definitely circumscribed area consisting of cellular reticulum, the meshes of which are charged with leucocytes and are in direct communication with lymph-vessels, or more rarely with blood-vessels. The following offer examples of lymphæa: solitary follicles, tonsils, thymus, lymph glands, hæmolymp glands and spleen. As stated above, whether the thymus should belong in the first or third division, I cannot say. Of the second type in this division, the bone marrow is the most important example. Of the third type, that of the genital glands, we have of course to distinguish two forms, the ovary and the testis.

With these explanations, I hope the accompanying table will be clear and I trust that the proposed new classification of glands will seem to you both more scientific and more available than the classification now prevalent, which I should like to see displaced.

TABLE II. CLASSIFICATION OF GLANDS.²

CLASS A. *Unicellular.*

CLASS B. *True Glands*, always developed with ducts.

DIVISION 1. *Simple Glands*, (*unifollicular or single glands*).

a. *Ectodermal.*

1. Sweat glands.
2. Sebaceous glands.
3. Buccal glands.

b. *Entodermal.*

1. Œsophageal.
2. Gastric.
3. Intestinal.

c. *Mesothelial.*

1. Uterine.

DIVISION 2. *Compound Glands (organic or true compound glands).*Type a, ductless epithelial branching (*with capillary circulation*).

1. Ectodermal.
Salivaries, tear gland, Harderian.
Mammary glands.
2. Entodermal.
Pancreas.
3. Mesothelial.
Appendicular glands of the urogenital system.

Type b, anastomosing (*with sinusoidal circulation*).

1. Liver.
2. Paraphysis (in *Necturus*).

Type c, ductless epithelial (*with secondary obliteration of duct*).

1. Thyroid.
2. Hypophysal gland.
3. Infundibular gland.
4. Pineal (*epiphysis*).

CLASS C. *False Glands*, never developed with ducts.DIVISION 1. *Epithelioid glands (exclusively entodermal?)*

1. Parathyroid.
2. Carotid.
3. Thymus (*cf. below*) (?).

DIVISION 2. *Mesenchymal ductless glands.*

1. Suprarenal cortex.
2. Coccyeal gland and other chromaffin cell organs.
3. Interstitial cells of genital glands (?).

DIVISION 3. *Cytogenic glands.*

a. Lymphæal structures.

1. Lymph glands and follicles (tonsil?).
2. Hæmolymph glands.
3. Spleen.
4. Thymus (?).

b. Sanguifactive organs.

1. Bone marrow.

c. Genital glands.

1. Ovary.
2. Testis.

I should like to include, in passing, reference to another general anatomical conception which, though not based strictly on embryological results, may be appropriately mentioned. I mean that unit of adult organization, which is sometimes referred to as the "*lobule*," but, as this term is somewhat confusing owing to the manifold meanings assigned to it, I venture to express the hope that the term "*structural unit*" will be

used instead, as has already been done by a few writers. We can then continue to employ the term lobule for the lung and the liver in the senses tradition gives to the term, as used for these two organs, and avoid confusion. The *structural unit*^s may be defined as the territory of an organ supplied by a single terminal branch of an afferent vessel (artery or vein). The volume of such a unit is often only 10-20 cubic millimeters. In the case of the liver, the structural unit comprises parts of several adjacent so-called lobules. It is a pleasure to recall that the recognition of the anatomical importance of these units is due to one of our most distinguished American investigators, Dr. Mall.

Finally, I should like to apply the principle of genetic interpretation to descriptive anatomy. It will, I think, sufficiently expound the point of view I am advocating to consider the application of the principle to a single organ, and for this purpose we may conveniently select the liver. In order to show that what I propose is practically a real and great innovation, let me indicate to you briefly the character of the anatomical descriptions of the liver to be found in some of the leading text-books of human anatomy.

In Cunningham's Anatomy (1902), the account of the liver is written by Professor Birmingham. He describes, 1, the general form of the surface; 2, the topographical relations and surfaces in detail; 3, the fissures, without giving their morphological relations; 4, the division into right and left chief lobes; 5, the peritoneal relations and ligaments; 6, the physical characteristics.

In the tenth edition of Quain's Anatomy (1896), the description opens, 1, with the dimensions and weight; 2, the surfaces; 3, the fissures; 4, the ligaments and the omentum; 5, the topographical relations; 6, vessels and nerves; 7, the ducts.

Testut in the third volume of his Anatomy (1894) gives, 1, the situation; 2, fixation; 3, volume and weight; 4, general confirmation, including the two chief right and left lobes; 5, the surfaces in detail.

The account of the liver in Poirier's Anatomy, Volume IV (1895), is written by Charpy, who begins with 1, the definition, and continues with 2, situation; 3, fixation; 4, data as to weight, consistency, etc.; 5, the form and surfaces. Under the head of fixation Charpy says:

"La foie est suspendu à la voute du diaphragme par deux moyens d'attache: par des replis péritonéaux et par la veine cave inferieure."

This misleading statement is the more deplorable because he mentions only incidentally that the liver adheres directly to the diaphragm. Quite at the end, the division into the right and left lobes is mentioned.

In the fourth edition (1901) of Merkel-Henle's *Grundriss*, there is, 1, a general account, which is distinctly not morphological in character; 2, detailed description of the surfaces and topography; 3, of the histology.

Gegenbaur in the seventh edition of his *Anatomy* (1899) proceeds very differently, for he has strong morphological inclinations. He gives, 1, the general account of the development of the liver; 2, general account of the surfaces, including the division into the chief lobes; 3, the relation of the veins to the omentum and the falciform ligament. Gegenbaur is the only author of a text-book of human anatomy, known to me, who gives a distinctly morphological account of the human liver, but even his presentation of the subject leaves much to be desired, chiefly because his knowledge of embryology was meagre, and quite insufficient for an adequate interpretation.

It would be easy to analyze descriptions in other text-books, but enough has been presented to show that they are usually characterized by certain common tendencies. The authors dwell upon the position and shape of the liver, seeking to emphasize its exact form, but not endeavoring at all to emphasize the essential characteristics of the organ, or to bring out the significance of its parts in a manner satisfactory to either an embryologist, a physiologist, a morphologist, or a pathologist. With the exception of Gegenbaur, none of the accounts rises above the level of sheer description.⁵ They simply perpetuate the tradition inherited from the time when human anatomy was only the description of what was actually found in the human adult. That tradition has undoubtedly been in part maintained by the demands of surgeons, whose interest is necessarily chiefly given to the exact determination of the topographical divisions in the body, hence the influence of the surgeons, when dominant in the anatomical laboratory, has often exerted an influence unfavorable to the becoming maintenance of a scientific-spirit, such as we ought to insist upon for the sake alike of anatomy and medicine.

If we review collectively the brief analyses just given of the actual descriptions in the text-books, we realize at once that those points, which the genesis of the liver reveals to us as fundamental, are scarcely heeded by the authors whom we have reviewed. This is not a fitting occasion to attempt a new description of the liver, and I can merely indicate to you the principal points upon which a scientific description ought, in my opinion, to be based. No little study and care would be necessary to work out practically the suggestions, embodied in the following schedule. Indeed, the schedule can doubtless be improved by others.

In order to prepare an adequate description of the liver, we must begin by laying aside certain bad habits which we have inherited and have

allowed ourselves to perpetuate. I mean the habit of applying the term ligaments, and the habit of applying the term fissures, to the liver; also the habit of describing the hepatic segment of the vena cava inferior as a vessel distinct from the liver, it being in reality, strictly, in every sense of the word, a portion of the organ. It may be further suggested that the introduction of a new term, *mesepatium*, may assist in clarifying the relations. The "*mesepatium*" is the membrane (French *méso*), which stretches from the ventral border of the stomach and duodenum to the median line of the ventral abdominal wall. It is in this membrane that the liver develops. Above the liver, between it and the stomach, is the dorsal mesepatium (lesser omentum). Between the liver and the body wall is the ventral mesepatium (falciform or suspensory ligament). Instead of speaking of the ligaments, we should speak of the insertion of the dorsal and ventral mesepatium into the liver; and instead of coronary and triangular ligaments, we should speak of the attachment of the liver to the diaphragm. This area of attachment might be called, as regards the diaphragm, the hepatic area, as regards the liver, the phrenic area.

With these preliminary explanations in mind, it may be suggested that a description of the liver must begin, as many authors have begun it already, with a general statement in regard to the position, size, color, and general form of the organ, and explaining that it is a gland, with a duct opening into the duodenum, and having the gall bladder appended to it, and that the circulation is sinusoidal, and not capillary.

Next, I should place a careful statement of the fundamental relations, as follows, *first*, of the broad connection of the liver with the diaphragm. This connection is primitive embryologically, is maintained throughout life and constitutes the phrenic area. It is not by the so-called ligaments or peritoneal folds, nor is it by the vena cava inferior that the liver is attached to the diaphragm. On the contrary it is by a large and characteristically shaped phrenic area of the organ that the connection is established. *Second*, the relation of the liver to the mesepatium, pointing out especially that the insertions of the dorsal and ventral mesepatia mark the division of the liver into right and left lobes and that the insertion is enlarged at one point towards the right to form the so-called porta of the liver, which admits from the dorsal mesepatium the hepatic artery, bile duct, and portal vein. *Third*, the relation of the veins to the organ, emphasizing that the portal vein marks the border of the dorsal mesepatium, and that its branches within the organ mark the so-called portal canals; emphasizing also that the umbilical vein or venous ligament marks the free edge of the ventral mesepatium, and explains the position,

origin and adult state of the ductus venosus. *Fourth*, the entrance and exit of the vena cava inferior. In this connection there should be made clear the rôle of the caval mesentery in furnishing a path for the *cava inferior*, and at the same time shutting off the lesser peritoneal space, and keeping the surface of the Spigelian lobe as part of the boundary of this space.

Next, again, might be presented the secondary features, especially the marking off of the caudate lobe from the chief right lobe by the vena cava inferior, and the marking off, similarly, of the quadrate lobe by the porta and the gall bladder.

Finally, according to this schedule, the description of the finer surface modelling and the contact with various adjacent organs, such as the stomach, colon, duodenum and kidney. Not one of these topographical relations is indispensable for a comprehension of the general character of the organ. Even from the standpoint of the surgeon and physician they are of minor importance. If they are put, as has been customary, in the forefront of text-book descriptions, attention is distracted from more essential things. Surely one need not argue to prove that a general comprehension of each organ is, first and last, the most important goal, to be striven for in the study of it.

In regard to almost every organ in the body it may be said, I think without injustice, that the current anatomical text-books offer bare and barren form-descriptions, seldom giving much, and often giving no, consideration to the essential morphological features of the parts. Take, for example, the urogenital system. We all know that the internal female genitalia are formed of two urogenital ridges, which fuse in the median line, making the so-called genital cord. There is in each ridge a longitudinal epithelial duct, which becomes the Fallopian tube, and by fusing with its fellow in the genital cord, produces the cavity of the uterus and vagina. A projection on one side of each ridge forms the ovary. Where the ridges have not united, rudiments of the Wolffian body of the embryo occur. The surface of the ridges, both where they are separate and where they are united, is covered by mesothelium. Around the duct (Fallopian tube), there is developed a muscular layer, and around the uterine portion of the fused ducts in the female a very powerful musculature is developed. By the union of the two ridges a partition is formed across the pelvic end of the abdomen, so that the abdominal cavity forms a pocket on the dorsal, and another on the ventral, side of the genitalia. Now the anatomical way of describing these organs is not to mention the ridges at all, but in the case of the female to speak of the uterus and its liga-

ments. It seems sometimes as if a deliberate effort were made by the descriptive anatomist to exclude all liberal use of the understanding and of the intelligence from the study of anatomy, and to reduce it almost to mere memorization of shapes and proportions, exceedingly difficult to fix in the mind by that method.

Is one not justified in condemning with great severity the perpetuation of this old type of anatomy? Is it not a grave mistake to fail to take advantage of the progress of anatomical science, and to utilize the best results of anatomical investigation to aid us in forming for ourselves, and still more, perhaps, for our students, clear notions of the essential characteristics of human organization? There has been within the last twenty-five years a very great progress in our knowledge of the topographical anatomy of the viscera, both thoracic and abdominal. When I plead for the presentation of the subject from the genetic standpoint, I do not mean to imply that this superior topographical knowledge should be slighted, but, on the contrary, I believe that if the student can first master the essential morphological relations of the body, it will be easier for him to master subsequently the finer, and often practically important, topographical details. Let our motto be, not "to memorize," but "*to comprehend*" the facts of anatomy.

Embryology illuminates anatomy. Its teachings give us the intellectual mastery of anatomical science, because embryology analyzes details, discriminates the essential from the secondary facts, and establishes the genetic interpretation, in the solvent light of which the obscurities of ancient anatomy vanish, and we see, where before was a dead sea of innumerable facts, new vital laws arising and guiding principles.

NOTES.

1. P. 247. Cytomorphosis was first used in the Middleton Goldsmith Lecture for 1901, entitled "The Embryological Basis of Pathology," *Science*, XIII, 481.

2. P. 256. Perhaps all or some of the salivary glands are entodermal. The submaxillary gland belongs among the organs, when it is a single large compound gland with a Bartholini's duct. When the submaxillary is represented by a group of small glands, they belong with the other simple buccal glands.

The position of the mammary gland must remain uncertain, until we can decide whether it is merely a group of glands, or morphologically a true compound gland. The significance of its peculiar development is still unsettled.

The hypophysis will perhaps, with more accurate study, be found to be an anastomosing gland with a sinusoidal circulation.

3. P. 258. The morphological characteristics of the structural (or histological) unit have been pointed out by Mall, so that the brief inadequate definition seems sufficient for the occasion.

4. P. 252. The account of the formation of sinusoids is somewhat schematic. We now know that the intercrecence of the vessels and parenchyma offers variations especially in its mode of beginning.

5. P. 259. Huntington's *Anatomy of the Peritonæum*, etc. (1903), is written entirely from the genetic and comparative standpoint. This excellent work, however, is not a general text-book, and in no sense belongs in the class of manuals criticized in the text. Even Huntington's account of the liver seems to me not to take sufficient advantage of our morphological knowledge, especially as regards the primary connection of the liver with the diaphragm and also as regards the sinusoidal circulation.