

**Researches on the primary stages of histogenesis and histolysis / by Robert D. Lyons, M.B.T.C.D., M.R.I.A. (Honorary Professor of Anatomy to the Royal Dublin Society, etc.).**

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Professor Bennett

With the autograph  
Compliments

RESEARCHES  
ON  
THE PRIMARY STAGES  
OF  
HISTOGENESIS AND HISTOLYSIS.

BY  
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RESEARCHES

THE PRIMAVERA

HISTOGENESIS AND HISTOLYSIS

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# RESEARCHES,

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MUCH yet remains to be achieved by chemical and microscopic researches, before we shall be in a position to understand thoroughly the laws, in obedience to which the elementary bodies combine to form organic compounds, and the processes by which these latter assume the determinate forms and distinctive characters of the various vegetable and animal tissues.

The term HISTOGENESIS is employed to designate the origin, development, and growth of animal and vegetable tissues, and under this head are included several of the most obscure and difficult problems in the entire domain of physiological science. Thus we have still to inquire what it is that determines the formation of plastic fluids; what are the forces brought into play to determine the growth of a tissue from an amorphous blastema, and, moreover, to give the elements of that tissue peculiar and characteristic properties; and, lastly, we have to inquire how various tissues combine to form organs. Each of these problems requires for its solution a greater amount of chemical and physico-physiological knowledge than we yet possess.

The researches of Turpin and Dumortier, Schleiden, Schwann, Henle, Valentin, Reichert, and others, have thrown considerable light on the manner of growth of tissues, and no reasonable doubt can be now entertained that the Cell-theory,



as elaborated by these and other observers, and specially applied to the development of animal structures by Schwann, fully and satisfactorily explains the mode of formation and development of several tissues and organs. Notwithstanding, however, the reception of this theory, even in its extreme and exclusive application, as insisted on by Schwann, in most schools, soon after its promulgation, it has been found defective in many points, and has been and is still questioned by several observers of authority. Having devoted much attention to this subject, I have become convinced by repeated observations that there are several tissues which at no period of their development exhibit any evidence of formation by cells, and consequently that cells cannot be considered as the only plastic germs or formative elements of organic life.

The following researches and observations appear to me to support the opinion now stated.

As the common hen's egg offers great facilities for the study of the formation of structures, I have made some careful observations of the microscopic elements, which it presents both before incubation and at certain periods after the commencement of that process.

1. A portion taken from the mass of the yolk, and submitted to a power of 420 D., exhibited the following elements :

*a.* An abundance of minute granules, covering the greater part of the field, of a light-yellowish colour, with a dark border and semi-opaque centre, moving freely on each other, and presenting the Brownian movement.

*b.* Bodies of larger size, strongly refractive, varying in diameter, and evidently oil-globules.

*c.* Vesicles of various sizes, round, oval, and elliptical, some presenting coarsely granular contents, others extremely fine, almost homogeneous, contents, their borders uniformly clear, dark, but fine, and readily seen ; these vesicles were, some as large as ordinary cells, others as small as nuclei. In none could I detect anything like a nucleus or nucleolus.



2. A portion of the germinal membrane was found to present—

*a.* Numerous granules, but in much less quantity than in the body of the yolk ; they were also clearer and more transparent.

*b.* Vesicles of various sizes, with fine pale contents, and clear but well-defined border, occasional oil-globules, granular corpuscles, with large, dark, spherical contents, and well-defined dark border. These corpuscles varied much in size ; aggregated masses of granules existed here and there, both of the light and dark variety of granules, and with corpuscles imbedded in them.

In no case did I see a distinctly nucleated cell in this preparation, many vesicles contained a central mass of spherules, but no distinct nucleus. The superposition of granules or vesicles is very likely to be mistaken for nuclei or nucleoli ; occasionally a motion in the fluid disturbs the granules, and they may then be seen to float freely away. I have often observed this.

3. In a preparation from near the germinal centre, after about twenty-four hours' incubation, the vesicles were much larger, more clearly seen, and very finely granular for the greater part ; a few presented central spherules, with or without granules, but I am doubtful, for the reasons just assigned, whether they are to be regarded as nuclei ; a few coarsely granular vesicles were to be seen ; also, isolated and aggregated granules.

4. From one of the halones, about a quarter of an inch external to the germinal centre, I took a fragment, which, when submitted to a power of 900 D., presented the following elements :

*a.* Large flat masses of a finely granular base or stroma, with superposed free granules, small vesicles, and oil-globules.

*b.* A considerable number of long flat bands or fibres, with a very fine, clear, double outline, and minutely granular centre, and occasional superposed and adjacent small vesicles and granules ; here and there a small vesicle was to be found lying



partly within and partly without the fibre. In some places the fibres appeared to me to terminate by tapering, indistinct granular ends, and I am much disposed to think that this indicates the true mode of their formation, viz., by the linear aggregation of granules. On the addition of acetic acid, I could get no indication of nuclei, or of the outlines of cells of any kind.

*c.* The large vesicles still exist in abundance, but I cannot see them anywhere to be distinctly engaged in forming any structure; I have looked in vain for nuclei in them; there appear to be two varieties of them—one finely granular, the other containing numerous large, dark globules. I think they become larger and more numerous for a certain time, and then break up; I look upon them as a-plastic, and consider their most probable use to be that of forming loci for the chemico-molecular elaboration of or change of combination of the chemical elements. The fibres above alluded to were found in the vicinity of granules, granular masses, and a small variety of cells.

5. In a preparation from near a blood islet I obtained a number of reddish-coloured elliptical corpuscles, some with nuclei, others without, also large finely granular vesicles, and a smaller kind of hyaline clearness, which burst on the addition of water.

6. In the plasma from a cut in my finger, five minutes after blood ceased to flow, I found not only granules, but granular corpuscles, hyaline vesicles, and granular masses. In another instance, one hour after the receipt of a wound in the hand, I examined the exudation, and found a well-marked granular base of considerable extent, abundance of granules, and a few examples of nucleated cells.

7. The observations of Robin and Handfield Jones, on the development of fat, likewise prove a mode of growth not reconcilable with the nucleo-cellular doctrine.

8. Another class of proofs may be deduced from the re-



sults of experimental or artificial Histogenesis, which go to prove the direct formation of tissues, without the intervention of cells.

Thus, in the well-known experiment of Ascherson, the contact of oil and albumen, two homogeneous fluids, gives rise to the formation of granules, granular base or stroma, vesicles, and simple membrane (hyaline membrane).

The experiments of Panum show the possibility of artificially forming granules, vesicles, and granular corpuscles.

The results obtained by Melsens, and fully confirmed by microscopic examination of his "*tissu cellulaire artificiel*" both by M. Gluge and myself, give us instances of the direct formation of at least three elements of organic bodies, independently of cells, viz., granules and granular base, fibres, and corpuscles.\* Similar results have been obtained by Parkes.

I am able to furnish another and valuable class of proofs from the results of my researches in Histolysis, which show, as will be fully detailed further on, that structures can originate under conditions when we cannot suppose any vital organic influence to be present, but when such forces as attraction, cohesion, fusion, endosmose and exosmose, and the mutual re-actions of elements differing in physical and chemical characters, are in full operation.

From the foregoing observations, and especially from the results of researches in Histolysis, I am induced to believe that in the formation of organic structures we may detect two quite distinct modes of growth and development, the one physical, the other organic (properly so called) or vital, the former taking place in obedience to certain physical laws alone; the latter, though operating by physical laws, yet guided and di-

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\* For an account of Melsens' experiments, see Dublin Quarterly Journal of Medical Science, February, 1852. For Panum's experiments, see Lyons' Annals of Micrology, British and Foreign Medico-Chirurgical Review, April, 1853.



rected by a force which, for the want of a better name, we are compelled to call vital.

The elements which result from these modes of growth differ widely in function and destination (the latter alone possessing the "gestaltungsfähigkeit"). There is reason, I think, to believe that the primary phases of Histogenesis are in a considerable measure similar to some of the artificial processes which have been above alluded to, and that in the history of development the following is the order of appearance of the elementary parts :

- I. An amorphous organic fluid, which in time exhibits the formation of—
- II. Primary organic granules, granular corpuscles, granular base or stroma, hyaline membrane, hyaline base or stroma, and hyaline vesicles.

Here we have an assemblage of elements of a simple kind which are to be met with, some or all variously combined in the examination of animal tissues and fluids: they are, in fact, the rubble work of the organic edifice, but have themselves no share in determining its development, being a-plastic, or incapable of generating higher tissues, though they may serve as pabulum for the more active plastic elements. But in the living organism we have elements of a still higher order, possessed of wonderful vitality, which we may suppose to be of later origin, and of whose mode of genesis we have still but very imperfect conceptions. These elements I will denominate Histo-plasts, or Histo-plastic Germs, and I conceive them to be of three kinds, Granules, Fibres, and Cells. The accompanying Table will exhibit more clearly my views of the order of precedence of the elementary parts of the organic fabric :



## AMORPHOUS ORGANIC FLUID.

From which become developed—

## I.

## A-PLASTIC ELEMENTS.

1. Primary Organic Granules :
  - (a) Isolated ;
  - (b) Aggregated ; and thus forming—
2. Granular Corpuscles ; or,
3. Granular Stroma or Base.
4. Hyaline Membrane (Cell Membrane, &c.)
5. Hyaline Stroma or Base.
6. Hyaline Vesicles.

## II.

## HISTO-PLASTS OR TRUE HISTO-PLASTIC GERMS.

7. Plastic Corpuscles, Granules, Nucleoli, Nuclei, and other Germs, if any.
8. Fibres (themselves formative elements).
9. Cells.
10. Definite Tissues.

It is unnecessary here to go farther into the study of these individual elements, the forms of which must be familiar to all experienced microscopic observers ; to the class of hyaline structures evidently belongs the membrane alluded to by Schwann, and whose formation even he found it difficult to reconcile with the exclusive adoption of his cell theory. He observes in reference to it : “ In many glands, as for instance the kidneys of a young mammalian fœtus, the stratum of cells surrounding the cavity of the duct is enclosed by an exceedingly delicate membrane, which appears to be an elementary structure, and not to be composed of areolar tissue ; the origin of this membrane is not at all clear, although we may imagine various ways of reconciling it with the formative process of cells.” Various cell walls are examples of hyaline membrane.



It is further to be remarked, that crystalline forms, whether organic or inorganic, have no place in this arrangement.

Several instances having come under my notice in which structures submitted to microscopic examination appeared to have undergone considerable alteration, by reason of a more or less advanced condition of decomposition, I was led to institute a series of observations for the purpose of discovering the order (if any) of the morphyic changes which take place in the passage of organized bodies through the several stages of putrefaction to their final dissolution and decay, until they return, "ashes to ashes," and "dust to dust." As I believe that the researches I have already made warrant me in stating that a certain order of morphyic changes is brought about, I have introduced the term HISTOLYSIS, to designate the morphyic changes of putrefying tissues, the use of a single word being convenient for the purposes of description and reference.

Not only will the study of Histolysis be found interesting in itself, as a portion of scientific inquiry, presenting, as it does, several beautiful and unexpected phenomena; but, moreover, the knowledge thereby acquired admits of several valuable and practical applications. Thus, it affords most favourable opportunities for the study of the intimate structure of complicated normal textures, which are thus, as it were, unfolded to our view by a process of natural dissection, in which the least possible violence is done to the most delicate parts. Furthermore, as I have already stated, I believe it furnishes us with means of elucidating some of the early and obscure phases of Histogenesis. Lastly, I feel confident that when the histolytic process will have been carefully and successfully studied in the chief tissues, fluids, and organs, the knowledge thus acquired will prove eminently useful in medico-legal inquiries, and will give a precision and accuracy to investigations of this nature which they are now incapable of. In pathological research, likewise, it will be highly useful. To study the morphyic changes of putrefaction, under what may be



termed its normal phases, it will be necessary to have the subjects of our intended examinations submitted to conditions of an equable mean temperature, with access of air and moisture. If none of these be in excess, the process is a sufficiently slow one; excess of any of them, if slight, will be found to rather hasten the putrefactive changes, while, if considerable, a condition may be produced in which the tissue will remain for a long time without farther change.

Extremes of heat, as is well known, will produce almost immediate dissolution, while, at a freezing temperature, structures will remain unaltered for almost an indefinite period. I now proceed to detail some of the observations which I have already made; they relate to cutaneous structures and fat, some varieties of human and animal blood, and muscular fibre. I omit for the present any notice of the general physical or chemical characters, though both are extremely important.

1. *Integument*.—This specimen had undergone change for four months. The epithelium of the cuticle was entirely destroyed, its place being supplied by a soft, pulpy mass, which presented an amorpho-granular mass under the microscope.

2. *Subcutaneous Structures after 6½ Months*.—They had the appearances of what is known as cadaveric fat; under the microscope, D. 900, there was seen an abundance of minute but well-defined granules, with fine, dark, well-marked border, and clear, transparent centre; they were arranged in masses, isolated, and in groups; small granular corpuscles of different sizes, and a few oil-globules; very large oval, pale, semi-opaque cells or vesicles; they had no nuclei; their borders were clear and well defined, but the most of them presented fissures, some as many as seven or eight, which extended inwards for about a sixth of the smaller axis; a very remarkable linear or moniliform arrangement of granules presented itself in certain parts of the field, sets or rows of granules being arranged longitudinally parallel or convergent, and apparently in connexion with very faint subjacent striations in the same direction—I am inclined



to regard this as an instance of granular disintegration of a band of fibre;—lastly, numerous stellate crystals, apparently of the fatty acids, lay scattered over the field, some also being included in cells, and appearing to be the stage of lysis of their previously granular contents, preparatory to the final rupture and dissolution of the including membrane.

3. *Blood*.—I have met with specimens of blood in which changes took place with great rapidity; I do not now allude to the corrugation and stellate appearance of the corpuscles, which is familiar to every one. In one specimen, after twenty-six hours, I found the hæmatine had escaped from numerous corpuscles, and had assumed the shape of granular masses, heaps, and crystals (hæmatoid crystals of Virchow). What pathological significance to give to this rapid change I do not know; but I am inclined to think that this, as well as other isolated facts which we now possess in reference to the blood, will be one day utilized.

4. *Blood Stains*.—This question is so important that I purpose making it the subject of a special inquiry. At present I will only add, that from specimens three months old, I have been able to figure the corpuscles, though much changed in form; also, a red granular base studded with corpuscles, and hæmatoid granules more or less aggregated.

2. *Histolysis in Fluid Blood*.—Blood of duck after two years (kept in a bottle). Here was presented an assemblage of forms widely different from those of the natural blood; none of the characteristic elliptical corpuscles of this animal's blood was to be found. There existed, firstly, abundance of granules, granular corpuscles, spherical vesicles of moderate size; square and oblong, apparently vesicular, bodies; large cells or vesicles, including one or more smaller ones: these several bodies were evidently the result of a process of secondary growth, taking place while the general process of dissolution was going on around, and constituting a kind of generation in death which may be termed thanato-genesis; in addition, there were nu-



merous prisms and needles of hæmatine, and large irregular hæmatine masses.

6. *Blood of Salmon*.—Of same date as last, and presenting nearly the same appearances; the granular bodies were, however, much larger; there existed also very large cells, including vesicles, and masses of granular base. Cells, including stellate crystals, were also visible. I am disposed to think that these forms resulted from the greater quantity of oil in the blood of fish, which, with the albuminous element, gave abundant means for these formations.

7. *Histolytic Changes in Muscle*.—The specimens examined had undergone the process of putrefaction for a considerable time; yet, by the aid of the microscope, the nature of the structures admitted of demonstration in the most clear and positive manner, though, I am satisfied, that by the unaided sight no amount of careful study would have sufficed for their recognition and identification. Under a power of 900 D., the following appearances were presented:—A semi-fluid granular mass, tinged of a light brown colour, in which granules, granular corpuscles, and spherules, were visible; here and there lay larger and smaller masses of elementary fibres, many of which retained, either in whole or part, their characteristic striæ, but presented internally more or less change.

There were seen several examples of elementary fibres. On more minutely examining these elementary fibres, it was found that some presented the transverse striation complete and perfect for a certain portion of their length; in others, the lines ceased at about half the transverse diameter; in other portions the edges only indicated the commencement of the striæ, which, however, were very clearly and well defined; almost all the elementary fibres which I was enabled to trace throughout their extent appeared to terminate indistinctly, a few only showed jagged and broken ends. A small number of the fibres continued clear and transparent throughout their entire extent, but, in the majority, the interior presented more or less change. Lastly, in a few instances I observed a number



of corpuscles of very peculiar and definite characters. These appeared to be perfectly spherical, were of a reddish-brown colour, and presented a well-marked edge sharply defined; in their interior lay another ring, having a diameter of about two-thirds of that of the outer, this enclosed a body or space which had the appearance of being depressed, and within which lay a dark central spot. These bodies varied somewhat in size, and lay, some mixed with other histolytic elements, some free and isolated on the field, and others again aggregated into masses, but showing no trace of any investing membrane. I am quite at a loss to understand the nature and origin of these peculiar corpuscles.

Scattered through the field lay granular masses, granular corpuscles, and cells; cells including numerous large corpuscles, formed, as it were, by endogenous growth; and finally, various stellate and acicular crystals, some within cells, others free on the field.

These results of the Histolysis of muscle are still very incomplete, yet I think they give us some indications of the mode in which the tissue breaks up. I may remark, incidentally, that from some of the appearances observed, I am led to adopt views different from those generally received, as to the nature of the striæ, which I am disposed to consider as belonging in greater part, if not entirely, to the sarcolemma.

In considering the chief results arrived at in the study of the process of putrefaction, I am led to believe—

1st. That concurrently with the first order of chemical changes, a certain order of morphyic changes takes place before the final dissolution of organic structures, by the action of chemical and physical forces.

2nd. That this series of changes may, under normal conditions, take place very slowly, so that, at the end of many months, and probably of even much longer periods, we are still enabled by the microscope to recognise and identify structures of great delicacy, such as elementary muscular fibre, and that this knowledge admits of important applications.



3rd. That in this process of Histolysis, the first changes consist in the softening, disunion, and separation from each other of the morphy constituents of the tissues, each of which is then subjected to a process of disintegration.

4th. That granules and granular corpuscles appear at an early period, arising probably from recombinations of the particles of the organic fluids. Animalcules appear at this stage.

5th. That granules, corpuscles, vesicles, cells, and granular masses of various kinds and sizes, may form in fluids and tissues undergoing Histolysis, in which no such elements exist when in their normal states.

6th. That generally in the progress of Histolysis, structures very similar to those which are arranged under the first group, or the a-plastic elements of Histogenesis, form at different stages, and that they exhibit the same modes of growth and development, but, like them, are incapable of producing higher forms.

7th. That these morphy elements of Histolysis pass gradually into lower forms, exhibiting occasional instances of endogenous fissiparition, granular disintegration, and other changes, and that the cellular and corpuscular elements, by forming media for endosmose and imbibition, may aid in the disintegration of contiguous structures.

8th. That certain elements may pass directly into a state of molecular disintegration.

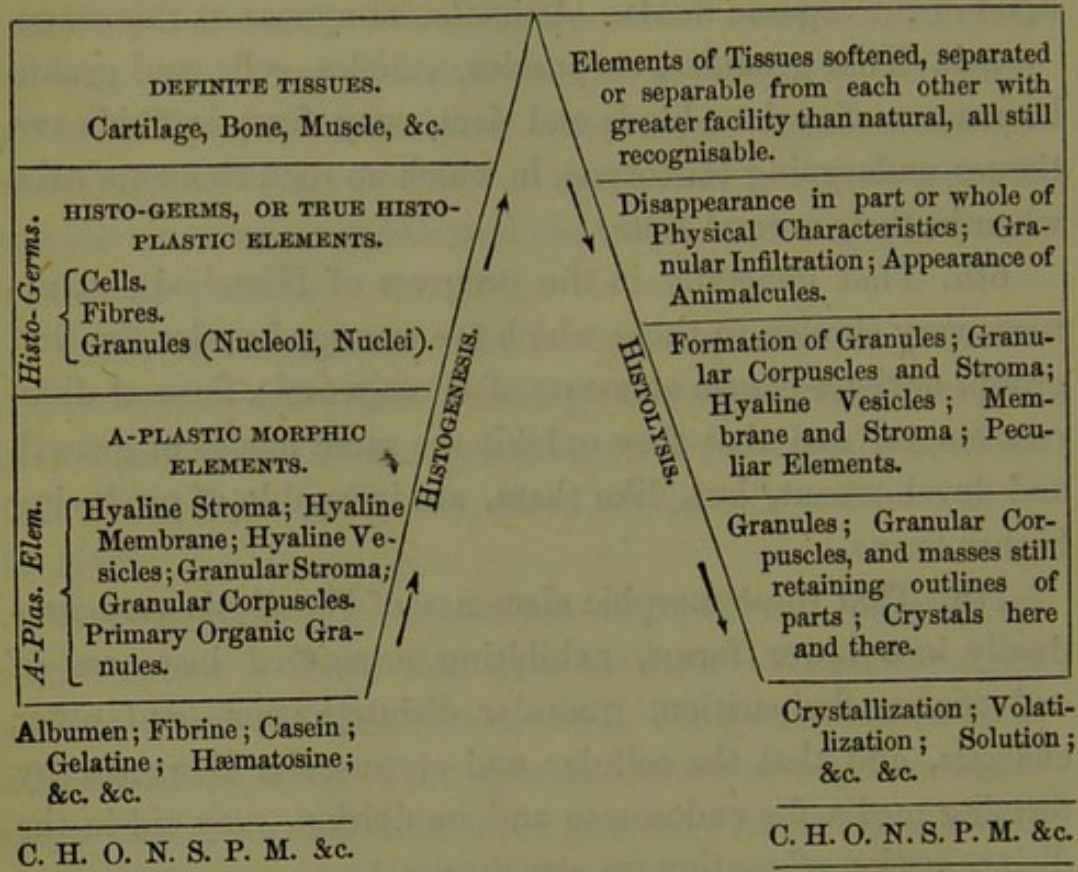
9th. That certain corpuscles of peculiar characters, and not identical with any known normal elements, are occasionally formed.

10th. That a period arrives at which chemico-physical forces prevail, which is evidenced by the passage of certain elements into crystalline forms, others passing off by volatilisation, solution, &c., and that in this way the final dissolution of a tissue is accomplished, the several morphy changes which take place probably facilitating and preparing the way for the action of chemical forces.



Lastly, it appears to me that the general scheme of the formation or Histogenesis of organic structures, and their final dissolution, or Histolysis, may be best represented in their mutual relations and analogies by a triangular figure, such as the following:—

S C H E M A.



Commencing from below, the left member of this scale presents us with the ascending series, corresponding to the growth and development or Histogenesis of Tissues, passing upwards in order from the simple bodies, carbon, oxygen, &c., through the organic compounds, albumen, fibrine, &c., till we reach the definite tissues. From the summit of the figure we then pass downwards, through the several phases of Histolysis, until finally, by the processes of crystallization, volatilization, &c., the organic compounds pass again to the state of simple elements. The study of this member of the scale is, of course, as yet in a very imperfect condition, and it offers an immense and highly interesting field for research.





