

CELLULAR PATHOLOGY

AS BASED UPON
PHYSIOLOGICAL AND PATHOLOGICAL
HISTOLOGY.

TWENTY LECTURES
DELIVERED IN THE
PATHOLOGICAL INSTITUTE OF BERLIN
DURING THE
MONTHS OF FEBRUARY, MARCH, AND APRIL, 1858.

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WITH
NOTES AND NUMEROUS EMENDATIONS, PRINCIPALLY FROM
MS. NOTES OF THE AUTHOR,
AND
ILLUSTRATED BY 144 ENGRAVINGS ON WOOD.

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PREFACE
TO THE
FIRST EDITION.

THE lectures which I herewith lay before the medical public at large were delivered in the early part of this year, in the new Pathological Institute of the University of Berlin, in the presence of a somewhat numerous assembly of medical men, for the most part physicians practising in the town. The object chiefly aimed at in them, illustrated as they were by as extensive a series of microscopical preparations as it was in my power to supply, was to furnish a clear and connected explanation of those facts upon which, according to my ideas, the theory of life must now be based, and out of which also the science of pathology has now to be constructed. They were more particularly intended as an attempt to offer in a better arranged form than had hitherto been done, a view of the cellular nature of all vital processes, both physiological and pathological, animal and vegetable, so as distinctly to set forth what even the people have long been dimly conscious of, namely, the unity of life¹ in all organized beings, in opposition to the one-sided humoral and neuristical (solidistic) tendencies which have been transmitted from the mythical days of

¹ See Lect. I, pp. 13—14, and Lect. XIV, pp. 284—286.—TRANS.

antiquity to our own times, and at the same time to contrast with the equally one-sided interpretations of a grossly mechanical and chemical bias—the more delicate mechanism and chemistry of the cell.

In consequence of the great advances that have been made in the details of science, it has been becoming continually more and more difficult to the majority of those who are engaged in practice, to obtain in the subjects treated on in these lectures that amount of personal experience which alone can guarantee a certain degree of accuracy of judgment. Day by day do those who are obliged to consume their best energies in the frequently so toilsome and so exhausting routine of practice find it becoming less and less possible for them, not only to closely examine, but even to understand the more recent medical works. For even the language of medicine is gradually assuming another appearance; well-known processes to which the prevailing system had assigned a certain place and name in the circle of our thoughts, change with the dissolution of the system their position and their denomination. When a certain action is transferred from the nerves, blood, or vessels to the tissues, when a passive process is recognized to be an active one, an exudation to be a proliferation, then it becomes absolutely necessary to choose other expressions whereby these actions, processes, and products shall be designated; and in proportion as our knowledge of the more delicate modes, in which the processes of life are carried on, becomes more perfect, just in that proportion must the new denominations also be adapted to this more delicate ground-work of our knowledge.

It would not be easy for any one to attempt to carry out the necessary reform in medical opinion with more respect for tradition than I have made it my endeavour to observe. Still my own experience has taught me that even in this there is a certain limit. Too great respect is a real fault, for it favours confusion; a well-selected expression renders at once accessible

to the understanding of all, what, without it, efforts prolonged for years would be able to render intelligible at most only to a few. As examples I will cite the terms, parenchymatous inflammation, thrombosis and embolia, leukæmia and ichor-rhæmia, osteoid and mucous tissue, cheesy and amyloid metamorphosis, and substitution of tissues. New names cannot be avoided, where actual additions to experimental (empirical) knowledge are being treated of.

On the other hand, I have already often been reproached with endeavouring to rehabilitate antiquated views in modern science. In respect to this I can, I think, say with a safe conscience that I am just as little inclined to restore Galen and Paracelsus to the position they formerly held, as I am afraid openly to acknowledge whatever truth there is in their views and observations. In fact, I find not only that the physicians of antiquity and the middle ages had not in all cases their senses shackled by traditional prejudices, but more than this, that among the people common sense has clung to certain truths, notwithstanding the criticism of the learned had pronounced them overthrown. What should hinder me from avowing that the criticism of the learned has not always proved correct, that system has not always been nature, and that a false interpretation does not impair the correctness of the fact? Why should I not retain good expressions, or restore them, even though false ideas have been attached to them? My experience constrains me to regard the term fluxion (active congestion—Wallung)¹ as preferable to that of congestion; I cannot help allowing inflammation to be a definite form in which pathological processes display themselves, although I am unable to admit its claims to be regarded as an entity; and I must needs, in spite of the decided counter-statements of many investigators, maintain tubercle to be a miliary granule, and

¹ See the Author's 'Handbuch der speciellen Path. und Therapie,' Vol. I, p. 141.

epithelioma a heteroplasmic, malignant new-formation (canceroid).

Perhaps it is now-a-days a merit to recognise historic rights, for it is indeed astonishing with what levity those very men, who herald forth every trifle, which they have stumbled upon, as a discovery, pass their judgment upon their predecessors. I uphold my own rights, and therefore I also recognize the rights of others. This is the principle I act upon in life, in politics and in science. We owe it to ourselves to defend our rights, for it is the only guarantee for our individual development, and for our influence upon the community at large. Such a defence is no act of vain ambition, and it involves no renunciation of purely scientific aims. For, if we would serve science, we must extend her limits, not only as far as our own knowledge is concerned, but in the estimation of others. Now this estimation depends in a great measure upon the acknowledgment accorded to our rights, upon the confidence placed in our investigations, by others; and this is the reason why I uphold my rights.

In a science so directly practical as that of medicine, and at a time when such a rapid accumulation of facts is taking place, as there is in ours, we are doubly bound to render our knowledge accessible to the whole body of our professional brethren. We would have reform, and not revolution: we would preserve the old, and add the new. But our contemporaries have a confused idea of the results of our activity. For only too much it is apt to appear as though nought but a confused and motley mass of old and new would thereby be obtained; and the necessity of combating rather the false or exclusive doctrines of the more modern, than those of the older writers, produces the impression that our endeavours savour more of revolution than reformation. It is, no doubt, much more agreeable to confine oneself to the investigation and simple publication of what one discovers, and to leave to others to "take it to market" (ver-

werthen—exploiter), but experience teaches us that this is extremely dangerous, and in the end only turns out to the advantage of those who have the least tenderness of conscience. Let us undertake, therefore, every one of us to fulfil the duties both of an observer and of an instructor.

The lectures, which I here publish with the view of accomplishing this double purpose, have found such very patient auditors, that they may perhaps venture to hope for indulgent readers likewise. How greatly they stand in need of indulgence, I myself feel very strongly. Every kind of lecture can only satisfy the actual hearers; and especially when it is chiefly intended to serve as an explanation of drawings on a board, and microscopical preparations, it must necessarily appear heterogeneous and defective to the reader. When the intention is to give a concise view of a comprehensive subject, it necessarily becomes impossible to bring forward all the arguments that could be advanced, and to support them by the requisite quotations. In lectures such as these too the personal views of the lecturer may seem to be brought forward with undue exclusiveness, but, as it is his business to give a clear exposition of the actual state of the science of which he treats, he is obliged to define with precision the principles, the correctness of which he has proved by his own experience.

I trust therefore that what I offer may not be taken for more than it is intended to be. Those, who have found leisure enough to keep up their knowledge by reading the current medical literature, will find but little that is new in these lectures. The rest will not, by reading them, be spared the trouble of being obliged to study the subjects, which are here only briefly touched upon, more closely in the special histological, physiological and pathological works. But they will at least be in possession of a summary of the discoveries which are the most important as far as the cellular theory is concerned, and they will easily be able to add their more accurate study

of the individual subjects to the connected exposition which I here give them of the whole. Nay, this very exposition may perhaps afford a direct stimulus for such more accurate study; and if it do but this, it will have done enough.

The time at my disposal was not sufficient to enable me to write out and revise a work like this. I was therefore constrained to have the lectures taken down in short-hand, just as they were delivered, and to publish them with but slight alterations. Herr Langenhaun has executed his stenographical task with great care. As far as the shortness of the time permitted, and wherever the text would otherwise have been difficult of apprehension to the inexperienced, I have had woodcuts made from the drawings on the board, and more particularly from the microscopical preparations which were sent round. Completeness in this respect could not be attained, seeing that, even as it is, the publication of the work has been delayed some months in consequence of the preparation of the woodcuts.

RUD. VIRCHOW.

MISDROY; *August 20th*, 1858.

PREFACE

TO THE

SECOND EDITION.

THE present attempt to bring the results of my experience, which are at variance with what is ordinarily taught, before the notice of the medical public at large, in a connected form, has produced unexpected results; it has found many friends and vigorous opponents. Both of these results are certainly very desirable; for my friends will find in this book no arbitrary settlement of questions, nothing systematical or dogmatical, and my opponents will be compelled at length to abandon their fine phrases and to set to work and examine the matters for themselves. Both can only contribute to the impulsion and advancement of medical science.

But still both have also their depressing point of view. When one has laboured for ten years with all the energy and zeal of which he was capable, and has laid the results of his investigations before the judgment of his contemporaries, one is only too apt to imagine that a considerable part, that perhaps the greater and more important portion of them, would be pretty generally known. This was, as I have learned by experience, not the case with my labours. One of my critics attributes it to my bringing forward too many arguments and lengthy cases in support of my views. It may be so, but then I might

	PAGE
Difference between formation and transformation. Fresh and growing, in opposition to macerated, bone. Nature of medullary tissue.—Growth in length of tubular [long] bones; proliferation of cartilage. Formation of marrow as a transformation of tissue; red and yellow, normal and inflammatory marrow. Osseous tissue, calcified cartilage, osteoid tissue. Bone-territories: caries, degenerative osteitis. Granulation of bone. Suppuration of bone. Maturation of pus. Ossification of marrow.—Growth of long bones in thickness; structure and proliferation of the periosteum.—Granulations as analogous to the medulla of bones, and as the starting-point of all heteroplastic development.	
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Consideration of some forms of pathological formation of bone. Soft osteoma of the maxillæ. Rickets. Formation of callus after fracture.—Theory of substitutive new formation in opposition to exudative. Destructive nature of new-formations. Homology and heterology (malignity). Ulceration. Mollities ossium. Proliferation and luxuriation. Medulla of bones and pus.—Suppuration. Its two forms: superficial, occurring in epithelium; and deep, in connective tissue. Eroding suppuration (skin, mucous membrane): pus- and mucus-corpuscles in their relations to epithelium. Ulcerative suppuration. Solvent properties of pus.—Connection of destruction with pathological growth and proliferation. Correspondence of the first stage in pus, cancer, sarcoma, &c. Possible duration of the life of pathologically new-formed elements, and of pathological new-formations considered as wholes (tumours). Compound nature of the larger tuberos tumours (Geschwulstknoten), and miliary character of the real foci (Heerde). Conditions of growth and recurrence: contagiousness of new-formations and import of the anastomoses of cells. Cellular pathology in opposition to the humoral and neuristic. General infection of the body. Parasitism and autonomy of new-formations.

LECTURE XX.—FORM AND NATURE OF PATHOLOGICAL NEW-FORMATIONS 462

Nomenclature and classification of pathological new-formations. Consistence as a principle of division. Comparison with individual parts of the body. Histological division. Apparent heterology of tubercle, colloid, &c.—Difference of form and nature: Colloid, Epithelioma, Papillary tumour, Tubercle.—Papillary tumours: simple (condylomata, papillomata) and specific (villous cancer and cauliflower-tumour).—Tubercle: infiltration and granulation. Inflammatory origin of tubercle. Its production from connective tissue. Miliary granules, and solitary masses. The cheesy metamorphosis.—Colloid: myxoma. Collonema. Mucous or gelatinous cancer.—Physiological types of heterologous new-formations: lymphoid nature of tubercle, hæmatoid of pus, epithelioid of cancer, canceroid, pearly and dermoid tumours, and connective-tissue-like of sarcoma. Infectiousness according to the amount of juice.—Comparison between pathological new-formations in animals and vegetables. Conclusion.

LECTURE I.

FEBRUARY 10, 1858.

CELLS AND THE CELLULAR THEORY.

Introduction and object.—Importance of anatomical discoveries in the history of medicine.—Slight influence of the cell-theory upon pathology.—Cells as the ultimate active elements of the living body.—Their nature more accurately defined.—Vegetable cells; membrane, contents, nucleus.—Animal cells; capsulated (cartilage) and simple.—Nuclei of.—Nucleoli of.—Theory of the formation of cells out of free cytoblastema.—Constancy of nucleus and its importance in the maintenance of the living cell.—Diversity of cell-contents and their importance as regards the functions of parts.—Cells as vital unities.—The body as a social organization.—Cellular, in contradistinction to humoral and solidistic, pathology.

Explanation of some of the preparations.—Young shoots of plants.—Growth of plants.—Growth of cartilage.—Young ova.—Young cells in sputa.

GENTLEMEN,—Whilst bidding you heartily welcome to benches which must have long since ceased to be familiar to you, I must begin by reminding you, that it is not my want of modesty which has summoned you hither, but that I have only yielded to the repeatedly manifested wishes of many among you. Nor should I have ventured either to offer you lectures after the same fashion in which I am accustomed to deliver them in my regular courses. On the contrary, I will make the attempt to lay before you in a more succinct manner the development which I myself, and, I think, medical science also, have passed through in the course of the last fifteen years. In my announce-

ment of these lectures, I described the subject of them in such a way as to couple histology with pathology; and for this reason, that I thought I must take it for granted that many busily occupied physicians were not quite familiar with the most recent histological changes, and did not enjoy sufficiently frequent opportunities of examining microscopical objects for themselves. Inasmuch as, however, it is upon such examinations that the most important conclusions are grounded which we now draw, you will pardon me if, disregarding those among you who have a perfect acquaintance with the subject, I behave just as if you all were not completely familiar with the requisite preliminary knowledge.

The present reform in medicine, of which you have all been witnesses, essentially had its rise in new anatomical observations, and the exposition also, which I have to make to you, will therefore principally be based upon anatomical demonstrations. But for me it would not be sufficient to take, as has been the custom during the last ten years, pathological anatomy alone as the groundwork of my views; we must add thereto those facts of general anatomy also, to which the actual state of medical science is due. The history of medicine teaches us, if we will only take a somewhat comprehensive survey of it, that at all times permanent advances have been marked by anatomical innovations, and that every more important epoch has been directly ushered in by a series of important discoveries concerning the structure of the body. So it was in those old times, when the observations of the Alexandrian school, based for the first time upon the anatomy of man, prepared the way for the system of Galen; so it was, too, in the Middle Ages, when Vesalius laid the foundations of anatomy, and therewith began the real reformation of medicine; so, lastly, was it at the commencement of this century, when Bichat developed the principles of general anatomy. What

Schwann, however, has done for histology, has as yet been but in a very slight degree built up and developed for pathology, and it may be said that nothing has penetrated less deeply into the minds of all than the cell-theory in its intimate connection with pathology.

If we consider the extraordinary influence which Bichat in his time exercised upon the state of medical opinion, it is indeed astonishing that such a relatively long period should have elapsed since Schwann made his great discoveries, without the real importance of the new facts having been duly appreciated. This has certainly been essentially due to the great incompleteness of our knowledge with regard to the intimate structure of our tissues which has continued to exist until quite recently, and, as we are sorry to be obliged to confess, still even now prevails with regard to many points of histology to such a degree, that we scarcely know in favour of what view to decide.

Especial difficulty has been found in answering the question, from what parts of the body action really proceeds—what parts are active, what passive; and yet it is already quite possible to come to a definitive conclusion upon this point, even in the case of parts the structure of which is still disputed. The chief point in this application of histology to pathology is to obtain a recognition of the fact, that the cell is really the ultimate morphological element in which there is any manifestation of life, and that we must not transfer the seat of real action to any point beyond the cell. Before you, I shall have no particular reason to justify myself, if in this respect I make quite a special reservation in favour of life. In the course of these lectures you will be able to convince yourselves that it is almost impossible for any one to entertain more mechanical ideas in particular instances than I am wont to do, when called upon to interpret the individual processes of life. But I think that we must

look upon this as certain, that, however much of the more delicate interchange of matter, which takes place within a cell, may not concern the material structure as a whole, yet the real action does proceed from the structure as such, and that the living element only maintains its activity as long as it really presents itself to us as an independent whole.

In this question it is of primary importance (and you will excuse my dwelling a little upon this point, as it is one which is still a matter of dispute) that we should determine what is really to be understood by the term cell. Quite at the beginning of the latest phase of histological development, great difficulties sprang up in crowds with regard to this matter. Schwann, as you no doubt recollect, following immediately in the footsteps of Schleiden, interpreted his observations according to botanical standards, so that all the doctrines of vegetable physiology were invoked, in a greater or less degree, to decide questions relating to the physiology of animal bodies. Vegetable cells, however, in the light in which they were at that time universally, and as they are even now also frequently regarded, are structures, whose identity with what we call animal cells cannot be admitted without reserve.

When we speak of ordinary vegetable cellular tissue, we generally understand thereby a tissue, which, in its most simple and regular form is, in a transverse section, seen to be composed of nothing but four- or six-sided, or, if somewhat looser in texture, of roundish or polygonal bodies, in which a tolerably thick, tough wall (*membrane*) is always to be distinguished. If now a single one of these bodies is isolated, a cavity is found, enclosed by this tough, angular, or round wall, in the interior of which very different substances, varying according to circumstances, may be deposited, *e. g.* fat, starch, pigment, albumen (*cell-contents*). But also, quite independently of these local varieties in the

contents, we are enabled, by means of chemical investigation, to detect the presence of several different substances in the essential constituents of the cells.

The substance which forms the external membrane, and is known under the name of cellulose, is generally found to be destitute of nitrogen, and yields, on the addition of iodine and sulphuric acid, a peculiar, very characteristic, beautiful blue

tint. Iodine alone produces no colour; sulphuric acid by itself chars. The contents of simple cells, on the other hand, do not turn blue; when the cell is quite a simple one, there appears, on the contrary, after the addition of iodine and sulphuric acid, a brownish or yellowish mass, isolated in the interior of the cell-cavity as a special body (*protoplasma*), around which can be recognised a special, plicated, frequently shrivelled membrane (*primordial utricle*) (fig. 1, *c*). Even rough chemical analysis generally detects in the simplest cells, in addition to the non-nitrogenized (external) substance, a nitrogenized internal mass; and vegetable physiology seems, therefore, to have been justified in concluding, that what really constitutes a cell is the presence within a non-nitrogenized membrane of nitrogenized contents differing from it.

It had indeed already long been known, that other

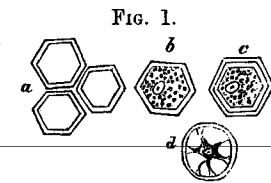


Fig. 1. Vegetable cells from the centre of the young shoot of a tuber of *Solanum tuberosum*. *a*. The ordinary appearance of the regularly polygonal, thick-walled cellular tissue. *b*. An isolated cell with finely granular-looking cavity, in which a nucleus with nucleolus is to be seen. *c*. The same cell after the addition of water; the contents (*protoplasma*) have receded from the wall (*membrane, capsule*). Investing them a peculiar, delicate membrane (*primordial utricle*) has become visible. *d*. The same cell after a more lengthened exposure to the action of water; the interior cell (*protoplasma* with the *primordial utricle* and nucleus) has become quite contracted, and remains attached to the cell-wall (*capsule*) merely by the means of fine, some of them branching, threads.

things besides existed in the interior of cells, and it was one of the most fruitful of discoveries when Robert Brown detected the *nucleus* in the vegetable cell. But this body was considered to have a more important share in the formation than in the maintenance of cells, because in very many vegetable cells the nucleus becomes extremely indistinct, and in many altogether disappears, whilst the form of the cell is preserved.

These observations were then applied to the consideration of animal tissues, the correspondence of which with those of vegetables Schwann endeavoured to demonstrate. The interpretation, which we have just mentioned as having been put upon the ordinary forms of vegetable cells, served as the starting point. In this, however, as after-experience proved, an error was committed. Vegetable cells cannot, viewed in their entirety, be compared with all animal cells. In animal cells, we find no such distinctions between nitrogenized and non-nitrogenized layers; in all the essential constituents of the cells nitrogenized matters are met with. But there are undoubtedly certain forms in the animal body which immediately recall these forms of vegetable cells, and among them there are none so characteristic as the cells of cartilage, which is, in all its features, extremely different from the other tissues of the animal body, and which, especially on account of its non-vascularity, occupies quite a peculiar position. Cartilage in every respect stands in the closest relation to vegetable tissue. In a well-developed cartilage-cell we can distinguish a relatively thick external layer, within which, upon very close inspection, a delicate membrane, contents, and a nucleus are also to be found. Here, therefore, we have a structure which entirely corresponds with a vegetable cell.

It has, however, been customary with authors, when describing cartilage, to call the whole of the structure

of which I have just given you a sketch (fig. 2, *a—d*) a cartilage-corpuscle, and in consequence of this having been viewed as analogous to the cells in other parts of animals, difficulties have arisen, by which the knowledge of the true state of the case has been exceedingly obscured. A cartilage-corpuscle, namely, is not, as a whole, a cell, but the external layer, the *capsule*, is the product of a later development (secretion, excretion). In young cartilage it is very thin, whilst the cell also is generally smaller. If we trace the development still farther back, we find in cartilage, also, nothing but simple cells, identical in structure with those which are seen in other animal tissues, and not yet possessing that external secreted layer.

You see from this, gentlemen, that the comparison between animal and vegetable cells, which we certainly cannot avoid making, is in general inadmissible, because in most animal tissues no formed elements are found which can be considered as the full equivalents of vegetable cells in the old signification of the word; and because, in particular, the cellulose membrane of vegetable cells does not correspond to the membrane of animal ones, and between this, as containing nitrogen, and the former, as destitute of it, no typical distinction is presented. On the contrary, in both cases we meet with a body essentially of a nitrogenous nature, and, on the whole, similar in composition. The so-called membrane of the vegetable cell is only met with in a few animal tissues, as, for example, in cartilage; the ordinary membrane of the animal cell corresponds, as I showed as far back as 1847,

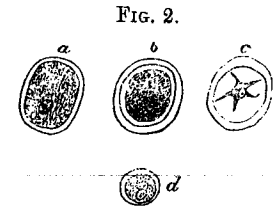


Fig. 2. Cartilage-cells, as they occur at the margin of ossification in growing cartilage, quite analogous to vegetable cells (cf. the explanation to fig. 1). *a—c*. In a more advanced stage of development. *d*. Younger form.

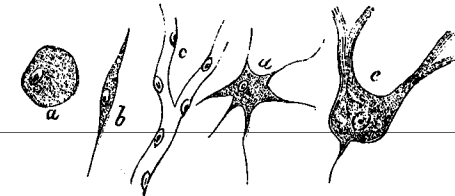
to the primordial utricle of the vegetable cell. It is only when we adhere to this view of the matter, when we separate from the cell all that has been added to it by an after-development, that we obtain a simple, homogeneous, extremely monotonous structure, recurring with extraordinary constancy in living organisms. But just this very constancy forms the best criterion of our having before us in this structure one of those really elementary bodies, to be built up of which is eminently characteristic of every living thing—without the pre-existence of which no living forms arise, and to which the continuance and the maintenance of life is intimately attached. Only since our idea of a cell has assumed this severe form—and I am somewhat proud of having always, in spite of the reproach of pedantry, firmly adhered to it—only since that time can it be said that a simple form has been obtained which we can everywhere again expect to find, and which, though different in size and external shape, is yet always identical in its essential constituents.

In such a simple cell we can distinguish dissimilar constituents, and it is important that we should accurately define their nature also.

In the first place, we expect to find a *nucleus* within the cell; and with regard to this nucleus, which has usually a round or oval form, we know that, particularly in the case of young cells, it offers greater resistance to the action of chemical agents than do the external parts of the cell, and that, in spite of the greatest variations in the external form of the cell, it generally maintains its form. The nucleus is accordingly, in cells of all shapes, that part which is the most constantly found unchanged. There are indeed isolated cases, which lie scattered throughout the whole series of facts in comparative anatomy and pathology, in which the nucleus also has a stellate or angular appearance; but these are extremely rare excep-

tions, and dependent upon peculiar changes which the element has undergone. Generally, it may be said that, as long as the life of the cell has not been brought to a close,

FIG. 3.



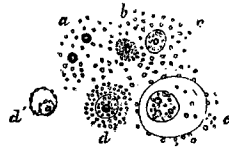
as long as cells behave as elements still endowed with vital power, the nucleus maintains a very nearly constant form.

The nucleus, in its turn, in completely developed cells, very constantly encloses another structure within itself—the so-called *nucleolus*. With regard to the question of vital form, it cannot be said of the nucleolus that it appears to be an absolute requisite; and, in a considerable number of young cells, it has as yet escaped detection. On the other hand, we regularly meet with it in fully developed, older forms; and it, therefore, seems to mark a higher degree of development in the cell. According to the view which was put forward in the first instance by Schleiden, and accepted by Schwann, the connection between the three coexistent cell-constituents was long thought to be on this wise: that the nucleolus was the first to show itself in the development of tissues, by separating out of a formative fluid (*blastema, cytoblastema*), that it quickly attained a certain size, that then fine granules were precipitated out of the blastema and settled around it, and that about these there condensed a membrane. That in this way a nucleus was

Fig. 3. *a.* Hepatic cell. *b.* Spindle-shaped cell from connective tissue. *c.* Capillary vessel. *d.* Somewhat large stellate cell from a lymphatic gland. *e.* Ganglion-cell from the cerebellum. The nuclei in every instance similar.

completed, about which new matter gradually gathered, and in due time produced a little membrane (the celebrated watch-glass form, fig. 4, *d'*). This

FIG. 4.



description of the first development of cells out of free blastema, according to which the nucleus was regarded as preceding the formation of the cell, and playing the part of a real cell-former (*cytoblast*), is the one which is

usually concisely designated by the name of the *cell-theory* (more accurately, theory of *free* cell-formation),—a theory of development which has now been almost entirely abandoned, and in support of the correctness of which not one single fact can with certainty be adduced. With respect to the nucleolus, all that we can for the present regard as certain, is, that where we have to deal with large and fully developed cells, we almost constantly see a nucleolus in them; but that, on the contrary, in the case of many young cells it is wanting.

You will hereafter be made acquainted with a series of facts in the history of pathological and physiological development, which render it in a high degree probable that the nucleus plays an extremely important part within the cell—a part, I will here at once remark, less connected with the function and specific office of the cell, than with its maintenance and multiplication as a living part. The specific (in a narrower sense, animal) function is most distinctly manifested in muscles, nerves, and gland-cells; the

Fig. 4. From Schleiden, 'Grundzüge der wiss. Botanik,' I, fig. 1. "Contents of the embryo-sac of *Vicia faba* soon after impregnation. In the clear fluid, consisting of gum and sugar, granules of protein-compounds are seen swimming about (*a*), among which a few larger ones are strikingly conspicuous. Around these latter the former are seen conglomerated into the form of a small disc (*b*, *c*). Around other discs a clear, sharply defined border may be distinguished, which gradually recedes farther and farther from the disc (the cytoblast), and, finally, can be distinctly recognised to be a young cell (*d*, *e*)."

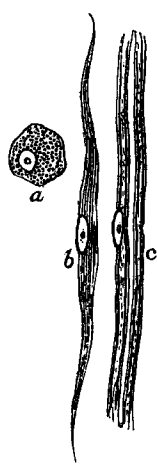
peculiar actions of which—contraction, sensation, and secretion—appear to be connected in no direct manner with the nuclei. But that, whilst fulfilling all its functions, the element remains an element, that it is not annihilated nor destroyed by its continual activity—this seems essentially to depend upon the action of the nucleus. All those cellular formations which lose their nucleus, have a more transitory existence; they perish, they disappear, they die away or break up. A human blood-corpuscle, for example, is a cell without a nucleus; it possesses an external membrane and red contents; but herewith the tale of its constituents, so far as we can make them out, is told, and whatever has been recounted concerning a nucleus in blood-cells, has had its foundation in delusive appearances, which certainly very easily can be, and frequently are, occasioned by the production of little irregularities upon the surface (Fig. 52). We should not be able to say, therefore, that blood-corpuscles were cells, if we did not know that there is a certain period during which human blood-corpuscles also have nuclei; the period, namely, embraced by the first months of intra-uterine life. Then circulate also in the human body nucleated blood-cells, like those which we see in frogs, birds, and fish throughout the whole of their lives. In mammalia, however, this is restricted to a certain period of their development, so that at a later stage the red blood-cells no longer exhibit all the characteristics of a cell, but have lost an important constituent in their composition. But we are also all agreed upon this point, that the blood is one of those changeable constituents of the body, whose cellular elements possess no durability, and with regard to which everybody assumes that they perish, and are replaced by new ones, which in their turn are doomed to annihilation, and everywhere (like the uppermost cells in the cuticle, in which we also can discover no nuclei, as soon as they begin to desquamate) have already reached a

stage in their development, when they no longer require that durability in their more intimate composition for which we must regard the nucleus as the guarantee.

On the other hand, notwithstanding the manifold investigations to which the tissues are at present subjected, we are acquainted with no part which grows or multiplies, either in a physiological or pathological manner, in which nucleated elements cannot invariably be demonstrated as the starting-points of the change, and in which the first decisive alterations which display themselves, do not involve the nucleus itself, so that we often can determine from its condition what would possibly have become of the elements.

You see from this description that, at least, two different things are of necessity required for the composition of a cellular element; the membrane, whether round, jagged, or stellate, and the nucleus, which from the outset differs in

FIG. 5.



chemical constitution from the membrane. Herewith, however, we are far from having enumerated all the essential constituents of the cell, for, in addition to the nucleus, it is filled with a relatively greater or less quantity of *contents*, as is likewise commonly, it seems, the nucleus itself, the contents of which are also wont to differ from those of the cell. Within the cell, for example, we see pigment, without the nucleus' containing any. Within a smooth muscular fibre-cell, the contractile substance is deposited, which appears to be the seat of the contractile force of muscle; the nucleus, however, remains a nucleus. The cell may develop itself into a nerve-fibre, but the nucleus remains, lying

Fig. 5. *a.* Pigment-cell from the choroid membrane of the eye. *b.* Smooth muscular fibre-cell from the intestines. *c.* Portion of a nerve-fibre with a double contour, axis-cylinder, medullary sheath and parietal, nucleolated nucleus.

on the outside of the medullary [white¹] substance, a constant constituent. Hence it follows, that the special peculiarities which individual cells exhibit in particular places, under particular circumstances, are in general dependent upon the varying properties of the cell-contents, and that it is not the constituents which we have hitherto considered (membrane and nucleus), but the contents (or else the masses of matter deposited without the cell, *intercellular*), which give rise to the functional (physiological) differences of tissues. For us it is essential to know that in the most various tissues these constituents, which, in some measure, represent the cell in its abstract form, the nucleus and membrane, recur with great constancy, and that by their combination a simple element is obtained, which, throughout the whole series of living vegetable and animal forms, however different they may be externally, however much their internal composition may be subjected to change, presents us with a structure of quite a peculiar conformation, as a definite basis for all the phenomena of life.

According to my ideas, this is the only possible starting-point for all biological doctrines. If a definite correspondence in elementary form pervades the whole series of all living things, and if in this series something else which might be placed in the stead of the cell be in vain sought for, then must every more highly developed organism, whether vegetable or animal, necessarily, above all, be regarded as a progressive total, made up of larger or smaller number of similar or dissimilar cells. Just as a tree constitutes a mass arranged in a definite manner, in which, in every single part, in the leaves as in the root, in the trunk as in the blossom, cells are discovered to be the ultimate elements, so is it also with the forms of animal life. *Every animal presents itself as a sum of vital unities*, every one of

¹ All words included in square brackets have been inserted by the Translator, and are intended to be explanatory.

which manifests all the characteristics of life. The characteristics and unity of life cannot be limited to any one particular spot in a highly developed organism (for example, to the brain of man), but are to be found only in the definite, constantly recurring structure, which every individual element displays. Hence it follows that the structural composition of a body of considerable size, a so-called individual, always represents a kind of social arrangement of parts, an arrangement of a social kind, in which a number of individual existences are mutually dependent, but in such a way, that every element has its own special action, and, even though it derive its stimulus to activity from other parts, yet alone effects the actual performance of its duties.

I have therefore considered it necessary, and I believe you will derive benefit from the conception, to portion out the body into *cell-territories* (Zellenterritorien). I say territories, because we find in the organization of animals a peculiarity which in vegetables is scarcely at all to be witnessed, namely, the development of large masses of so-called *intercellular substance*. Whilst vegetable cells are usually in immediate contact with one another by their

FIG. 6.

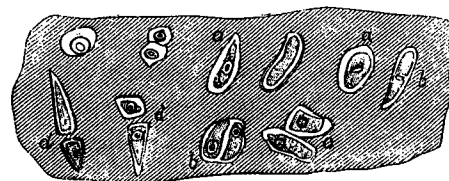


Fig. 6. Cartilage from the epiphysis of the lower end of the humerus of a child. The object was treated first with chromate of potash, and then with acetic acid. In the homogeneous mass (intercellular substance) are seen, at *a*, cartilage-cavities (Knorpelhöhlen) with walls still thin (capsules), from which the cartilage-cells, provided with a nucleus and nucleolus, are separated by a distinct limiting membrane. *b*. Capsules (cavities) with two cells, produced by the division of previously simple ones. *c*. Division of the capsules following the division of the cells. *d*. Separation of the divided capsules by the deposition between them of intercellular substance—Growth of cartilage.

external secreted layers, although in such a manner that the old boundaries can still always be distinguished, we find in animal tissues that this species of arrangement is the more rare one. In the often very abundant mass of matter which lies between the cells (*intermediate, intercellular substance*), we are seldom able to perceive at a glance, how far a given part of it belongs to one or another cell; it presents the aspect of a homogeneous intermediate substance.

According to Schwann, the intercellular substance was the *cytoblastema*, destined for the development of new cells. This I do not consider to be correct, but, on the contrary, I have, by means of a series of pathological observations, arrived at the conclusion that the intercellular substance is dependent in a certain definite manner upon the cells, and that it is necessary to draw boundaries in it also, so that certain districts belong to one cell, and certain others to another. You will see how sharply these boundaries are defined by pathological processes (Fig. 129), and how direct evidence is afforded, that any given district of intercellular substance is ruled over by the cell, which lies in the middle of it and exercises influence upon the neighbouring parts.

It must now be evident to you, I think, what I understand by the territories of cells. But there are simple tissues which are composed entirely of cells, cell lying close to cell. In these there can be no difficulty with regard to the boundaries of the individual cells, yet it is necessary that I should call your attention to the fact that, in this case, too, every individual cell may run its own peculiar course, may undergo its own peculiar changes, without the fate of the cell lying next it being necessarily linked with its own. In other tissues, on the contrary, in which we find intermediate substance, every cell, in addition to its own contents, has the superintendence of a certain quantity of matter external to it, and this shares in its changes, nay, is frequently affected even earlier than the interior of the

cell, which is rendered more secure by its situation than the external intercellular matter. Finally, there is a third series of tissues, in which the elements are more intimately connected with one another. A stellate cell, for example, may anastomose with a similar one, and in this way a reticular arrangement may be produced, similar to that which we see in capillary vessels and other analogous structures. In this case it might be supposed that the whole series was ruled by something which lay who knows how far off; but upon more accurate investigation, it turns out that even in this chainwork of cells a certain independence of the individual members prevails, and that this independence evinces itself by single cells undergoing, in consequence of certain external or internal influences, certain changes confined to their own limits, and not necessarily participated in by the cells immediately adjoining.

That which I have now laid before you will be sufficient to show you in what way I consider it necessary to trace pathological facts to their origin in known histological elements; why, for example, I am not satisfied with talking about an action of the vessels, or an action of the nerves, but why I consider it necessary to bestow attention upon the great number of minute parts which really constitute the chief mass of the substance of the body, as well as upon the vessels and nerves. It is not enough that, as has for a long time been the case, the muscles should be singled out as being the only active elements; within the great remainder, which is generally regarded as an *inert mass*, there is in addition an enormous number of active parts to be met with.

Amid the development which medicine has undergone up to the present time, we find the dispute between the humoral and solidistic schools of olden times still maintained. The humoral schools have generally had the greatest success, because they have offered the most con-

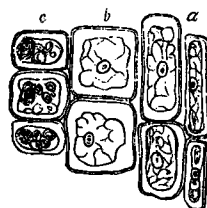
venient explanation, and, in fact, the most plausible interpretation of morbid processes. We may say that nearly all successful practical, and noted hospital, physicians have had more or less humoro-pathological tendencies; aye, and these have become so popular, that it is extremely difficult for any physician to free himself from them. The solidopathological views have been rather the hobby of speculative inquirers, and have had their origin not so much in the immediate requirements of pathology, as in physiological and philosophical, and even in religious speculations. They have been forced to do violence to facts, both in anatomy and physiology, and have therefore never become very widely diffused. According to my notions the basis of both doctrines is an incomplete one; I do not say a false one, because it is really only false in its exclusiveness; it must be reduced within certain limits, and we must remember that, besides vessels and blood, besides nerves and nervous centres, other things exist, which are not a mere theatre (Substrat) for the action of the nerves and blood, upon which these play their pranks.

Now, if it be demanded of medical men that they give their earnest consideration to these things also; if, on the other hand, it be required that, even among those who maintain the humoral and neuro-pathological doctrines, attention at last be paid to the fact, that the blood is composed of many single, independent parts, and that the nervous system is made up of many active individual constituents—this is, indeed, a requirement which at the first glance certainly offers several difficulties. But if you will call to mind that for years, not only in lectures, but also at the bedside, the activity of the capillaries was talked about—an activity which no one has ever seen, and which has only been assumed to exist in compliance with certain theories—you will not find it unreasonable, that things which are really to be seen, nay are, not unfrequently, after practice,

accessible even to the unaided eye, should likewise be admitted into the sphere of medical knowledge and thought. Nerves have not only been talked about where they had never been demonstrated; their existence has been simply assumed, even in parts in which, after the most careful investigations, no trace of them could be discovered, and activity has been attributed to them in parts where they absolutely do not penetrate. It is therefore certainly not unreasonable to demand, that the greater part of the body be no longer entirely ignored; and if no longer ignored, that we no longer content ourselves with merely regarding the nerves as so many wholes, as a simple, indivisible apparatus, or the blood as a merely fluid material, but that we also recognise the presence within the blood and within the nervous system of the enormous mass of minute centres of action.

In conclusion, I have still some preparations to explain, and will begin with a very common object (Fig. 7). It has been taken from the tuber of a potato, at a spot where

FIG. 7.



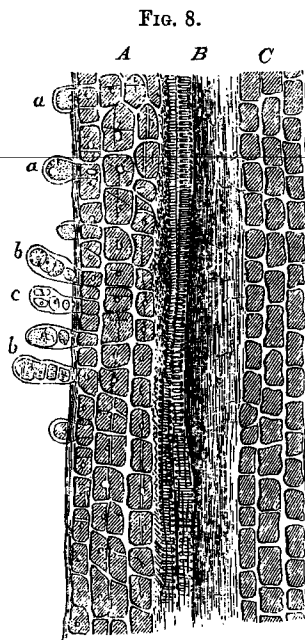
you can view in its perfection the structure of a vegetable cell, where the tuber, namely, is beginning to put forth a new shoot, and there is, consequently, a probability of young cells being found, at least, if we suppose that all growth consists in the development of new cells.

In the interior of the tuber all the cells are, as is well known, stuffed full with

granules of starch; in the young shoot, on the other hand,

the starch is used up, in proportion to the growth, and the cell is again exhibited in its more simple form. In a transverse section of a young sprout near its exit from the tuber, about four different layers may be distinguished—the cortical layer, next a layer of larger, then a layer of smaller, cells, and lastly, quite on the inside, a second layer of larger cells. Here we see nothing but regular structures; thick capsules of hexagonal form, and within them one or two nuclei (Fig. 1). Towards the cortex (corky layer) the cells are four-sided, and the farther one proceeds outwards, the flatter do they become; still, nuclei may be distinctly recognised in them also. Wherever the so-called cells come in contact, a boundary line may be recognised between them; then comes the thick layer of cellulose, in which fine streaks may be observed; and in the interior of the capsular cavity you see a compound mass, in which a nucleus and nucleolus may be easily distinguished, and after the application of reagents the primordial utricle also makes its appearance as a plicated, wrinkled membrane. This is the perfect form of a vegetable cell. In the neighbouring cells lie a few larger, dimly lustrous, laminated bodies, the remains of starch (Fig. 7, *c*). The next object is of importance in my eyes, because I shall afterwards have to refer to it when instituting a comparison with new formations in animals. It is a longitudinal section of a young lilac bud, developed by the warm days we have had this month (February). In the bud a number of young leaves have already begun to develop themselves, each composed of numerous young cells. In these, the youngest parts, the external layers are composed of tolerably regular layers of cells, which have a rather flat, four-sided appearance, whilst in the internal layers the cells are more elongated, and in a few parts spiral vessels show themselves. Especially would I call your attention to the little outgrowths (leaf-hairs—Blatthaare), which protrude every-

where along the border, and very much resemble certain animal excrescences, *e. g.*, in the villi of the chorion, where they mark the spots at which young, secondary villi will shoot out. In our preparation, you see the little, club-



shaped protuberances, which are repeated at certain intervals, and are connected internally with the rows of cells in the cambium. They are structures in which the more delicate forms of cells can best be distinguished, and, at the same time, the peculiar mode of growth be discovered. This growth is effected thus: a division takes place in some of the cells, and a transverse septum is formed; the newly-formed parts continue to grow as independent elements, and gradually increase in size. Not unfrequently divisions take place also longitudinally, so that the parts become thicker (Fig. 8, *c*).

Every protuberance is therefore originally a single cell, which, by continual subdivision in a transverse direction (Fig. 8, *a, b*), pushes its divisions forwards, and then, when occasion offers, spreads out also in a lateral direction. In this way the hairs shoot out, and this is in general the

mode of growth, not only in vegetables, but also in the physiological and pathological formations of the animal body.

In the following preparation—a piece of costal cartilage, in a state of morbid growth—changes are evident even to the naked eye, namely, little protuberances upon the surface of the cartilage. Corresponding to these the microscope shows a proliferation of cartilage-cells, and we find the same forms as in the vegetable cells; large groups of cellular elements, each of which has proceeded from a single previously existing cell, arranged in several rows, and differing from proliferating vegetable cells only in this—that there is intercellular substance between the individual groups.

In the cells we can as before distinguish the external capsule, which, indeed, in the case of many cells, is composed of two, three, or more layers, and within them only does the real cell come with its membrane, contents, nucleus, and nucleolus.

In the following object you see the young ova of a frog, before the secretion of the yolk-granules has begun. The very large ovum (Eizelle) (Fig. 10, *C*) contains a nucleus likewise very large, in which a number of little vesicles are dispersed—and tolerably thick, opaque contents, beginning, at a certain spot, to become granular and brown. Around

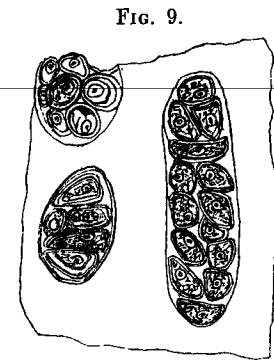
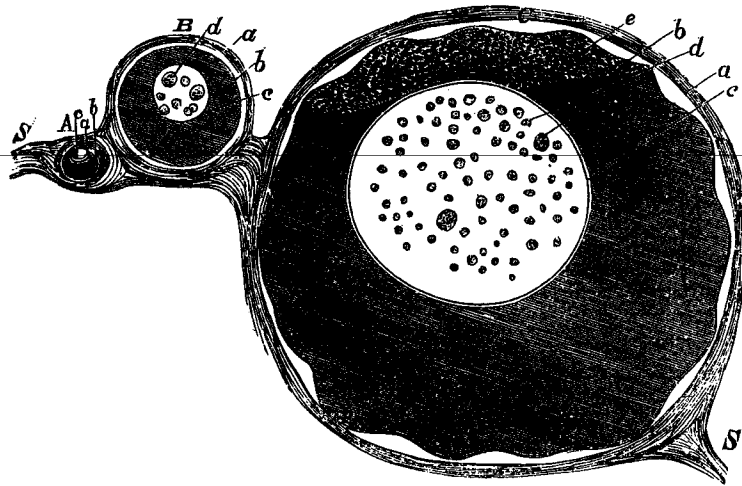


Fig. 9. Proliferation of cartilage; from the costal cartilage of an adult. Large groups of cartilage-cells within a common envelope (wrongly so-called parent-cells), produced from single cells by successive subdivisions. At the edge, one of these groups has been cut through, and in it is seen a cartilage-cell invested by a number of capsular layers (external secreted masses). 300 diameters.

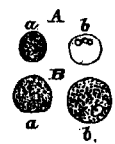
the cell may be remarked the relatively thin, connective tissue of the Graafian vesicle, with a hardly visible layer of

FIG. 10.



epithelium. In the neighbourhood are lying several smaller ova, which show the gradual progress of their growth.

FIG. 11.



As a contrast to these gigantic cells, I place before you an object from the bed-side; cells from fresh catarrhal sputa. You see cells in comparison very small, which, with a higher

Fig. 10. Young ova from the ovary of a frog. *A*. A very young ovum. *B*. A larger one. *C*. A still larger one, with commencing secretion of brown granules at one pole (*e*), and shrunken condition of the vitelline membrane from the imbibition of water. *a*. Membrane of the follicle. *b*. Vitelline membrane. *c*. Membrane of the nucleus. *d*. Nucleolus. *S*. Ovary. 150 diameters.

Fig. 11. Cells from fresh catarrhal sputa. *A*. Pus-corpuscles. *a*. Quite fresh. *b*. When treated with acetic acid. Within the membrane the contents have cleared up, and three little nuclei are seen. *B*. Mucus-corpuscles. *a*. A simple one. *b*. Containing pigment granules. 300 diameters.

power, prove to be of a perfectly globular shape, and, in which, after the addition of water and reagents, a membrane, nuclei, and, when fresh, cloudy contents can clearly be distinguished. Most of the small cells belong, according to the prevailing terminology, to the category of pus-corpuscles; the larger ones, which we may designate mucus-corpuscles or catarrhal cells, are partly filled with fat or greyish-black pigment, in the form of granules.

These structures, however small their size, possess all the typical peculiarities of the large ones; all the characters of a cell displayed by the large ones again present themselves in them. But this is, in my opinion, the most essential point—that, whether we compare large or small, pathological or physiological, cells, we always find this correspondence between them.