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.

BY

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TRANSLATED FROM THE SECOND EDITION OF THE ORIGINAL.

BY

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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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TO

JOHN GOODSIR, F.R.S., Etc.,

PROFESSOR OF ANATOMY IN THE UNIVERSITY OF EDINBURGH,

AS ONE OF THE EARLIEST AND MOST ACUTE OBSERVERS OF

CELL-LIFE,

BOTH PHYSIOLOGICAL AND PATHOLOGICAL.

THIS WORK ON

CELLULAR PATHOLOGY

Is Dedicated

AS A SLIGHT TESTIMONY OF HIS DEEP RESPECT

AND SINCERE ADMIRATION,

BY

THE AUTHOR.

AUTHOR'S PREFACE.

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 life* in all organized beings, in opposition to the one-sided humoral and neuristical (solidistic) tendencies which have been transmitted from the mythical days of 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

* See Lect. I., p. 40 and Lect. XIV., pp. 322–324.—Trans.

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 ichorrhæmia, 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)* 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 epithelioma a heteroplastic, malignant new-formation (cancroid).

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

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

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 combatting 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" (verwerthen—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 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.

AUTHOR'S 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 perhaps have been allowed to expect that other critics would have sought for the proofs, which they did not find here in sufficient abundance, in the original works. For I had in the preface to the first edition expressly pointed out that those who had kept up their knowledge, by reading the current medical literature, would here find but little that was new to them.

In this new edition I have contented myself with improving the language, with expressing in more precise terms what was liable to be misunderstood, and with expunging repetitions. There no doubt, still even now, remains a great deal requiring correction; but it seemed to me that the whole ought as far as possible to preserve the fresher impress of oral discourse, and of the unshackled range of thought which there prevails, if it were for the future still to serve as an active ferment to the labourers in the so very various fields of medical science and practice. For the book will have fulfilled its object, if it assists in the propagation, not of cellular pathology, but in general only of independent thought and investigation.

RUD. VIRCHOW.

BERLIN, *June 7th*, 1859.

TRANSLATOR'S PREFACE.

Professor Virchow and his works are so well known wherever the science of medicine is studied, that I think it quite unnecessary to give any account of them here.

When I arrived in Berlin in March, 1858, these lectures were in the course of delivery, and I was present at a few of the concluding ones. Subsequently, whilst attending the lectures, classes, and post-mortem examinations* which are held in the Pathological Institute by Professor Virchow, I had ample opportunities for seeing practical illustrations of most of the doctrines advocated in this book. It was natural, therefore, that I should feel a desire to translate these lectures, the more especially as I had every reason to suppose that the views put forward in them still remained unknown—in consequence, no doubt, of their German dress—to a large proportion of the English medical public, although they had already, many of them several years previously, appeared in Professor Virchow's larger works.

The translation will in many instances be found to differ somewhat from the original, for numerous additions, subtractions, and substitutions have been made, many of them at the suggestion of the Author, many at my own, but all with the Author's sanction.

A few notes will be found, especially in the later lectures. Of these some are literal, some free translations of, or are based upon, answers I received from Professor Virchow to questions I had put to him, whilst others (pp. 352, 406, 415-416) were made entirely at

* From 700 to 800 bodies are examined annually in the Institute.

his own suggestion, and are literal translations of his words. In all cases, however, the notes have been submitted to the Author, and approved by him.

An index too, I thought might be of service, and I have therefore added a tolerably full one.

I cannot sufficiently thank Professor Virchow for the very great trouble—a trouble of which nobody but myself can have any idea—which he has taken in revising this translation, nor for the exceeding courtesy and kindness with which he has replied to the very numerous questions—many of them put for my own private information—which I have plagued him with. He has written me fully fifty letters, most of them very long ones; and when I reflect that he daily passes eight or nine hours at the Charité, that he reads all the more important German, French, and English medical works which appear, and is besides constantly engaged in publishing something fresh, I can scarcely conceive how he has managed to find time to write these letters, of which a large proportion reached me by return of post.

To Dr. Harris I must return my best thanks for the assistance he has rendered me in reading the proof-sheets, and correcting any errors of language into which I might have fallen, and also for kindly permitting me to consult him whenever I met with any difficulty—a permission of which I have availed myself most freely.

The engravings will, I think, be found to be pretty faithful copies of the original woodcuts.

51 Wimpole Street, *August 10th*, 1860.

LIST OF WOOD-ENGRAVINGS.

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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 announcement 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 be 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-nitro-

Fig. 1.

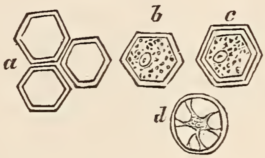


Fig. 1. Vegetable cells from the centre of the young shoot of a tuber of *Solanum tuberosum*. *a.* The ordinary appearance of the regularly polygonal, thick-walled cellular tissue. *b.* An isolated cell with finely granular-looking cavity, in which a nucleus with nucleolus is to be seen. *c.* The same 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.

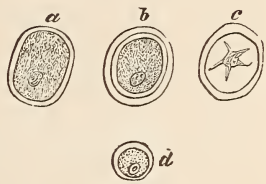
genized membrane of nitrogenized contents differing from it.

It had indeed already long been known, that other 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.

Fig. 2.



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

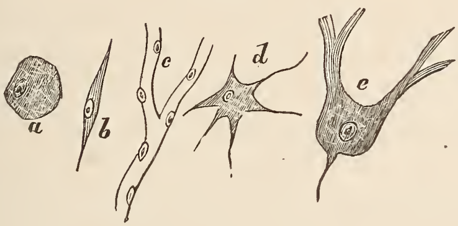
Fig. 2. Cartilage-cells as they occur at the margin of ossification in growing cartilage, quite analogous to vegetable cells (cf. the explanation to fig. 1). *a—c*. In a more advanced stage of development. *d*. Younger form.

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, 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 criteterion 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 exceptions, 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

Fig. 3.



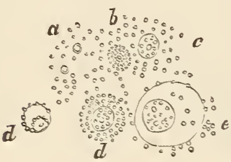
brought to a close, as long as cells behave as elements still endowed with vital power, the nucleus maintains a very nearly constant form.

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

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.

connection between the three coexistent cell-constituents was long thought to be on this wise: that the nucleolus was the first to shew 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 completed, about which new matter gradually gathered, and in due time produced a little membrane (the celebrated watch-glass form, fig. 4, *d'*). This 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.

Fig. 4.



You will hereafter be made acquainted with a series

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*)."

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 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 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 on the outside of the medullary [white[1]] 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

FIG.

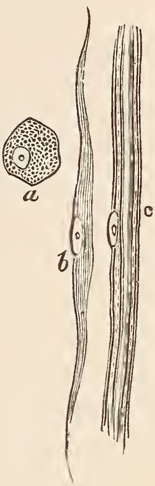


Fig. 5. *a.* Pigment-cell from the choroid membrane of the eye. *b.* Smooth muscular fibre-cell from the intestines. *c.* Portion of a nerve-fibre with a double contour, axis-cylinder, medullary sheath and parietal, nucleolated nucleus.

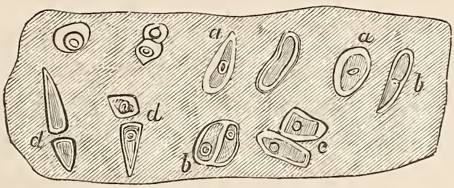
[1] All words included in square brackets have been inserted by the Translator, and are intended to be explanatory.

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 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 external secreted layers, although in such a manner that the old boundaries can still always

FIG 6.



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 bounda-

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.

ries in it also, so that certain districts belong to one cell, and certain others to another. Yow 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 convenient 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 solido-pathological 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 you can view in its pefection 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 hex-

Fig. 7.

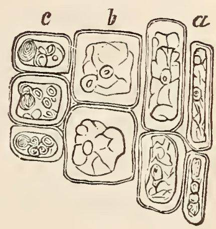


Fig. 7. From the cortical layer of a tuber of solanum tuberosum, after treatment with iodine and sulphuric acid. *a.* Flat cortical cells, surrounded by their capsule (cell-wall, membrane). *b.* Larger, four-sided cells of the same kind from the cambium; the real cell (primordial utricle), shrunken and wrinkled, within the capsule. *c.* Cells with starch-granules lying within the primordial utricle.

agonal 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 out-growths (leaf-hairs—Blatthaare), which protrude everywhere 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 subdivison 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.

Fig. 8.

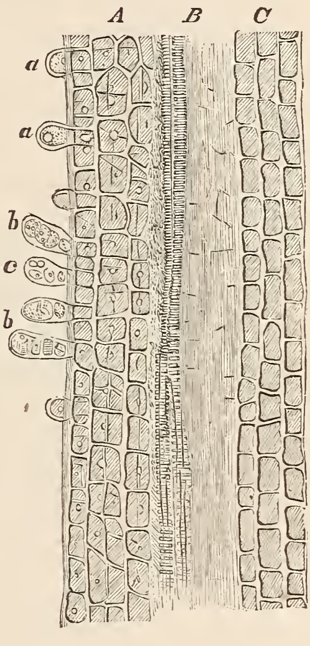


Fig. 8. Longitudinal section of a young February-shoot from the branch of a syringa. *A*. The cortical layer and cambium; beneath a layer of very flat cells are seen larger, four-sided, nucleated ones, from which, by successive transverse division, little hairs (*a*) shoot out, which grow longer and longer (*b*), and, by division in a longitudinal direction (*c*), thicker. *B*. The vascular layer, with spiral vessels. *C*. Simple, four-sided, oblong, cortical cells.—Growth of Plants.

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.

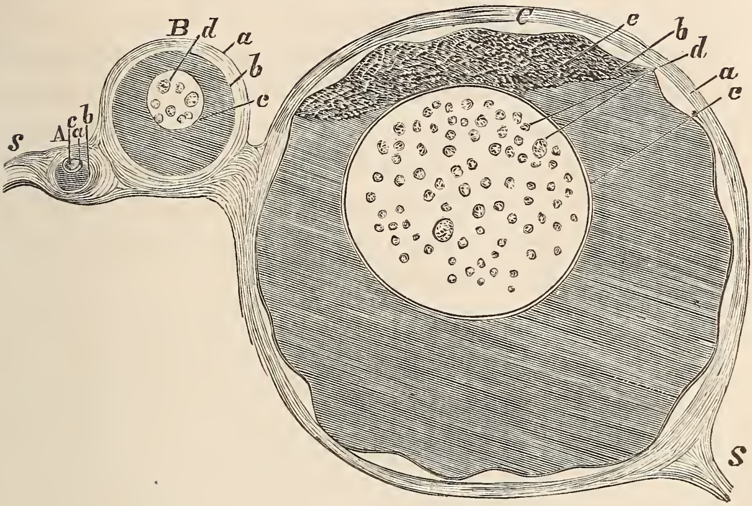
Fig. 9.

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 the cell may be remarked the relatively thin, connective tissue of the Graafian vesicle, with a hardly visible layer of epithelium. In the neigh-

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.

bourhood are lying several smaller ova, which show the gradual progress of their growth.

FIG. 10.



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 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

FIG. 11.

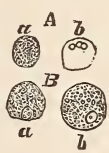


Fig. 10. Young ova from the ovary of a frog. *A*. A very young ovum. *B*. A larger one. *C*. A still larger one, with commencing secretion of brown granules at one pole (*e*), and shrunken condition of the vitelline membrane from the imbibition of water. *a*. Membrane of the follicle. *b*. Vitelline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

Fig. 11. Cells from 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.

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.

LECTURE II.

FEBRUARY 17, 1858.

PHYSIOLOGICAL TISSUES.

Falsity of the view that tissues and fibres are made up of globules (elementary granules)—The investment theory (Umhüllungstheorie)—Equivocal [spontaneous] generation of cells—The law of continuous development.

General classification of the tissues—The three categories of General Histology—Special tissues—Organs and systems, or apparatuses.

The Epithelial Tissues—Squamous, cylindrical, and transitional epithelium—Epidermis and rete Malpighii—Nails, and their diseases—Crystalline lens—Pigment—Gland-cells.

The Connective Tissues—The theories of Schwann, Henle, and Reichert—My theory—Connective tissue as intercellular substance—Cartilage (hyaline, fibro- and reticular)—Mucous tissue—Adipose tissue—Anastomosis of cells; juice-conveying system of tubes or canals.

In my first lecture, gentlemen, I laid before you the general points to be noted with regard to the nature and origin of cells and their constituents. Allow me now to preface our further considerations with a review of the animal tissues in general, and this both in their physiological and pathological relations.

The most important obstacles which, until quite recently, existed in this quarter, were by no means chiefly of a pathological nature. I am convinced that pathological conditions would have been mastered with far less difficulty if it had not, until quite lately, been utterly impossible to give a simple and comprehensive sketch of the physiological tissues. The old views, which have in part come down to us from the last century, have exercised such a preponderating influence upon that part of histology which is, in a pathological point of view, the most important, that not even yet has unanimity been arrived at, and you will therefore be constrained, after you have inspected the preparations I shall lay before you, to come to your own conclusions as to how far that which I have to communicate to you is founded upon real observation.

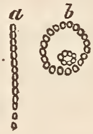
If you read the 'Elementa Physiologiæ' of Haller, you will find, where the elements of the body are treated of, the most prominent position in the whole work assigned to *fibres*, the very characteristic expression being there made use of, that the fibre (fibra) is to the physiologist what the line is to the geometrician.

This conception was soon still further expanded, and the doctrine that fibres serve as the groundwork of nearly all the parts of the body, and that the most various tissues are reducible to fibres as their ultimate constituents, was longest maintained in the case of the very tissue in which, as it has turned out, the pathological difficulties were the greatest—in the so-called cellular tissue.

In the course of the last ten years of the last century there arose, however, a certain degree of reaction against this fibre-theory, and in the school of natural philosophers another element soon attained to honour, though it had its origin in far more speculative views than the former, namely, the *globule*. Whilst some still clung to their fibres, others, as in more recent times Milne Edwards, thought fit to go so far as to suppose the fibres, in their turn, to be made up of globules ranged in lines. This view was in part attributable to optical illusions in microscopical observation. The objectionable method which prevailed during the whole of the last and a part of the present century—of making observations (with but indifferent instruments) in the full glare of the sun—caused a certain amount of dispersion of light in nearly all microscopical objects, and the impression communicated to the observer was, that he saw nothing else than globules. On the other hand, however, this view corresponded with the ideas common amongst natural philosophers as to the primary origin of everything endowed with form.

These globules (granules, molecules) have, curiously enough, maintained their ground, even in modern histology, and there are but few histological works which do not begin with the consideration of elementary granules. In a few instances, these views as to the globular nature of elementary parts have, even not very long ago, acquired such ascendancy, that the composition, both of the primary tissues in the embryo and also of the later ones, was based upon them. A cell was considered to be produced by the globules arranging themselves in a spherical form, so as to constitute a membrane, within which other globules remained, and formed the contents. In this way did even Baumgärtner and Arnold contend against the cell theory.

Fig. 12.



This view has, in a certain manner, found support even in the history of development—in the so-called *investment-theory* (Umhüllungstheorie)—a doctrine which for a time occupied a very prominent position. The upholders of this theory imagined, that originally a number of elementary globules existed scattered through

Fig. 13.

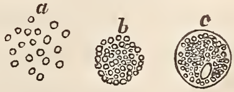


Fig. 12. Diagram of the globular theory. *a*. Fibre composed of elementary granules (molecular granules) drawn up in a line. *b*. Cell with nucleus and spherically arranged granules.

Fig. 13. Diagram of the investment- (cluster-) theory. *a*. Separate elementary

a fluid, but that, under certain circumstances, they gathered together, not in the form of vesicular membranes, but so as to constitute a compact heap, a globe (mass, cluster—Klümpchen), and that this globe was the starting point of all further development, a membrane being formed outside and a nucleus inside, by the differentiation of the mass, by apposition, or intussusception.

At the present time, neither fibres, nor globules, nor elementary granules, can be looked upon as histological starting-points. As long as living elements were conceived to be produced out of parts previously destitute of shape, such as formative fluids, or matters (*plastic matter*, *blastema*, *cytoblastema*), any one of the above views could of course be entertained, but it is in this very particular that the revolution which the last few years have brought with them has been the most marked. Even in pathology we can now go so far as to establish, as a general principle, *that no development of any kind begins* de novo, *and consequently as to reject the theory of equivocal* [spontaneous] *generation just as much in the history of the development of individual parts as we do in that of entire organisms.* Just as little as we can now admit that a tænia can arise out of saburral mucus, or that out of the residue of the decomposition of animal or vegetable matter an infusorial animalcule, a fungus, or an alga, can be formed, equally little are we disposed to concede either in physiological or pathological histology, that a new cell can build itself up out of any non-cellular substance. Where a cell arises, there a cell must have previously existed (*omnis cellula e cellula*), just as an animal can spring only from an animal, a plant only from a plant. In this manner, although there

granules. *b.* Heap of granules (cluster). *c.* Granule-cell, with membrane and nucleus.

are still a few spots in the body where absolute demonstration has not yet been afforded, the principle is nevertheless established, that in the whole series of living things, whether they be entire plants or animal organisms, or essential constituents of the same, an eternal law of *continuous development* prevails. There is no discontinuity of development of such a kind that a new generation can of itself give rise to a new series of developmental forms. No developed tissues can be traced back either to any large or small simple element, unless it be unto a cell. In what manner this continuous *proliferation of cells* (Zellenwucherung), for so we may designate the process, is carried on, we will consider hereafter; to-day, my especial object only was to deter you from assuming as the groundwork of any views you might entertain with regard to the composition of the tissues, these theories of simple fibres or simple globules (elementary fibres or elementary globules).—

If it be wished to classify the normal tissues, a very simple point of view, founded upon marked characteristics, offers itself, upon which their division into three categories may be based.

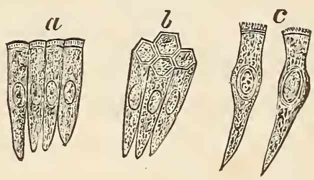
We either have tissues which consist exclusively of cells, where cell lies close to cell—in fact, cellular tissue in the modern sense of the word—or we find tissues, in which one cell is regularly separated from the other by a certain amount of intermediate matter (intercellular substance), and, therefore, a kind of uniting medium exists, which, while it visibly connects the individual elements, yet holds them separate. To this class belong the tissues which are now-a-days generally comprehended under the name of connective tissues (Gewebe der Bindesubstanz), and of which what was formerly universally called cellular tissue constitutes the chief portion. Finally, there is a third group of tissues, in which the cells have attained specific, higher forms of development, by means of which their constitution has acquired a type entirely peculiar ; indeed, in part so peculiar, as to appertain exclusively to the animal economy. These are the tissues which are really characteristic of animals, although a few among them exhibit transitions of vegetable forms. To this class belong the nervous and muscular systems, the vessels and the blood. Herewith is the list of tissues concluded.

You must now proceed to consider, in what respect, in this summary of the result of histological researches, a contrast is afforded to what was formerly, chiefly in imitation of Bichat, regarded as constituting a tissue. Bichat's tissues would, for the most part, not so much represent what we now regard as the subjects of General Histology, as what we must rather designate as belonging to Special Histology. For, if we regard the tissues in the light they were formerly regarded ; if we, for example, separate tendons, bones, and faciæ, from one another, we then obtain an extraordinary variety of categories (Bichat had twenty-one), but there are not quite as many simple forms of tissue to correspond to them.

In accordance with modern notions, the whole domain of anatomy should first be divided into the categories of General Histology (*tissues* properly so called). Special Histology, then, takes up the instances, in which a combination of tissues, sometimes very different, into a single whole (*organ*) takes place. Thus we speak, for example, of osseous tissue ; but this tissue, the tela ossea of general histology, does not of itself form bone, for no bone consists entirely of tela ossea, but it has necessarily superadded at least periosteum and vessels. Nay, and from this simple conception of a bone, every bone of considerable size, for example, a long bone differs; for that is a real organ, in which we can distinguish at least four different tissues. We have in it the tela ossea properly so called, the cartilaginous layer, the stratum of connective tissue belonging to the periosteum, and the peculiar medullary tissue. These several parts again are exceedingly heterogeneous in their nature, inasmuch as, for example, vessels and nerves enter into the composition of the marrow, the periosteum, etc. All these must be taken together to constitute the entire organism of a bone. Before we come, therefore, to *systems* or *apparatuses*, properly so called, the special subject of descriptive anatomy, a long series of gradations must be traversed, and in discussions we must always begin by having a clear idea of what the question is. When bone and osseous tissue are confounded together, the extremest confusion is occasioned, and so also when it is sought to identify nervous with cerebral matter. The brain contains many things which are not of a nervous nature, and its physiological and pathological conditions cannot be comprehended if they are regarded as occurring in an aggregation of purely nervous parts, and no consideration is paid to the membranes, the interstitial substance, and the vessels, as well as the nerves.

If, now, we consider the first of the classes into which we have divided General Histology, namely, the simple cellular tissues, a little more attentively, we find that those of which we can best obtain a general idea are unquestionably the *epithelial formations*, such as we meet with in the epidermis and the rete Malpighii, upon the external surface of the body, and in the cylindrical and scaly epithelium of mucous and serous membranes. Their general plan is, that cell lies close to cell, so that in the most favorable specimens, as in plants, four- or six-sided cells lie in immediate apposition one to the other, and nothing at all is found between them. The same is the case in many places with the scaly or pavement-epithelium (Fig. 16). These forms are evidently in a great measure due to pressure. For all the elements of a cellular tissue to possess perfect regularity of form, it is requisite that they should all grow in a perfectly uniform manner, and simultaneously. If their development takes place under circumstances such that less resistance is offered in one direction, it then may come to pass that, as in the case of columnar or cylindrical epithelium, the cells will shoot out in this one direction and become very long, whilst in the other direction they remain very narrow. But even one of these cells, when seen in transverse section, will present an hexagonal shape, and if we look down upon the free surface of cylindrical epithelium, we see in it, too, regularly polygonal forms (Fig. 14, *b*).

Fig. 14.

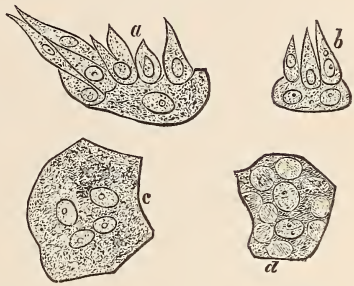


Contrasting with these, singularly irregular forms are met with in places where the cells shoot up in an irregular manner, and accordingly they are found with remarkable constancy on the surface of the urinary passages, in their whole extent from the calyces of the kidneys down to the urethra. In all these parts it is very common to meet with instances in which a cell is round at one end, whilst at the other it terminates in a point, or where it exhibits the appearance of a somewhat thick spindle, or is

Fig. 14. Columnar or cylindrical epithelium from the gall-bladder. *a.* Four contiguous cells seen in profile, each with a nucleus and nucleolus, their contents slightly marked with longitudinal striæ; along the free (upper) edge, a thickish border, marked with fine, radiated lines. *b.* Similar cells, with their free (upper, outer) surface seen obliquely, so as to show the hexagonal form of a transverse section, and their thick border. *c.* Cells altered by imbibition, somewhat swollen up and with the upper border split into fibrils.

slightly rounded on one side and excavated on the other, or where a cell is so thrust in between others as to assume a clubbed or jagged form. But in these cases also the one cell always corresponds with the other in form, and it is not any peculiarity in the cell which gives rise to its shape, but the way in which it lies, its relations to the neighbouring cells, and its having to adapt itself to the arrangement of the parts next to it. In the direction of the least resistance the cells acquire points, jaggs and projections of the most manifold description. As they did not well admit of classification, Henle gave them the name, which has since been adopted, of transitional epithelium, to express their gradual transition into distinct scaly and cylindrical epithelium. Sometimes, however, this is not the case, and another name for them might just as well have been adopted.

Fig. 15.



On account of the importance of the subject, I will just add a few words with regard to the cuticle (epidermis). In this it fortunately happens that, what is not the case in many mucous membranes, many layers of cells lie one above the other, and that the young layers (the *rete Malpighii* [mucosum]) can easily and conveniently be separated from the older ones (the *epidermis proper*).

Fig. 15. Transitional epithelium from the urinary bladder. *a.* A large cell, with excavations along its border, into which more delicate club- and spindle-shaped cells fit. *b.* The same; the larger cell with two nuclei. *c.* A larger, irregularly angular cell, with four nuclei. *d.* A similar cell, with two nuclei and nine depressions, as seen from above, corresponding to the excavations of the border. (Comp. 'Archiv. für path. Anat. und Phys.,' vol iii., plate i., fig. 8.)

On examining a perpendicular section of the surface of the skin, we for the most part see externally a very dense stratum, of variable thickness, which at the first glance is discovered to consist of nothing but flattened cells, that, when viewed edgeways, look like lines. They might be taken for fibres, piled up one above the other, and with slight differences of level making up the the whole external layer. Beneath these layers we find, differing in thickness and substance, the so-called rete Malpighii, and next to this, in a downward direction, the papillæ of the skin. If, now, we examine the boundary between the epidermis and the rete, the result we obtain by nearly every method of examination is,

Fig. 16.

Fig. 16. Perpendicular section through the surface of the skin of a toe, treated with acetic acid. *P. P.* Extremities of cut papillæ, in each of which a vascular loop,

that to the innermost layer of the epidermis, very closely and almost abruptly, there succeed cells, which at first are also flattened, but in a less degree, and within which very distinct nuclei may be distinguished. These tolerably large cells mark the transition from the oldest layers of the rete Malpighii to the youngest of the epidermis. This is the point from which proceeds the regeneration of the epidermis, in itself an inert mass, which is gradually removed from the surface. And here is also generally the boundary, at which pathological processes set in. The farther we advance inwards, the smaller do the cells become ; the last of them standing in the form of little cylinders upon the surface of the papillæ (Fig. 16 *r*, *r*).

On the whole, the relations of the individual parts throughout the whole surface of the skin are everywhere the same, however manifold the peculiarities of detail may be, which the individual layers offer in respect to thickness, position, firmness, and connection. A section of a nail, for example, which in its external appearance certainly widely differs from ordinary epidermis, presents, nevertheless, on the whole, the same conformation, and has only one essentially distinctive feature, that, namely, in it two different epidermoidal structures are thrust, the one over the other, and thus a complication arises, which, if not duly attended to, may lead to the assumption of certain specific differences between it and other parts of the epidermis, whilst it really consists only in a peculiar change in the position of certain layers of

and near it little spindle-shaped, connective-tissue corpuscles, displaying at the base a reticulated arrangement, may be observed; to the left, a bulging out of the papillæ, corresponding to a tactile corpuscle, no longer visible, and situated at a deeper level. *R. R.* The rete Malpighii; immediately around the papilla a very dense layer of small, cylindrical cells (*r*, *r*); more externally, polygonal cells, gradually increasing in size. *E.* Epidermis, consisting of flat and more closely packed layers of cells. *S S.* Duct of a sweat gland passing through. 300 diameters.

the epidermis with regard to one another. The extremely dense and hard scales, which constitute the uppermost part, the so-called *body of the nail* (Nagelblatt), may, by different methods, be restored to forms in which they present the ordinary appearances of cells , and this is best seen after treatment with an alkali, when every scale swells up into a large, broadly oval, cell.

In the uppermost layers of the epidermis the cells become everywhere flatter, and towards the external surface no more nuclei at all can be discovered in them. Still there is no original difference between the epidermis and the rete Malpighii ; the latter is only the matrix of the epidermis, or indeed its youngest layer, inasmuch as from it there is a constant apposition of new parts taking place, which gradually become flatter and flatter, and move upward as fast as the scales on the outside disappear through friction of the surface, washing, or rubbing. But between the lowest layer of the rete and the surface of the cutis vera there are no intervening layers ; there is no amorphous fluid or blastema to be found there in which the cells could be generated, but they lie in direct contact with the papillæ of connective tissue of the cutis. There is therefore nowhere any space here, as there was thought to be even a short time ago, into which fluid transudes from the papillæ and the vessels contained therein, in order that new cells may arise and develop themselves out of it. Of such a fluid there is absolutely nothing discernible, but throughout the whole series of the layers of cells of the rete and epidermis the same relations exist that we are familiar with in the bark of a tree. The cortical layer of a potato (Fig. 7) exhibits in a similar manner, externally, corky, epidermoidal cells, and underneath, as in the rete Malpighii, a layer of nucleated cells, the cambium, constituting the matrix for the subsequent growth of the cortex.

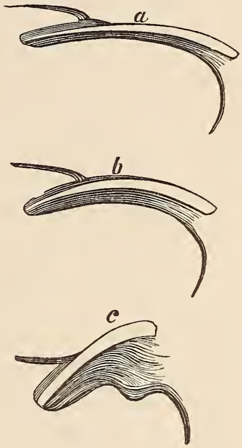
Very much the same is the case with the nails. On examining the section of a nail, made transversely to the long axis of the finger, we see virtually the same structure as in ordinary skin, only every single indentation of the inferior surface does not correspond to a conical prolongation of the cutis, or papilla, but to a ridge which runs along the entire length of the bed of the nail, and may be compared with the ridges which are to be seen upon the palmar surface of the fingers. Upon these ridges of the bed of the nail are dwarfish, stunted papillæ, and upon them rests the rather cylindrically shaped youngest layer of the rete Malpighii; then follow cells continually increasing in size, until at last the really hard substance comes, which corresponds to the epidermis.

Nevertheless—to discuss the subject at once, seeing that I shall not again have occasion to mention it—the structure of the nails has been difficult to make out, because they were conceived to be a simple formation. Nearly all the discussions, therefore, which have taken place, have turned upon the question where the matrix of the nail was, and whether the growth of the latter took place from the whole surface or from the little fold into which it is received behind. If we consider the nail with respect to its proper firm substance, its compact *body* (Nagelblatt), this only grows from behind, and is pushed forwards over the surface of the so-called *bed of the nail* (Nagelbett), but this in its turn also produces a definite quantity of cellular elements, which are to be regarded as the equivalents of an epidermic layer. On making a section through the middle of a nail, we come, most externally, to the layer of nail which has grown from behind, next to the substance which has been secreted by the bed of the nail, then to the rete Malpighii, and lastly to the ridges upon which the nail rests.

Thus the nail lies in a certain measure loose, and can easily move forwards, pushing itself over a moveable substratum, while it is kept in place by the ridges with which its bed is beset. When a section is made transversely through a nail, we see, as already mentioned, essentially the same appearance presented as that offered by the skin, only that a long ridge corresponds to every single papilla seen in ordinary sections of the skin ; the undermost part of the nail has slight indentations corresponding to these ridges, so that, while gliding along over them, it can execute lateral movements only within certain limits. In this manner, the body of the nail which grows from behind moves forwards over a *cushion* of loose epidermic substance (Fig. 17, *a*) in grooves which are provided by the ridges and furrows of the bed of the nail. The uppermost part of the nail, if examined when fresh, is composed of so dense a substance that it is scarcely possible to distinguish individual cells in it without applying reagents, and at many points an appearance is presented like that which we see in cartilage. But by treating it with potash, we can convince ourselves that this substance is composed of nothing but epidermis-cells. From this mode of development you will see how easily intelligible distinctions may be drawn between the different diseases of the nails.

There are diseases of the bed of the nail which do not affect the growth of its body, but may give rise to changes in its position. When there is a very abundant development of cells in the bed of the nail, the body may be pushed upwards (Fig. 17, *b*) ; nay, it sometimes happens that the nail, instead of growing horizontally, shoots perpendicularly upwards, the space underneath being filled with a thick accumulation of the loose cushiony substance (Polstermasse) (Fig. 17, *c*). Thus suppuration may take place in the bed of the nail without the development of its body being thereby impeded. The most singular changes occur in small pox. When a pock forms upon the bed of the nail, there is nothing to be seen but a yellowish, somewhat uneven, spot; but if, on the other hand, it is developed upon the fold, then its traces are left in the shape of a circularly depressed, and, as it were, excavated spot in the body of the nail as it gradually advances, a proof of a loss of substance precisely similar to that which takes place in the epidermis.

Fig. 17.



I will not to-day, gentlemen, enter more particularly into the special history of the formation of epidermis and epithelium, although it is of great importance for the right comprehension of many pathological processes, but content myself with calling your attention to the fact, that, under particular circumstances epithelial cells may undergo a series of transformations, through which they become extremely unlike what they originally were, and gradually assume appearances which render it impossible for those who are unacquainted with the history of their development to realize their original epidermic nature. The greatest abnormity of the kind is met with in the *crystalline lens* of the eye, which is originally a mere

Fig. 17. Diagrammatic representation of a longitudinal section of a nail. *a.* The normal condition; a gently curved, horizontal nail, implanted in its fold, and separated from its bed by a thin cushion. *b.* A more markedly curved and somewhat thicker nail, with great thickening of the cushion, and much increased curvation of the bed, the fold being shorter and wider. *c.* Onychogryphosis; the nail, short and thick, reared up at a considerable angle, the fold short and wide, the bed furrowed on its surface, the cushion very thick and composed of layers of loose cells, piled up one above the other.

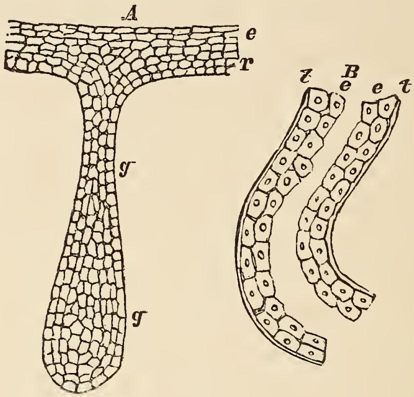
accumulation of epidermis. It has its origin, as is well known, in a saccular involution of the external skin. At first its connection with the external parts continues to be maintained by means of a delicate membrane, the *membrana capsulo-pupillaris;* afterwards this atrophies and leaves the lens isolated in the interior of the eye. The fibres of the lens are therefore, as C. Vogt has shown, nothing more than epidermoidal cells which have been developed in a peculiar manner, and their regeneration, after the extraction of a cataract for example, is only possible as long as there still remains epithelium in the capsule to undertake the new formation, and to represent, as it were, a thin layer of rete Malpighii. This reproduces the lens in the same way that the ordinary rete Malpighii of the external surface does the cuticle. Amongst the other changes of epithelial structures we shall in due time revert to the peculiar pigment cells that are produced in the most different parts by the direct transformation of epidermic cells, the contents of which either become coloured by imbibition, or have pigment engendered in them by a (metabolic) transposition of their elements.

With the history of epithelial elements properly so called is immediately connected that of a peculiar class of structures which play a very important part in the accomplishment of the functions of an animal, namely the *glands.* The really active elements of these organs are essentially of an epithelial nature. One of Remak's greatest merits consists in his having shown that in the normal development of the embryo the outer and inner of the well-known three layers of the germinal membrane chiefly produce epithelial structures, from a gradual proliferation of the elements of which glandular structures arise. Other observers, for example, Kölliker, had indeed before him made similar observations, but by

Remak was first established the law that the formation of glands in general must be regarded as consequent upon a direct process of proliferation on the part of epithelial structures. Previously large quantities of cytoblastema had been conceived to exist, in which, spontaneously, glandular substance took its rise ; but, with the exception of the lymphatic glands, and perhaps those belonging to the sexual organs, their mode of origin is everywhere this—that at a certain point, in a manner very similar to that which I described to you in the foregoing lecture, when speaking of the excrescences of plants, an epithelial cell begins to divide, and goes on dividing again and again, until by degrees a little process composed of cells grows inwards, and, spreading out laterally, gives rise to the development of a gland, which thus straightway consitutes a body continuous with layers of cells originally external. Thus arise the glands of the surface of the body (the sudoriferous and sebaceous glands of the skin and the mammary gland), and thus also arise the internal glands of the digestive tract (the stomach glands and liver.) The most simple forms which glands can present do not occur at all in man. In inferior animals, however, *uni-cellular glands* have recently been discovered. The glands of the human body are invariably made up of a number of elements, which can, however, ultimately be traced back to a nearly simple type. Besides, in our own glands, in consequence of their size and complicated structure, other necessary constituents generally enter into their composition, so that, regarded as organs, they certainly do not consist of gland-cells only. But all parties are now pretty well agreed that the gland-cells are the really essential elements, just as the primitive bundles are in muscle, and that the specific action of a gland is dependent upon the properties and peculiar arrangement of these elements.

Generally speaking, therefore, glands consist of accumulations of cells, which usually form open canals. With

Fig. 18.



the exception of the glands, whose functions are uncertain, such as the thyroid body and supra-renal capsules, there are in the human body only the ovaries which form an exception to this rule, inasmuch as their follicles are only open at times ; yet they too must be open when the specific secretion of the ova has to take place. In most glands there is found indeed besides a certain quantity of transuded fluid, but this only constitutes the vehicle which floats off either the cells themselves, or their specific products. Suppose, for example, that in one of the ducts of the testicle a cell, in which there is a production of spermatozoa, becomes detached, then there transudes at the same time a certain quantity of fluid, which carries them away ; but what makes the semen, semen, and constitutes the specific character of the action

Fig. 18. *A*. Development of sweat-glands by means of the proliferation of the cells of the rete Malpighii in an inward direction. *e*. Epidermis. *r*. Rete Malpighii. *g g*. Solid process, constituting the first rudiments of a gland. After Kölliker.

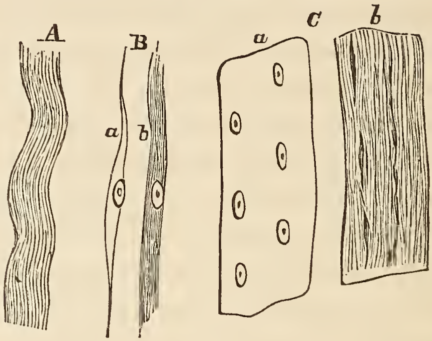
B. Portion of the duct of the sweat-gland in a state of complete development. *t t*. Tunica propria. *e e*. Layers of epithelium.

is the peculiar power of the cell; the mere transudation from vessels is no doubt a means of conveyance onwards, but does not constitute the specific action of the gland nor the real secretion. In an analogous manner, in all the glands of which we can follow the action in all its details with precision, the essential peculiarities of their energy are derived from the development and transformation of epithelial cells.

The second histological group is formed by the *connective* tissues (Gewebe der Bindesubstanz). This is the subject in which I take the most interest, because it was here that my own observations, which have led to the result to which I directed your attention at the beginning of these lectures, originated. The alterations which I have succeeded in introducing in the views of histologists with regard to the whole group have, at the same time, enabled me to give a certain degree of roundness and completeness to the cellular theory.

Previously, connective tissue had nearly universally been regarded as essentially composed of fibres. On examining loose connective tissue in different regions, as, for example, beneath the corium, in the pia mater, subserous and submucous cellular tissue, we find wavy bundles of fibres, the so-called *wavy connective tissue* (Fig. 19, *A*). This wavy character, which is interrupted at certain intervals, so as to give rise to a kind of fasciculation, could, it was thought, with the less hesitation be attributed to the presence of separate fibres, because at the end of each bundle isolated filaments could in reality be seen to protrude. In spite of this, however, an attack was made upon this very hypothesis, somewhat more than ten years ago, and has proved of very great importance, though in a manner different to to that which was intended. Reichert endeavoured, namely, to show that the fibres were only an optical illusion produced by folds, and that connective tissue in all parts formed a homogeneous mass, endowed with a great tendency to the formation of folds.

FIG. 19.



Schwann had, in reference to the formation of connective tissue, assumed that there originally existed spindle-shaped cells, the *caudate corpuscles* (geschwänzte Körperchen) (fibro-plastic corpuscles of Lebert), which afterwards became so famous ; and that out of these cells fasciculi of connective tissue were directly developed by the splitting up of the body of the cell into distinct fibrils, whilst the nucleus remained as such (Fig. 19, *B*). Henle, on the other hand, thought the only conclusion his observations would warrant was, that there were originally no cells at all, but that nuclei only were formed in the blastema at certain intervals ; whilst the

Fig. 19. *A*. Bundle of common, wavy, connective tissue (intercellular substance), splitting at its end into fine fibrils.

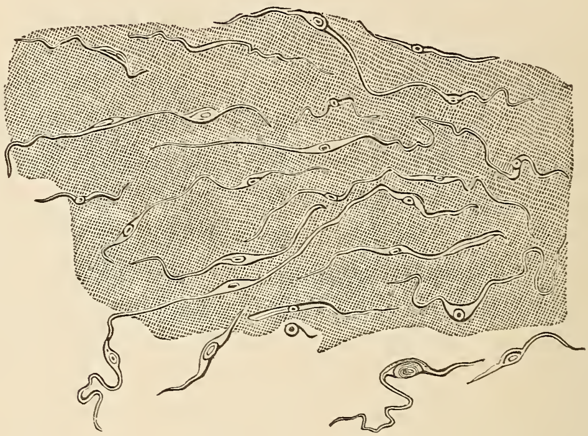
B. Diagram of the development of connective tissue according to Schwann. *a*. Spindle-shaped cell (caudate corpuscle, fibro-plastic corpuscle of Lebert), with nucleus and nucleolus. *b*. Cleavage of the body of the cell into fibrils.

C. Diagram of the development of connective tissue, according to Henle. *a*. Hyaline matrix (blastema), with nucleolated nuclei regularly distributed through it. *b*. Fibrillation of the blastema (direct formation of fibrils), and transformation of the nuclei into nucleus-fibres.

fibres, which afterwards appeared, were produced by a direct fibrillation of the blastema; and that, whilst the intermediate substance was thus being differentiated into fibres, the nuclei gradually became elongated, so as at length to run into one another, and thus give rise to peculiar longitudinal fibres, *nucleus-fibres* (Kernfasern) (Fig. 19, *C*). Reichert took an extremely important step in opposition to these views. He showed, namely, that originally there were only cells, and those in great abundance, between which intercellular substance was deposited. But the membrane of the cells became, he thought, at a certain period, blended with the intercellular tissue, and then a stage was reached analogous to that described by Henle, in which there no longer existed any boundary between the original cells and the intermediate substance. And, finally, he imagined that the nuclei, too, entirely disappeared in some instances, whilst they were preserved in others. On the other hand, he positively denied the occurrence of the spindle-shaped cells of Schwann, and declared all such, as well as the caudate and jagged cells, to be just as much artificial products as the fibres, which were said to be seen in the intervening substance, were a false interpretation of an optical image.

Now, my own investigations have shown, that both Schwann's and Reichert's observations, up to a certain point, have some foundation in truth. That, in the first place, in opposition to Reichert, spindle-shaped and stellate cells indisputably do exist (Fig. 20); and secondly, in opposition to Schwann, and with Reichert, that a direct splitting up of the cells into fibres does not take place, but that on the contrary, what is afterwards presented to our sight as connective tissue has really taken the place of the previously homogeneous intercellular substance. I have found, moreover, that Reichert, Henle, and Schwann, were wrong in maintaining that ultimately at best only nuclei or nucleus-fibres remained;

Fig. 20.



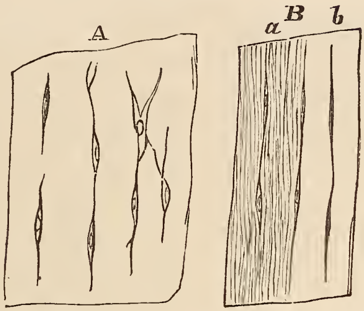
and that, on the contrary, in most cases the cells themselves preserve their integrity. The connective tissue of a later period is therefore not distinguished in its general structure and disposition in any respect from that of an earlier date. There is not an embryonic connective tissue with spindle-shaped cells and a perfectly developed one without them, but the cells remain the same, although they are often not easy to see.

Essentially, therefore, this whole series of lower tissues may be reduced to one simple plan. Usually, the greater part of the tissue is composed of intercellular substance, in which, at certain intervals, cells lie imbedded, which in their turn present the most manifold forms. But these tissues cannot be distinguished by one's con-

Fig. 20. Connective tissue from the embryo of a pig, after long-continued boiling. Large spindle-shaped cells (connective-tissue corpuscles (Bindegewebskörperchen)), some isolated, some still imbedded in the basis-substance, and anastomosing one with the other. Large nuclei, with their membrane detached; cell-contents in some cases shrunken. 350 diameters.

taining only round, another's, on the contrary, only caudate or stellate, cells. but in all connective tissues

Fig. 21.



round, long and angular cells may occur. The simplest case is where round cells lie at certain intervals, and intercellular substance appears between them. This is the form which we see most beautifully shown in hyaline cartilage, as in that lining the joints, for example, in which the intercellular matter is perfectly homogeneous, and we see nothing but a substance which, though, perhaps, slightly granulated here and there, is on the whole quite as clear as water, so that as long as we do not see the edges of the preparation, doubt may arise as to whether anything at all exists between the cells.

This substance is characteristic of *hyaline cartilage*. Now we find that, under certain circumstances, the round cells became even in cartilage transformed into oblong

Fig. 21. Diagram of the development of connective-tissue, according to my investigations. *A*. Earliest stage. Hyaline basis- (intercellular) substance, with largish cells (connective-tissue corpuscles); the latter drawn up in rows at regular intervals; at first separated, spindle-shaped, and simple; at a later period anastomosing and branched. *B*. More advanced stage; at *a*, the basis-substance which has become striated (fibrillated), presents a fasciculated appearance on account of the cells imbedded in it in rows, the cells becoming narrower and smaller; at *b*, the striation of the basis-substance has disappeared under the influence of acetic acid, and the fine and long anastomosing fibre-cells (connective-tissue corpuscles), still retaining their nuclei, are seen.

spindle-shaped ones, as, for example, with great regularity in the immediate neighbourhood of the articular surfaces. The nearer, in the examination of articular cartilage, we approach to the free surface (Fig. 22, *a*,) the smaller do the cells become; and, at last, nothing more is seen but small, flatly lenticular bodies, the substance intervening between which sometimes presents a slightly striated appearance. Here, therefore, without the tissue's having ceased to be cartilage, a new type displays itself, which we much more regularly meet with in pure connective tissue, and hence the idea might easily arise that articular cartilage is invested with a special membrane. This is, however, not the case, for there is no synovial membrane spread over the cartilage, but its boundary towards the cavity of the joint is everywhere formed of cartilage itself. The synovial membrane only begins where the cartilage ceases—at the edge of the bone. On the other hand, we see that at certain points the cartilage passes directly into forms in which the cells become stellate, and the way is paved for their final anastomosis; ultimately, spots are met with at which it is no longer possible to say where the one cell ends and the other begins, inasmuch as they communicate so directly one with another that it is impossible to detect a line of separation between their membranes. When

Fig. 22.

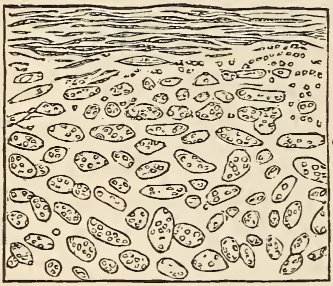


Fig. 22. Perpendicular section through the growing cartilage of a patella. *a.* The articular surface, with spindle-shaped cells (cartilage-corpuscles) disposed in layers parallel to it. *b.* Incipient proliferation of the cells. *c.* Advanced proliferation; large, roundish groups—within the enlarged capsules a continually increasing number of round cells. 50 diameters.

such a case occurs, the cartilage, which up to that time had remained hyaline and homogeneous, becomes heterogeneous and striated, and has long since been called *fibro-cartilage.*

From these forms a third has been distinguished, the so-called *reticular* [yellow or spongy] *cartilage*, as seen in the ear and nose, in which the cells are round, but encircled by a peculiar kind of thick, stiff fibres, whose mode of production has not yet been thoroughly made out, but they are, perhaps, derived from the metamorphosis of the intercellular substance.

Under these different types, presented by cartilage in its different localities, all the different aspects which the other connective tissues offer are included. There is also true connective tissue with round, long, and stellate cells. Just in the same manner we find, for example, in the peculiar tissue which I have named *mucous tissue* (Schleimgewebe), round cells in a hyaline, or spindle-shaped ones in a striated, or reticular ones in a meshy, basis-substance. The only criterion we possess for distinguishing them consists in the determination of the chemical constitution of the intercellular substance. Every tissue is called connective tissue whose basis-substance yields gelatine when boiled ; the intercellular substance of cartilage produces chondrine ; mucous tissue, on expression, a substance, mucin, precipitable by acetic acid, and insoluble in an excess of it, though dissolving in muriatic acid when added in considerable quantity.

Besides these, a few solitary points of difference in regard to peculiarity of form and contents may be presented by individual cells at some later period of their existence. What we concisely designate *fat* is a tissue which is intimately connected with those of which we have been treating, and is distinguished from the rest by the fact that some of the cells enlarge and become stuffed full of fat, the nucleus being thereby thrust to one side. In itself, however, the structure of adipose tissue is precisely the same as that of connective tissue, and, under certain circumstances, the fat may so completely disappear that the adipose tissue is once more reduced to the state of simple, gelatinous connective, or mucous tissue.

Amongst these different species of connective tissue the most important for our present pathological views, are, generally speaking, those in which a reticular arrangement of the cells exists, or, in other words, in which they anastomose with one another. Wherever, namely, such anastomoses take place, wherever one cell is connected with another, it may with some degree of certainty be demonstrated that these anastomoses constitute a peculiar system of tubes or canals which must be classed with the great canalicular system of the body, and which particularly, forming as they do a supplement to the blood- and lymphatic vessels, must be regarded as a new acquisition to our knowledge, and as in some sort filling up the vacancy left by the old vasa serosa which do not exist. This reticular arrangement is possible in cartilage, connective tissue, bone and mucous tissue in the most different parts; but in all cases those tissues which possess anastomoses of this description may be distinguished from those whose elements are isolated, by the greater energy with which they are capable of conducting different morbid processes.

LECTURE III.

FEBRUARY 20, 1858.

PHYSIOLOGICAL AND PATHOLOGICAL TISSUES.

The higher animal tissues: muscles, nerves, vessels, blood.

Muscles—Striped and smooth—Atrophy of—The contractile substance and contractility in general—Cutis anserina and arrectores pili.

Vessels—Capillaries—Contractile vessels—Nerves.

Pathological tissues (Neoplasms), and their classification—Import of vascularity—Doctrine of specific elements—Physiological types (reproduction)—Heterology (heterotopy), heterochrony (heterometry), and malignity—Hypertrophy and hyperplasy—Degeneration—Criteria for prognosis.

Law of continuity—Histological substitution and equivalents—Physiological and pathological substitution.

In my last lecture I portrayed to you the first two groups of tissues, the one embracing epithelium or epidermis, and the other the different kinds of connective tissue. What still remains forms a somewhat heterogeneous group, the individual members of which do not, indeed, in the degree that is the case with epithelium and connective tissue, bear a real relationship to one another, yet, on the whole, present a certain correspondence, in that they constitute the higher animal structures, and are distinguished by their specific mode of development from the less highly organized epithelial and connective tissues. Moreover, most of them appear under the form of connected, more or less tubular, structures. If a comparison be instituted between muscles, nerves, and vessels, the idea very readily suggests itself that we have in all three structures to deal with real tubes, filled with now more, now less, moveable contents. But this notion, however well it may accord with a superficial view of the matter, does not express the whole truth, inasmuch as we cannot compare the contents of the different tubes.

The blood which is contained in the vessels, cannot, at least at present, be regarded as analogous to the axis-cylinder, or the medullary [white] substance of a nerve-tube, or to the contractile substance of a primitive muscular fasciculus (Muskelprimitivbündel [muscular fibre]). I must, indeed, here remark, that the original development of all the structures which may be included in this group is still a subject of great controversy, and that the view maintaining the simply cellular structure of most of these elements is by no means completely established. This much, however, appears to be certain, that, at any rate in fœtal parts, the blood-corpuscles are just as much cells as the individual constituents of the walls of the vessels within which the blood flows; and that the vessel cannot be designated as a tube which invests the blood-corpuscles, as the cell-membrane does its contents. It is therefore necessary in the case of the vessels to draw a line between their contents and proper walls, and to repudiate the seeming resemblance between the vessels, and the nerves and muscular fibres. Again, if we wished to adopt the mode of origin of the several tissues as the basis of our classification, we should, in accordance with prevailing views, have to associate the lymphatic glands also with the blood, and might be rather reminded of a connection such as we have seen to exist in the relations between the epidermis and the rete mucosum. But here I must once more impress upon you that the lymphatic glands are distinguished from glands properly so called, not only by their not possessing any excretory duct in the ordinary sense of the word, but also because from the mode of their development they by no means occupy the same position as ordinary glands, but are on the contrary at every period of their existence nearly allied to the connective tissues, and that, therefore, the temptation would rather be to class them with the tissues which we see produced by the transformation of the connective tissues. Yet this would at the present moment be still rather a venturous undertaking.

Amongst all the forms of which we have here to treat, the *elements of muscle* have generally been regarded as the most simple. If we examine an ordinary red muscle (I do not say a voluntary one, inasmuch as in the heart also we meet with fibres of the same form) we find it to be essentially composed of a number of cylinders, for the most part of equal thickness (primitive fasciculi [fibres]), which on a transverse section are seen to have a cylindrical form, and on which we at once perceive the well-known transverse striæ, that is, broad lines which generally run transversely through the fasciculus with a somewhat wavy outline, and are almost as broad as the intervals that separate them. In addition to this transverse striation we also see, especially when certain modes of preparation have been adopted, striæ fol-

Fig. 23.

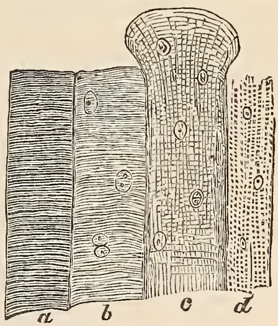


Fig. 23. A group of primitive muscular fasciculi [fibres]. *a.* The natural appearance of a fresh primitive fasciculus, with its transverse striæ (bands or discs). *b.* A fasciculus gently acted upon by acetic acid; the nuclei stand out distinctly, and in one of them two nucleoli are visible, whilst in another the division is complete. *c.* A fibre acted upon more strongly by acetic acid; the contents are swollen up at the end, so as to protrude from the sheath (sarcolemma). *d.* Fatty atrophy. 300 diameters.

lowing a longitudinal direction, and these, indeed, in some preparations preponderate to such a degree, that the muscular fasciculus appears to be striated almost exclusively in this direction. If now we add acetic acid, there are forthwith disclosed immediately beneath the sheath, and now and then also more towards the centre, nuclei which are tolerably large, and mostly contain large nucleoli in greater or less number. In this manner, therefore, after we have cleared up the internal substance by the application of acetic acid, we again obtain an appearance which reminds us of the original cell-form ; and there has been the greater tendency to regard the whole of a primitive fasciculus as having sprung from a single cell, because, according to the view which was formerly entertained, the individual primitive fasciculi of every muscle were thought to extend from the point of origin to that of insertion, and were therefore held to be as long as the muscle itself. This latter supposition has, however, been shaken by investigations which were set on foot in Vienna, under Brücke's direction by Rollet, for he demonstrated that in the course of muscles the ends of primitive fasciculi are to be seen running into points, so that a primitive muscular fasciculus would comport itself like a large fibre-cell (Fig. 105, *A*). These ends fit one into the other, and, according to this, the length of a primitive fasciculus would by no means correspond to the whole extent of the muscle.

On the other hand, I must remark, that observations have been made in different quarters quite recently, which are rather of a nature to throw doubts upon the uni-cellular nature of these elements. Leydig regards them as rather containing a series of cells of a smaller kind, between which the contractile substance is lodged, his idea being based upon the circumstance that every nucleus (Figs. 23, *b*, *c*; 24, *B*) is enclosed in a special elongated cavity.[1] In discussions respecting these ultimate elements of muscle, extremely difficult relations are involved, and I for my own part must confess that, however much I am inclined to admit the uni-cellular nature of the primitive fasciculi, I am still too familiar with the peculiar appearances in their interior not to be obliged to allow that another view may be advanced. For the present, however, we must bear in mind that we have to do with a structure in which an external membranous sheath (sarcolemma) and contents are to be distinguished. In the latter, acetic acid causes nuclei to show themselves, and, when they (the contents) are in their natural condition, the peculiar transverse and longitudinal striation may be recognised in them. This

Fig. 24.

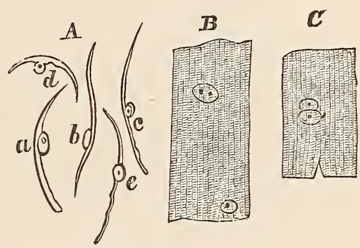


Fig. 24. Muscular elements from the heart of a puerperal woman. *A.* Peculiar spindle-shaped cells precisely like the fibre-cells of the pulp of the spleen, probably belonging to the sarcolemma and set free in teasing out the preparation. *a.* Crescentically curved cell, somewhat flat at one end, viewed on its surface. *b.* A similar one, seen in profile, with flat nucleus. *c, d.* Cells, the nuclei of which lie in a hernial protrusion of the membrane. *e.* A similar cell, viewed on its surface, with its nucleus, as it were, lying upon it. *B.* A primitive fasciculus, without its sheath (sarcolemma), with distinct longitudinal fibrils and large, roundish nuclei, of which one contains two nucleoli (incipient partition). *C.* A primitive fasciculus, which has been teased asunder and slightly cleared up by acetic acid; besides a divided nucleus, fine, awl-shaped, nucleus-like bodies are seen imbedded between the longitudinal fibrils. 300 diameters.

[1] This cavity Leydig supposes to be lined by a membrane, and therefore really to constitute a cell (connective-tissue corpuscle). The nuclei of every primitive fasciculus would, therefore, according to this view, be the nuclei of connective-tissue corpuscles, and the contractile substance, lying between these, would be equivalent to the intercellular substance of ordinary connective tissue. The nuclei here alluded to are the ordinary nuclei of muscle, as seen in the figs. quoted above and must not be confounded with the awl-shaped bodies represented in fig. 24, *C*, lying between the fibrils; for, though these bodies look like nuclei, they are really, according to Leydig, portions of the divided processes of some of his connective-tissue corpuscles.—*From a MS. note by the Author.*

striation is altogether internal and not external. The membrane in itself is perfectly smooth and even; the transverse striation belongs to the contents, which, when seen in a mass, form the red substance of the muscle.

Now it is this substance which has the property of contractility indubitably inherent in it, and even varies in appearance according to its state of contraction, becoming broader when contracted, whilst the intervals between the individual transverse bands become somewhat narrower, so that a change in the arrangement of its minutest constituents takes place, and this, as seems probable from the investigations of Brücke, not merely in the case of its physical molecules, but also in that of its visible anatomical constituents. Brücke, namely, by examining muscle by polarized light, has discovered different optical properties in the individual layers of substance—in those which compose the transverse striæ and those which form the intervening mass. On the adoption of certain methods of preparation, every primitive muscular fasciculus appears to be made up of plates or discs of a different nature, piled up one above another, and these in their turn to be entirely composed of minute granules (Bowman's sarcous elements). In reality, however, the contents of a primitive fasciculus consist of a certain number of fine, longitudinal fibrils, every one of which contains minute granules corresponding in position to the transverse striæ or apparent discs of the primitive fasciculus, and held together by a pale, intervening substance. Now, since a considerable number of primitive fibrils lie in apposition side by side, there arises, in consequence of the symmetrical position of the little granules, this very appearance of discs which really do not exist. In proportion to the activity of the muscle these parts assume an altered position with regard to one another; during contraction the granules are approximated, whilst the intervening substance becomes shorter and, at the same time, broader.

Compared with this, the structure of the *smooth*, *organic*, or, although this is a less expressive term, *involuntary muscular fibres*, appears much more simple. On examining any part of those organs in which smooth muscular fibres are contained, we find in the majority of cases, first of all, just as was the case with the transversely striated muscles, little fasciculi—as, for example, in the muscular coat of the urinary bladder. Within these fasciculi, upon further investigation, a series of distinct elements can be distinguished, of which a certain number, six, ten, twenty, or more, are held together by a common connective substance. According to the notion which universally prevailed until quite recently, every one of these elements was analogous to the primitive fasciculus of striped muscle. For as soon as we succeed in separating these fasciculi of smooth muscle into their more minute constituents, we find their ultimate elements to consist of long, spindle-shaped cells, which usually contain a nucleus in their centre (Fig. 5, *b*). According to the view on the contrary, which, especially in consequence of the impulsion given by Leydig's investigations, has quite lately

Fig. 25.

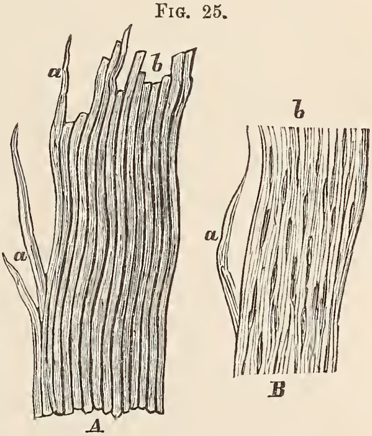


Fig. 25. Smooth muscular fibres from the parietes of the urinary bladder. *A*. Fasciculus still coherent, out of which at *a*, *a* single isolated fibre-cells protrude, whilst at *b* their simple divided ends appear. *B*. A similar fasciculus after being treated with acetic acid, whereby the long and narrow nuclei have become evident. *a*. and *b*, as above. 300 diameters.

begun to be mooted in various quarters, we should have to regard the bundle, in which a whole series of fibre-cells is contained, rather as analogous to a transversely striated primitive fasciculus. Until, however, this point has been satisfactorily settled, I consider it advisable and more in accordance with known facts to regard each fibre-cell as the equivalent of a primitive fasciculus. Should, however, any change of opinion shortly occur, you will now at any rate be prepared for it.

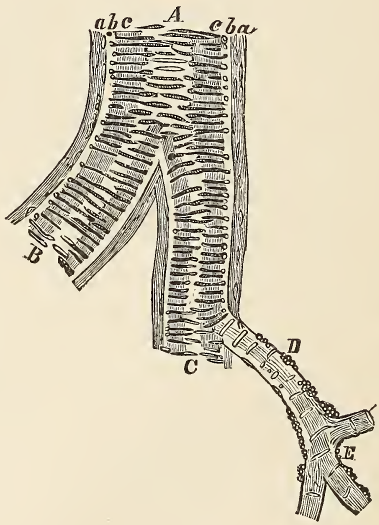
In one of these spindle-shaped or fibre-cells it is difficult to distinguish anything particular. In very large cells of this kind, and with a high magnifying power, we can certainly frequently distinguish a fine longitudinal striation (Fig. 5, *b*), so that it looks as if here, too, fibrils of some sort were disposed lengthways in the interior, whilst ordinarily no trace of any transverse striæ is perceptible. Yet the pale, smooth muscles exhibit, chemically speaking, a pretty close agreement with the transversely striped ones, since a similar substance (the so-called Syntonian of Lehmann) can, by the help of diluted hydrochloric acid, be extracted from both ; and one of the most characteristic substances which is met with in red muscles, namely Creatine, is met with also, according to the investigations of G. Siegmund, in the smooth muscular fibres of the uterus.

One of the preparations of red muscle which I have placed before you exhibits an appearance which is also pathologically interesting ; among the fasciculi, namely, is one which presents the condition of the so-called *progressive* (fatty) *atrophy*. The degenerated fasciculus is smaller and narrower, and at the same time little fat-globules are seen arranged in rows between the longitudinal fibrils (Fig 23, *d*). Atrophy in muscles is chiefly characterized by a diminution in the diameter of the primitive fasciculi affected ; in fatty atrophy the more palpable change is added, that little rows of fat-globules appear in the interior of the primitive fasciculus, during the accumulation of which the proper contractile substance decreases in bulk. The more fat there is, the less contractile substance ; or, in other words, the muscle becomes less capable of performing its functions in proportion as the normal contents of its fibres diminish. Pathological experience, therefore, also designates as the seat of the contractile power a definite substance, the occurrence of which, as especially the important investigations of Kölliker have taught us, is connected with certain histological elements. Whilst formerly many other things besides the substance of muscle, as for example, certain forms of connective tissue, were assumed to be contractile, lately the whole theory of contractility in the human body has been withdrawn within the limits of that substance, and observers have succeeded in tracing back nearly all the peculiar phenomena of motion to the existence of minute parts of a really muscular nature. Thus, in the human skin there lie little muscles about as large as the smallest fasciculi in the parietes of the urinarybladder, bundles consisting of diminutive fibre-cells, which run from the base of the hair-follicles towards the surface of the skin, and, when they contract, approximate the two. The result of this is naturally that the skin becomes uneven, and we get what is called a goose-skin. This singular phenomenon, which was previously regarded as inexplicable, has been simply explained by the demonstration of these purely microscopical muscles, the *arrectores pilorum.*

So also we now know that the greater part of the muscular layers in vessels is composed of elements of this kind, and that the phenomena of contraction exhibited by the vessels must be referred solely and exclusively to the action of muscular fibres, which are contained in them in the form of circular or longitudinal layers. A small vein or a small artery can contract only in proportion to the quantity of muscle with which it is provided, and they are only distinguished by the circumstance that either the longitudinal or the transverse muscular layers are the more strongly developed.

I have called your attention to this point because you

Fig. 26.



can see from it, how a simple anatomical discovery may supply the most important information with regard to

Fig. 26. Small artery from the base of the cerebrum after the application of acetic acid. *A*. Small trunk; *B* and *C*, larger branches; *D* and *E*, branches of the smallest size (capillary arteries). *a*, *a*. External coat, with nuclei, which run in the direction of the length of the vessel, and are seen first in a double and afterwards in a single layer, with a striated basis-substance; at *D* and *E* the coat is reduced to a single layer, with longitudinal nuclei, which here and there have been replaced by masses of fat-granules (fatty degeneration). *b*, *b*. Middle coat (circular fibrous, or muscular, coat), with long, cylindrical nuclei, which run transversely around the vessel, and at its borders (where they look as though they had been cut across) present the appearance of round bodies; at *D* and *E* transverse nuclei of the middle coat becoming continually scarcer. *c*, *c*. Internal coat, at *D* and *E* with longitudinal nuclei. 300 diameters.

physiological facts, which are widely separated from one another, and how the demonstration of definite morphological elements may at once most essentially contribute to the elucidation of functions, which, without any such data, would be utterly incomprehensible.

I will omit to speak here of the more intimate structure of the nervous system, because I shall have occasion hereafter to consider it in a more connected form, else this would be the subject which would most suitably come next, seeing that there exist many points of resemblance in the structure of muscular and nerve-fibres. But in the nervous system we find, in addition, nerve-cells (Ganglienzellen), which connect the individual fibres with one another, and must be regarded as the most important storehouses for all nervous energy.

Concerning the structure of the vascular system also I will not here treat in detail, but will only say as much as is necessary to give a cursory view of the matter.

A capillary vessel is a simple tube (Fig. 3, *c*), in which we have, with the aid of our present appliances, hitherto only been able to discover a simple membrane, beset at intervals with flattened nuclei, which, when seen in the middle of the surface of the vessel, present the same appearance as in the elements of muscle, only that they usually lie more at the sides, and therefore frequently have an awl-shaped appearance, from their sharp border alone being perceived. It is this, the most simple class of vessels, which we now-a-days solely and exclusively cali capillaries, and with regard to them we cannot say that they become wider or narrower by means of any action of their own, but at most that their elasticity renders a certain degree of contraction possible. Nowhere are there to be witnessed in them genuine processes of contraction or relaxation succeeding it. The discussions which formerly took place with regard to the contractility of the capillaries really had reference to small arteries and veins, the calibre of which grows narrower through the contraction of their muscular coats, or wider upon the occurrence of relaxation in consequence of the pressure of the blood. This is one of the first facts, and an important one it is, which have resulted from the more accurate histological knowledge of the smaller and larger vessels, and it shows us that we cannot speak of the general properties of vessels, inasmuch as the capillaries differ essentially in structure from the small arteries and veins. These are composite structures, partaking of the nature of organs, whilst a capillary vessel is rather a simple *histological* element.

Now that we have, gentlemen, completed a very general survey of the physiological tissues, the question arises, how the pathological ones in their turn comport themselves. By pathological tissues, of course, those only can be meant which really constitute pathological new formations, and not physiological parts which have simply undergone alteration in consequence of some deviation from the normal processes of nutrition. We have in them to deal with genuine *neoplasms*, with the additional matter furnished by the growth of new tissues in the course of pathological processes, and the question is, whether the general types which we have established for the physiological tissues will also be found to hold good in the case of the pathological ones. To this I unreservedly reply, yes ; and however much I herein differ from many of my living contemporaries, however positively the peculiar (specific) nature of many pathological tissues has been insisted upon during the last few years, I will nevertheless endeavour in the course of these lectures to furnish you with proofs that every pathological structure has a physiological prototype, and that no form of morbid growth arises which cannot in its elements be traced back to some model which had previously maintained an independent existence in the economy.

The classification of pathological new formations, of genuine neoplasms, was formerly by most observers attempted to be based upon their different degrees of *vascularity*. If you examine the different treatises which appeared upon this subject up to the time of the cell-theory, you will find that the question of organization was always decided by that of vascularity. Every part which contained vessels was regarded as organized, and every part as unorganized which was destitute of vessels. But this, according to present notions, is an incorrect view of the matter, inasmuch as we have also physiological tissues without vessels, as for example, cartilage.

But at a time when the more minute elements of tissues were at most only known as globules, and when very different virtues were attributed to these globules, it was quite excusable that everything should be referred to the vessels, particularly after the comparison John Hunter made between pathological new formations and the development of the chick in the egg, when he endeavoured to show that, just as the punctum saliens in the hen's egg constitutes the first phenomenon of life, the vessels also where the first things to show themselves in pathological formations. You no doubt still remember how several "parasitical" new formations were described by Rust and Kluge as provided with an independent vascular system, which without having any connection with the old vessels, developed itself quite independently, as is the case in the chick. Many attempts had indeed been made even before this to refer the apparently so irregular forms of new formations to physiological paradigms, and herein essential service has been rendered by natural philosophers. At the time when theromorphism played a conspicuous part, and many analogies were discovered between pathological processes and the normal states of inferior animals, comparisons also began to be instituted between new formations and familiar parts of the body. Thus, Johann Friedr. Meckel, the younger, spoke of mammary and pancreatic sarcoma. What has very recently been described in Paris as heteradenia (Heteradenie), or a heterologous formation of glandular substance, was in the school of the natural philosophers a pretty generally accepted fact.

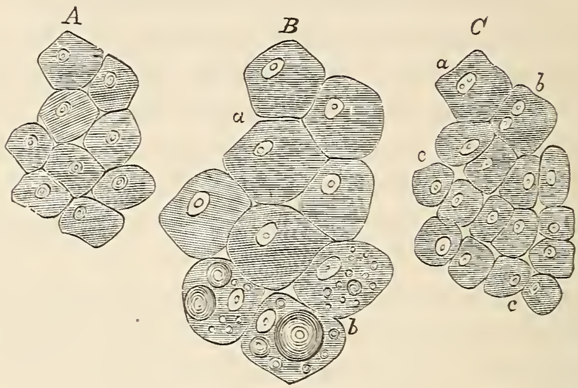
Since the study of embryology has been prosecuted in a more histological manner, the conviction has gradually more and more been acquired, that most new formations contain parts which correspond to some physiological tissue, and in the micrographical schools of the west a certain number of observers have come to the conclusion, that in the whole series of new formations there is only one particular structure which is specifically different from natural formations, namely cancer. With regard to this, the most important points urged are, that it differs altogether from every other tissue, and that it contains elements *sui generis*, whilst, singularly enough, a second formation, between which and cancerous tissue the older writers were wont to draw parallels, namely tubercle, has—although to it too nothing strictly analogous could be discovered—been much neglected, owing to its having been regarded as an incomplete and somewhat crude product, and as a structure which had never become properly organized. Yet, upon a more careful examination of cancer or tubercle, we shall find that everything depends upon our searching for that stage in their development, in which they are exhibited in their perfect form. We must not examine at too early a period, when their development is incomplete, nor yet at too late a one, when it has proceeded beyond its highest point. If we restrict our observations to the time when development is really at its height, a physiological type may be found for every pathological formation, and it is just as possible to discover such types for the elements of cancer as to find them, for example, for pus, which, if it be sought to maintain the specific nature of certain formations, is just as much entitled to be regarded as something peculiar as cancer. Both of them stand upon precisely the same footing in this respect, and when the older writers spoke of cancer-pus they were in a certain measure right, inasmuch as cancer-juice is only distinguished from pus by the higher degree of development to which its individual elements have attained.

A classification of pathological structures also may be made upon exactly the same plan as that which we have already ventured upon in the case of the physiological tissues. In the first place, there are also among these structures some which, like the epithelial ones, are essentially composed of cellular elements, without the addition of anything else of consequence. In the second place, we meet with tissues which are allied to those called connective, inasmuch as in addition to the cells a certain quantity of intercellular substance is present. In the third and last place come those formations which are akin to the more highly organized structures, blood, muscles, nerves, etc. Now, a point to which I must at once direct your attention is, that in pathological formations those elements the more frequently exist, and the more decidedly prevail, which do not represent the higher grades of really animal development, and that, therefore, on the whole, those elements are most rarely imitated which belong to the more highly organized, and especially, to the muscular and nervous, systems. Still, these formations are by no means excluded; we find pathological new formations of every description, no matter to what tissue they may be analogous, provided it possesses distinctive features. It is only with regard to their frequency and importance that a difference prevails, and this is of such a nature that the great majority of pathological productions contain cells analogous to epithelial cells, or to the corpuscles of the connective tissues, and that of those structures which we have included in the last class of normal tissues, the vessels and parts which may be compared with lymph and lymphatic glands are the most frequently met with as new formations, whilst real blood, muscles, and nerves, are the most seldom found as such.

But, if we ultimately arrive at such a simple view of the matter, the question of course arises, what becomes of the doctrine of the *heterology* of morbid products, to the upholding of which we have long been accustomed, and to which the most simple reflection almost inevitably conducts us. Hereunto I can return no other answer than that there is no other kind of heterology in morbid structures than the abnormal manner in which they arise, and that this abnormity consists either in the production of a structure at a point where it has no business, or at a time when it ought not to be produced, or to an extent which is at variance with the typical formation of the body. So then, to speak with greater precision, there is either a *Heterotopia*, an aberratio loci, or an aberratio temporis, a *Heterochronia*, or lastly, a mere variation in quantity, *Heterometria*. But we must be very careful not to connect this kind of heterology in the more extended sense of the word with the notion of *malignity*. Heterology is a term that, in its histological meaning may be applied to a large proportion of pathological new formations, which, as far as the prognosis is concerned, may unquestionably be called benignant; it is not rare for a new formation to occur at a point where it is certainly entirely misplaced, but at the same time does not occasion any considerable mischief. A lump of fat may very likely arise in a place where we should expect no fat, as, for example, in the submucous tissue of the small intestines, but, let the worst come to the worst, the result is only a polypus, which protrudes on the inner surface of the bowel, and may become tolerably large without giving rise to any symptoms of disease.

If we consider the structures which are called heterologous in the more restricted sense of the word, with reference, namely, to the points at which they arise, they may be easily separated from the homologous ones (homœoplastic ones of Lobstein), by their deviating from the type of the part in which they arise. When a fatty tumour arises in fatty tissue, or a connective tissue (fibrous) tumour Bindegewebs-Geschwulst) in connective tissue, the type followed in the formation of the new structure is homologous to the type followed in the formation of the old one. All such formations are, as usually designated, included under the term hypertrophy, or under that of *hyperplasia*, if we adopt the name I have proposed for the sake of more accurate distinction. Hypertrophy, according to the meaning which I attach to the word, designates those cases in which the individual elements af a structure take up a considerable amount of matter, and thereby become larger; and in consequence of the simultaneous enlargement of a number of elements, at last the whole of an organ may become swollen. When a muscle becomes thicker, all its primitive fasciculi become thicker. A liver may become hypertrophied simply in consequence of a considerable enlargement of its individual cells. In this case there is real hypertrophy without, properly speaking, any

Fig. 27.



new formation. Essentially different from this process are the cases in which an enlargement takes place in consequence of an *increase in the number of the elements.* A liver, namely, may also become enlarged by a very abundant development of a series of small cells in the place of the ordinary ones. Thus, when simply hypertrophied, we see the panniculus adiposus of the skin swell up in consequence of every single fat-cell's absorbing a larger quantity of fat than usual, and when this takes place in thousands upon thousands, nay, we may say, in hundreds of thousands and millions of cells, the result is very obvious and strikes the eye (polysarcia). but it is just as possible for new cells to form in addition to the old ones, and for an increase of size to take place without any enlargement of the individual cells.

Fig. 27. Diagrams of hepatic cells. *A.* Their simple physiological appearance. *B.* Hypertrophy: *a*, simple; *b*, with accumulation of fat (fatty degeneration, fatty liver). *C.* Hyperplasy (numerical or adjunctive hypertrophy). *a.* Cell with nucleus and divided nucleolus. *b.* Divided nuclei. *c, c.* Divided cells.

These are essentially different processes, and may be styled *simple and numerical hypertrophy.*

Hyperplastic processes (numerical hypertrophy) in all cases produce a tissue similar to that of the original part ; hyperplasia of the liver gives rise to new hepatic cells ; that of a nerve to new nerve-substance ; that of the skin to a fresh production of the elements of the skin. A heteroplastic process, on the contrary, engenders histological elements which correspond, indeed, to natural forms, elements, for example, resembling in structure those peculiar to glands, nerve-substance, the connective and epithelial tissues, but these elements do not arise in consequence of a simple increase in the number of such as previously existed, but in consequence of a change in the original type of the parent tissue. When cerebral matter forms in the ovary, it does not arise out of pre-existing cerebral matter, nor through any act of simple cell-proliferation ; when epidermis springs up in the muscular substance of the heart, however much it may correspond to that on the external surface of the skin, it is, notwithstanding, a heteroplastic structure. When we find hairs quite natural in structure in the substance of the brain, however great the correspondence they exhibit with the hairs of the external surface, they will nevertheless be heteroplastic hairs. In like manner we see cartilaginous tissue arise, without the existence of any essential difference between it and ordinary, familiar cartilage, as, for example, an enchondromata. Still, an enchondroma is a heteroplastic tumour, even when occurring in bone, for perfect bone has no longer any cartilage in the parts where the enchondroma forms, and the term *cartilage* of bone (Knochenknorpel), as a designation for the organic basis of bone, is nothing but a term. It is either from osseous or medullary tissue that the enchondroma springs, and at the very point where real cartilage exists, for example, at the articular ends of the bone, no cartilaginous tumours, in the ordinary sense of the word, arise. It is not, therefore, with an hypertrophy of pre-existing cartilage that we have here to deal, but with a genuine new formation, which begins with a change in the local histological type. According to this manner of viewing the subject which is essentially different from that previously current, no attention is therefore paid, in considering the question of the heterologous nature of a new formation, to the composition of the structure as such, but only to the relations which subsist between it and the parent soil from which it springs. Heterology, in this sense, designates the difference of development in the new, as contrasted with the old, tissue, or, as we are wont to say, a *degeneration*, a deviation from the typical conformation.

This is, as you will see, also really the most important point upon which we can ground our prognosis. We find tumours, which present the most striking resemblance to the most familiar physiological tissues. An epidermic [epithelial] tumour (Epidermis-Geschwulst) may, as I have already pointed out, in its elementary structure entirely correspond to ordinary epidermis, but in spite of this it is not always a benignant tumour of merely local import, which may be traced to a merely hyperplastic increase in pre-existing tissues, for it sometimes arises in the midst of parts which are far from containing epidermis or epithelium, as, for example, in the interior of lymphatic glands, or in that of thick layers of connective tissue, which are at a distance from any surface, and even in bone. In these cases the formation of epidermis is certainly quite as heterologous as it is possible to conceive anything to be. But practical experience has shown us that it was altogether incorrect to conclude from the mere correspondence of the pathological tissue with a physiological one, that the case would continue to follow a benignant course.

It has been, as I must remark with particular emphasis, one of the greatest, and at the same time best-founded, reproaches which have been levelled against the most recent micrographical doctrines, that, regarding the subject from the certainly excusable point of view, namely, the correspondence between many normal and abnormal structures, they have declared every pathological new formation to be innocuous which exhibits a reproduction of pre-existing and familiar tissues of the body. If what I have communicated to you as my view be correct, namely, that throughout the whole range of pathological growths no structure of an absolutely new form is to be found, but that we everywhere meet with structures which may in one way or another be regarded as the *reproduction of physiological tissues*, then this point of view falls to the ground. In support of my view, I can at least adduce the fact that I have, in all disputes concerning the innocent or malignant nature of definite forms of tumours, up to the present time always proved to be in the right.

Before we quit the consideration of General Histology, I would invite your attention for a few moments to a few points of primary importance which obtrude themselves upon us on nearly every occasion. Whilst, namely, the animal tissues were being studied in their affinities to one another, questions relating to these affinities were at different times stumbled upon, which gave rise to generalizations that were more of a physiological character.

When Reichert undertook to collect the connective tissues into one larger group, he set out with this position chiefly, that the demonstration of the *continuity of tis-*

sues must be regarded as a decisive proof of their intimate relationship. That as soon as one part could be made out to be continuously (by union, not mere juxtaposition) connected with another, both must be regarded as parts of a common whole. In this manner he sought to prove that cartilage, periosteum, bone, tendons, fasciæ, etc., really formed a continuous mass, a kind of basis-tissue (Grundgewebe) for the body, a *connective substance*, which had only experienced certain changes in these different localities, without their being, however, of such a nature as to destroy the character of the tissue as such. This so-called *law of continuity* soon suffered the most violent shocks, and quite recently such a terrible breach has been made in it, that it can scarcely any longer be possible to derive therefrom any general criterion for the determination of the nature of a tissue. On the other hand, namely, new facts have been continually brought forward in support of the continuity ot such histological elements as, according to Reichert, would be separated *toto cœlo* from one another, as, for example, of epithelial and connective tissue ; and there has been a continually increasing mass of evidence in support of the assertion that cylindrical epithelium is capable of becoming elongated into fibres, which in the shape of filaments anastomose with connective-tissue corpuscles. Nay, it has been quite recently asserted by a whole series of observers that these superficial cells are prolonged inwardly, and then enter into direct connection with nerve-fibres. With regard to this last point, I must confess that I am not yet convinced of the correctness of the representation ; but with respect to the former one, that is a matter which will probably end in the demonstration of the real continuity of the elements. It would seem, therefore, that it is even now no longer possible to mark out the exact limits which divide every kind of epithelium from every kind of connective tissue, but only where scaly epithelium is met with, whilst the limits are doubtful wherever cylindrical epithelium exists.

Just in the same manner elsewhere also do the boundary lines become obliterated. Whilst formerly the limits which separate the elements of muscle from those of tendon were considered to be most distinctly defined, extremely decisive proofs have in this case also been afforded, and first by Hyde Salter and Huxley, that fibres proceed from connective-tissue corpuscles, which whilst pursuing their course in an inward direction, all at once assume the character of transversely striped muscle. So, then, in the case of connective tissue, it would seem there exists a continuous connection between the elements of the surface and the more highly developed ones of the deeper parts. Now if, on the other hand, it has turned out to be very probable that the corpuscles of connective tissue have definite relations to the vascular system, we are, as you see, almost justified in regarding this tissue as a kind of *neutral ground* for parts to *meet upon* (indifferenter Samelpunkt), as a peculiar arrangement for their intimate connection, an arrangement which, though certainly not exercising any great influence upon the higher functions of the animal, is yet of great importance as far as its nutrition is concerned.

In the place of the law of continuity, therefore, we must necessarily put something else. And here, I think, the doctrine which has the strongset claims to our attention is that of *histological substitution.* In the case of all tissues of a like nature it is quite possible, even whilst confining our attention to what occurs physiologically in the various classes of animals. to find one tissue at a certain fixed point of the body replaced by an analogous one belonging to the same group, or, in other words, by an *histological equivalent.*

A spot invested with cylindrical, may acquire scaly epithelium. A surface upon which cilia were originally seen, may afterwards be found to have ordinary epithelium. Thus, on the surface of the ventricles of the brain we meet at first with ciliated, and at a later period with simple scaly, epithelium. Thus, too, we see the mucous membrane of the uterus usually covered with ciliated epithelium, but during pregnancy we find the layer of ciliated cylinders replaced by one of squamous epithelium. Thus, also, in places where soft epithelium ordinarily is found, epidermis may, under particular circumstances, be generated, as, for example, in the prolapsed vagina. Thus, again, in the sclerotic coat of the eyes of fish, cartilage is found, whilst in man this tunic consists of dense connective tissue ; in many animals bone is found in parts of the skin, where in man there is only connective tissue ; but in man, too, in many places where there was original cartilage, osseous tissue is afterwards discovered. But the most striking instances of such substitutions are met with in muscles. One animal has transversely striped muscular fibres in the same place that another has smooth ones.

In diseased conditions *pathological substitutions* occur, in which a given tissue is replaced by another ; but even when this new tissue is produced from the previously existing one, the new formation may deviate more or less from the original type. There is therefore a great chasm between physiological and pathological substitution, or at least, between the physiological and certain forms of the pathological one.

Physiologically, the substitution is constantly effected by the introduction of another tissue of the same group (*homology*) ; pathologically, very frequently by the agency of a tissue belonging to another (*heterology*). To this we must reduce the whole doctrine of the specific elements of pathology which have played so conspicuous a part in the last twenty years.

LECTURE IV.

FEBRUARY 24, 1858.

NUTRITION AND ITS CHANNELS.

Action of the vessels—Relations between vessels and tissues—Liver—Brain—Muscular coat of the stomach—Cartilage—Bone.

Dependence of tissues upon vessels—Metastases—Vascular territories [Gefässterritorien] (vascular unities)—Conveyance of nutriment in the juice-conveying canals (Saftkanäle) of the tissues—Bone—Teeth—Fibro-cartilage—Cornea—Semilunar cartilages.

According to the ideas usually entertained with regard to nutrition, the vessels are regarded as the canals by means of which not only the interchange of material (Stoffverkehr) is accomplished, but upon the assistance of which, sometimes actively and sometimes passively afforded, reliance is placed whenever it is required to control an individual part in its interchange of material. The regulating principle in the process of nutrition was long designated by an expression which has even crept into the language of the present day, namely, the "action of the vessels," as if they were endowed with a special power of actively influencing the condition of the neighbouring histological constituents.

As I pointed out to you the last time, when upon the subject of muscular fibres (p. 85), we can now-a-days only speak of action in the vessels as far as muscular fibres are present in them, and the vessels are thus enabled by the contraction of these fibres to grow narrower or shorter. This narrowing of their channel may have the effect of impeding transudation of fluids, whilst, on the contrary, in the case of the relaxation or paralysis of the muscular fibres, the widening of the vessel may favour such transudation. Let us admit this for the present, but allow me, before proceeding farther, to enter somewhat into the analysis of the mass of tissue which lies around the vessels, and is generally conceived to be of a very simple and uncomplicated nature.

If we select parts where the vessels lie very closely packed, and there is perhaps nearly as much vessel as tissue, as, for example, the *liver*, in which this condition really does occur (for a liver, when its vessels are full, contains nearly as large a volume of vessels as it does of proper hepatic substance), we see that the interstices which are left between the vessels are filled with quite a small number of cells.

If we examine a single acinus of the liver by itself, we find, when a very lucky transverse section has been obtained, in its centre the vena centralis or intralobularis, which runs into the hepatic vein, at the periphery branches of the portal vein, which send capillary twigs into the interior. These at once form a network, which at first has long, but afterwards more regularly shaped, meshes, and extends in the direction of the central (or hepatic) vein, and at last terminates in it. The blood, therefore, after it has en-

Fig. 28.

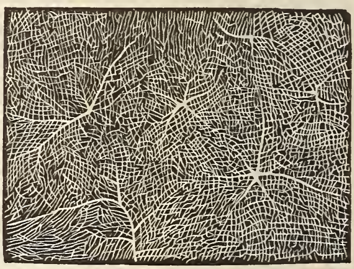


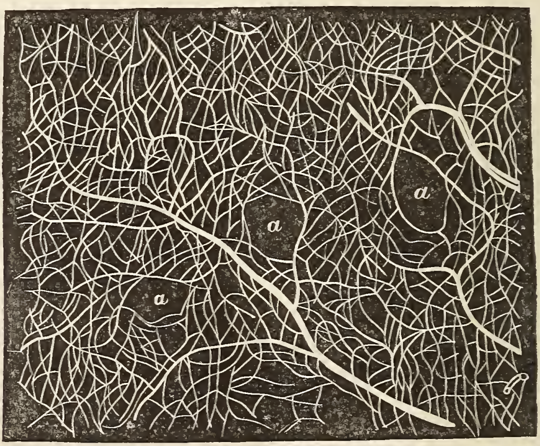
Fig. 28. Section from the periphery of the liver of a rabbit; the vessels completely injected. 11 diameters.

tered by the interlobular (or portal) vein, flows through the capillary network into the intralobular vein, whence, by means of the hepatic veins, it is conducted back again to the heart. Now, in the case of an injected liver, this network is seen to be so close that what interstices there are left seem almost to occupy less room than the vessels themselves. We can thus easily imagine how the older anatomists, such as Ruysch, came to be led by their injections to the supposition that nearly everything in the body was made up of vessels, and that the different organs were only distinguished by differences in the arrangement of their vessels. But just the opposite to what is observed in an injected preparation does the proportion between vessel and tissue appear to be in an ordinary specimen from a liver. In this the vessels are scarcely perceptible. A similar network is indeed seen, but it is the network formed by the hepatic-cells (Fig. 27), which, closely crowded, one against the other, fill up all the inter-spaces of the vessels. It is plain, therefore, that the capillary and hepatic-cell networks are interwoven in the most intricate manner, so that cells belonging to the parenchyma of the liver everywhere lie in almost immediate contact with the walls of the vessels, there being at most a fine layer between the cells and the walls, concerning which it is still a matter of dispute amongst histologists whether it is to be regarded as a peculiar coat, constituting the finest gall-ducts, or only as a very small quantity of connective tissue accompanying the vessels.

In this extremely simple case, a tolerably simple relation may certainly be assumed to exist between the vessels and the cells ; it may be conceived that the blood which flows through the vessels may, in proportion to the degree in which they are contracted or dilated, and to its own quantity, exercise a direct influence upon the adjoining cells. It might indeed be objected, with regard to the conditions of nutrition, that we have here to deal with quite a peculiar arrangement of the vessels, which are essentially of a venous nature, as being composed of ramifications of the portal and hepatic veins, but the hepatic artery also enters into the formation of this capillary network, so that the blood in it cannot be resolved into its individual arterial and venous constituents. Injections from each of the vessels named ultimately find their way into the same capillary network.

In most parts, however, the relations do not present such a simple form as in the liver ; considerable interspaces often separate the individual cells, and no inconsiderable quantities of these elements are enclosed in every capillary mesh. I show you here a second object derived from a fresh human *brain*—from a lunatic who died with his cerebrum in a highly hyperæmic state.

Fig. 29.



The section has been made through the corpus striatum, which was of a deep red colour. You have a good view

Fig. 29. Natural injection of the corpus striatum of a lunatic. *a*, *a*. Gaps destitute of vessels, and corresponding to the strands of nervous fibres which traverse the ganglion. 80 diameters.

of the naturally injected vessels ; and the width of the individual meshes of the capillary network may be clearly seen. The section has been carried transversely through the corpus striatum, and at certain intervals large, roundish spots may be distinguished, which appear dark by transmitted light (Fig. 29, *a*, *a*, *a*), but by reflected light and to the naked eye look white, and are formed by transverse sections of the nervous fibres which run in long strands towards the spinal marrow. The vessels scarcely penetrate into them. The rest of the mass, on the other hand, consists of the proper grey substance of the corpus striatum, within which a vascular network with very fine meshes is distributed, the grey substance of the nervous centres being everywhere, both in their interior and in their cortical substance, distinguished from the white by its greater vascularity. A few large vessels are observable in the object, giving off branches, the ramifications of which continually diminish in size, until at last they terminate in capillary networks with very fine meshes. Still, however close this network may be, every element of the substance of the brain by no means comes into immediate contact with a capillary vessel.

The third object is a very slightly magnified injected preparation from the *muscular coat of the stomach*, in which, with a high power, the direction of the muscular fibres is indicated by fine longitudinal striæ ; here the vessels form tolerably regular networks, connected with one another by

Fig. 30.

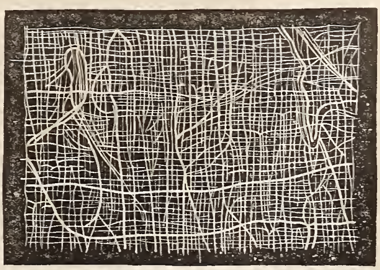
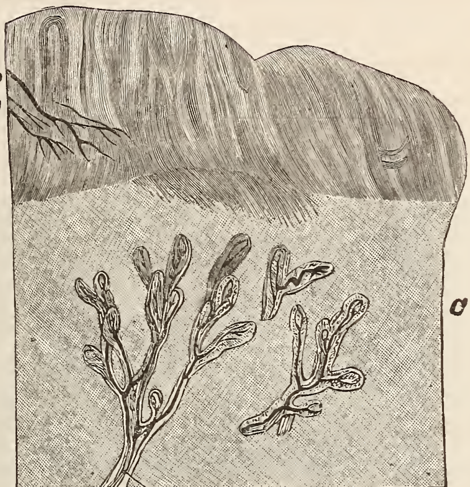


Fig. 30. Injected preparation from the muscular coat of the stomach of a rabbit, magnified 11 diameters.

transverse anastomoses, and splitting up into smaller and smaller vessels, which form fine networks within the tissue, so that the whole of it is by this means mapped out into a series of irregularly four-sided divisions. To each of the ultimate intervascular spaces is allotted a certain number of muscular elements, so that the vessels are in some parts in contact with the muscular fibres, whilst in others they lie at a greater distance from them.

If we go on in this way examining the structure of the different organs and tissues, we pass from such as, when injected, seem to consist almost entirely of vessels, in time to those which contain scarcely any, and at last to such as really have none at all. This is most strikingly the case with the connective tissues, and the most important amongst these are *bone* and *cartilage.* Perfectly developed cartilage has no longer any vessels at all; perfectly developed bone certainly contains vessels, but in a very variable degree. That perfectly developed cartilage contains no vessels, you will not, I suppose, call upon me to convince you by any additional, special proofs, inasmuch as you have seen various preparations of cartilage, in which not a trace of them was to be observed. (Figs. 6, 9, 22.) I now place before you a piece of young cartilage, because you can see in it what the arrangement of the vessels in cartilage is at an earlier period. It is a section from the calcaneum of a new-born child, and in it the vessels run up from the already-formed central osseous mass into the cartilage which still remains. The preparation shows along the outermost surface of the cartilage the transition from it into the perichondrium, whilst the lower part of the section is taken from the border of the already-formed bone. From this part large vessels are seen running up and terminating in the middle of the cartilage by the formation of loops and plexuses, as it were a tree of villi (Zottenbaum) in the cartilage, and very much resembling a villus of the chorion of the ovum. In fact, the vessels mount up into the cartilage from the nutrient artery of the bone, but only to a certain height. There they form real loops, and at length break up into a fine

Fig. 31.



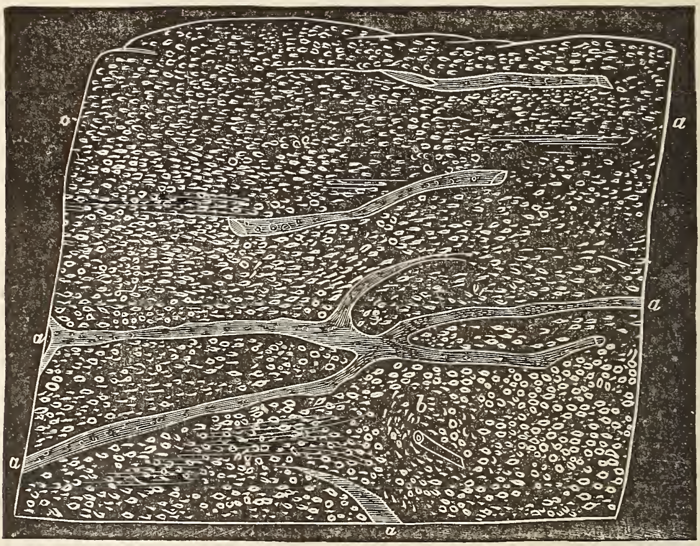
plexus of capillaries, out of which veins are ultimately formed, and run out again pretty near the spot where the artery entered. But the whole of the rest of the mass consists of non-vascular cartilage, the corpuscles of which, with a low power, look like fine points. Thus there is a whole host of cartilage-corpuscles lying between the terminal loops and the external surface, and the whole of this layer is therefore dependent for its

Fig. 31. Section of cartilage from the calcaneum of a new-born child. *C.* The cartilage, with its cells indicated by fine points. *P.* Perichondrium and adjoining fibrous tissue. *a.* Inferior border very near to the line of junction between the cartilage and the bone, with the vascular loops ascending from the nutrient artery. *b, b.* Vessels which make their way through the perichondrium in the direction of the cartilage. 11 diameters.

nutrition upon the juice which exudes from the terminal loops and permeates the tissue, though to a trifling extent also upon the materials which the scanty vessels of the perichondrium convey to it. The vessels which spring from the nutrient artery mark in all bones, at a tolerably early period, pretty exactly the limits to which the ossification subsequently proceeds, whilst the remnants of the cartilage which remain bordering upon the joint never contain vessels.

With regard to the *bones* themselves, the disposition of their blood-vessels is in itself tolerably simple, but at

Fig. 32.

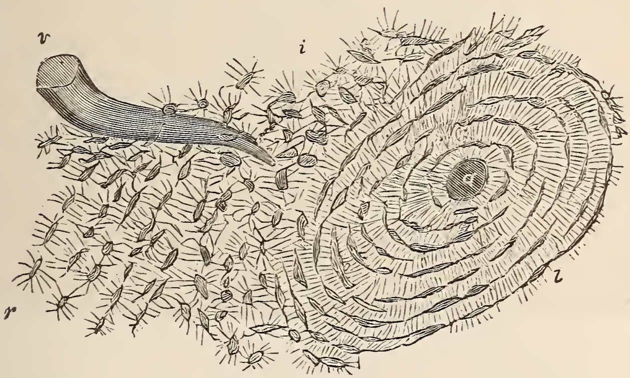


the same time very characteristic. If we examine the compact substance, we can usually, even with the naked eye, distinguish upon its surface small openings through which vessels enter from the periosteum. With a mode-

Fig. 32. Longitudinal section from the cortex of a sclerotic tibia. *a*, *a*. Medullary (vascular [Haversian]) canals, between them the bone-corpuscles for the most part parallel; but at *b* (in transverse section) concentrically arranged. 80 diameters.

rately high power we discover that these vessels (Fig. 32, *a*) immediately beneath the surface form a network with somewhat long meshes, or a series of tubes anastomosing with one another and, generally speaking, running longitudinally, for though they sometimes take a somewhat more oblique course inwardly, they still essentially maintain a longitudinal direction. Between these meshes there remain comparatively wide interspaces, within which, precisely as we before saw the cartilage cells, we here see the bone-corpuscles, and indeed also in a longitudinal direction, parallel to the surface. If the same part be examined in transverse section, we of course see, where the longitudinal canals were previously observed, nothing but their transverse sections here and there united by oblique communications! Between them lies the proper osseous tissue, deposited in lamellar layers, some of them parallel to

Fig. 33.



the surface, some concentrically arranged around the vessels. In the deeper layers of the compact substance

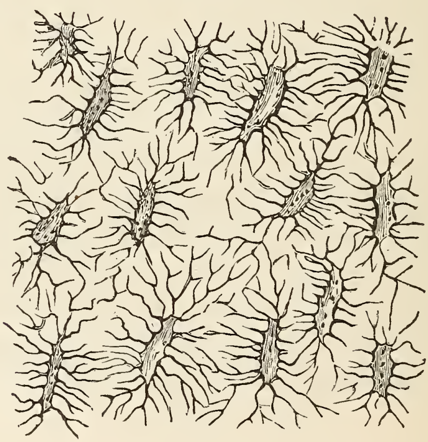
Fig. 33. Section of bone. *a.* Transverse section of medullary (vascular [Haversian]) canal, around which the concentric lamellæ, *l*, lie with bone-corpuscles and anastomosing canaliculi. *r.* Lamellæ divided longitudinally and parallel. *i.* Irregular arrangement in the oldest layers of bone. *v.* Vascular canal. 280 diameters.

this concentric arrangement around the vessels constantly prevails.

Between these more lamellated parts is left a small quantity of osseous substance (Fig. 33, *i*) which does not present the same structure, but is arranged upon another, and independent, plan. Upon more accurate examination it is seen to be formed of little columns, which are generally perpendicular to the long axis of the bone, but sometimes curve round, and so become parallel to the long axis. These are the remains of the spicula first formed during the growth of the bone in thickness, and are therefore of older date.

As in the sections which are obtained by grinding down bone, the vessels themselves cannot for the most part any longer be distinguished, the cavities [Haversian

FIG. 34.



canals] (Fig. 32, *a*, 33, *a*, *v*,) in which they run have been named medullary canals, improperly, inasmuch as

Fig. 34. Bone-corpuscles from a morbid formation of bone in the dura mater of the brain. Their branching and anastomosing prolongations (canaliculi) are seen, as well us minute spots upon their walls, marking the funnel-shaped commencements of the canaliculi. 600 diameters.

there is usually no marrow contained in these narrow channels; they should properly be called vascular canals; still the other term is so universally received, that it is even employed in cases where the wall of the vessel is in immediate contact with the internal surface of the cavity. Immediately surrounding these canals we see a series of peculiar structures; oblong or roundish bodies which usually appear black when the object is not fully brought into focus, and are provided with jaggs or processes. They used to be called bone-corpuscles, and their processes bone-canals (canaliculi ossei); and as the view was originally entertained that the calcareous matter was really deposited in them, and that the dark appearance which they usually present when viewed by transmitted light resulted from the presence of this matter, the canals were also termed canaliculi chalicophori, a name which has now been altogether abandoned, because convincing proofs have been obtained that, so far from being contained in them, the lime is, on the contrary, diffused throughout the homogeneous basis-substance which lies between them.

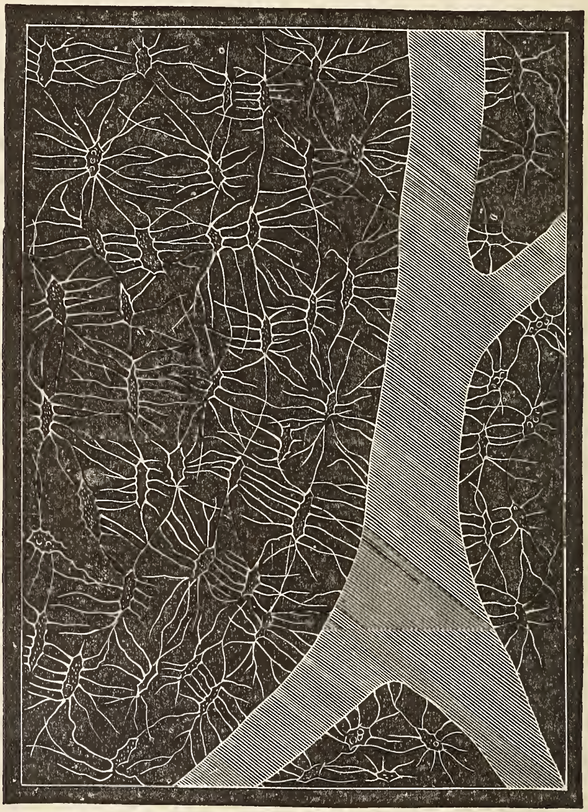
As soon as this discovery was made, that, namely, the distribution of the lime in the osseous tissue took place in a manner just the reverse of that in which it had been supposed it did, the other extreme was immediately run into, and for the name of bone-corpuscles that of bone-cavities (lacunæ) was substituted, and it was assumed that bone contained nothing but a series of empty cavities and canals, which were indeed penetrated by a fluid, but still were really nothing more than fissures in the bone. Some few observers indeed actually called them bone fissures Now I have endeavoured to demonstrate in various manners that they are real corpuscles, and not mere cavities in a dense basis-tissue, but structures provided with special walls and boundaries of their own, which separate them from the intermediate substance. For by the help of chemical reagents (concentrated mineral acids, and particularly hydrochloric acid) we are enabled, by dissolving the basis-substance, namely, to disengage the corpuscles from it. In this way we furnish, I think, the most complete demonstration that they are really independent structures. Besides, a nucleus may be distinguished within these bodies; and, even without entering into the history of their development, we discover that here too we have once more to deal with cellular elements of a stellate form. Bone therefore exhibits in its composition a tissue, containing, in an apparently altogether homogeneous basis-substance, peculiar, stellate bone-cells distributed in a very regular manner.

The intervals which exist between every two of the vessels in bone are often very considerable; whole systems of lamellæ, beset with numerous bone-corpuscles, thrust themselves in between the medullary canal. Here it is certainly difficult to conceive the nutrition of so complicated an apparatus to depend upon the action of vessels some of them so remote, and especially so, to understand how every individual particle of this extensive compound mass can manage to maintain a special relation of nutrition to the vessels. For experience shows us that every single bone-corpuscle really possesses conditions of nutrition peculiar to itself.

I have laid these details before you, in order to point out to you the gradual transition which takes place from the vascular and abundantly vascular, to the scantily vascular and non-vascular parts. If we would form a simple conception of the conditions of nutrition, I think we must lay it down as a logical principle, that whatever is enunciated with regard to the nutrition of very vascular parts, must also hold good for that of scantily and non-vascular parts; and that, if the nutrition of individual parts is considered to be directly dependent upon the vessels or the blood, it must at all events be demonstrated that all the elements which stand in immediate connection with one and the same vessel, and are assigned to a single vessel for their support, present conditions of life essentially similar. In the case of bone it would be necessary to show that every system of lamellæ which has only one vessel for its nutrition, always exhibits a similar state of nutrition. For if that vessel, or the blood which circulates in it, be the active agent concerned in the nutrition, the utmost that can be admitted is, that one part of the elements may be more, another less, subjected to their influence; but still it must essentially be a common and similar influence which they experience. That this is no unreasonable requirement, that a certain dependency of definite territories of tissue upon definite vessels must undoubtedly be admitted, the most beautiful illustrations are afforded us in the doctrine of metastases, in the study of the changes which are effected by the occlusion of single capillary vessels, and with which we have become acquainted from the history of capillary embolia. In such cases, in fact, we see that a whole portion of tissue, as far as its immediate connection with a vessel extends, in its pathological relations also constitutes a whole—a *vascular unity*. But this vascular unity to a finer apprehension still appears a compound, and it is not sufficient to split up the body into vessel-territories (Gefässterritorien) alone, but within them a further division must be made into cell-territories (Zellenterritorien).

This view has, I think, been essentially furthered by our having discovered, as I lately pointed out to you (p. 76), the existence of a special system of anastomosing elements in the connective-tissues, and by our having in this manner filled the place of the vasa serosa (which the older writers imagined as a complement to the capillaries for these ultimate purposes of nutrition) with something definite, by means of which the circulation of nutritive juices is rendered possible in parts which are in themselves poor in vessels. To keep to *bone*, we should

Fig. 35.



scarcely be justified in assuming the existence of vasa serosa in it. The hard basis-substance is throughout

Fig. 35. Section of an osseous plate from the arachnoid of the cerebrum, but quite normal in its structure. A branching vascular (medullary) canal is seen with canaliculi opening into it, and leading to the bone corpuscles. 350 diameters.

uniformly filled with calcareous salts, so uniformly indeed, that no interval can be perceived between the individual calcareous particles. Though some few writers have assumed that little granules can be distinguished in it, this is an error. The only differentiation which can be seen is caused by the prolongation into the basis-substance of the canaliculi, which all ultimately lead back to the bodies of the bone-cells (bone-corpuscles) and in their turn give out branches. The peripheral extremities of these little branches or processes extend right up to the surface of the vascular (medullary) canal. They are therefore inserted exactly where the membrane of the vessel begins (Fig. 35), for they can be distinctly perceived as very minute orifices upon the wall of the canal. Now since the different bone-corpuscles are in their turn distinctly connected with one another, means are afforded by which a certain quantity of juice taken up from the surface of the vascular canal is not diffused throughout the whole mass of tissue, but confined to these delicate, continuous, and specially provided channels, and forced to move onwards in canals which are inaccessible to injections from the vessel. For a time it was believed that the canaliculi could be injected from the vessel, but this is only possible when the vascular canal has become empty by maceration.

This is a condition precisely similar to what we observe in the *teeth*, in which the canaliculi can be injected from the pulp-cavity when empty. If a solution of carmine be injected into this cavity, the dental canaliculi are displayed in the form of numerous tubules running up to the surface side by side in a radiated manner. The substance of the teeth also forms a tolerably broad layer of non-vascular material. Vessels are found nowhere but in the pulp-cavity, in proceeding from which outwards we find nothing but the proper substance of the tooth (dentine) with its system of tubes, which extend nearly up to the surface, and in the root of the tooth are directly continuous with a layer of real bony substance (cement) the corpuscles of which are seated upon the ends of the tubes. A provision for the conveyance of the juices similar to that which in bone originates in the marrow, here takes its rise in the pulp, whence the nutritive fluid can be conveyed up to the surface by the means of tubes.

These systems of tubes which are found in such a very marked form in bone and the teeth, are to be seen with far less distinctness in the soft structures, and it is chiefly for this reason, I imagine, that the analogy which exists between the soft connective tissues and the hard texture of bone has not been clearly comprehended. These systems are most distinctly seen in parts which are more of a cartilaginous nature, as, for example, in fibro-cartilage. But it is a fact of great significance that we find a series of transitional forms between cartilage and the other connective tissues, in which the same conditions are constantly repeated. In the first place, parts which chemically belong to the class of cartilages, for example, the cornea, which yields chondrine when boiled, although nobody regards it as real cartilage. But more striking is the arrangement in those parts in which the external appearance speaks in favour of a cartilaginous nature, but the chemical properties do not correspond, as for example, in the semi-lunar cartilages (Bandscheiben) of the knee-joint, which are interposed between the femur and tibia for the purpose of protecting the articular cartilages from too violent contact. These parts, which even now are generally described as cartilage, yield no chondrine on boiling, but gelatine ; and yet, in this hard connective tissue, we meet with the same system of anastomosing corpuscles that prevails in the cornea and in fibro-cartilage, and it is displayed with unusual distinctness and clearness. Vessels are almost entirely wanting in these cartilages, but in exchange they contain a system of tubes of rare beauty. On making a section, we see that the whole is in the first place mapped out into large divisions, exactly like a tendon; these are subdivided into smaller ones, and these are pervaded by a fine, stellate system of tubes, or, if you will, of cells, inasmuch as the notion of a tube and that of a cell here quite coincide. The networks of cells which here form the system of tubes, terminate externally in the septa bounding the individual divisions, and we here see in close proximity considerable collections of spindle-shaped cells. In these cartilages, too, the whole mass of tissue is only connected by its exterior with the circulatory system; everything that penetrates into the interior must pass by a very circuitous route through a system of canals with numerous anastomoses, and the nutrition of the internal parts is altogether dependent upon this mode of conveyance. The semi-lunar cartilages are structures of considerable extent and great density, and as they are entirely dependent for their nutrition upon this ultimate, minute system of cells, we have in them, much more

Fig. 36.

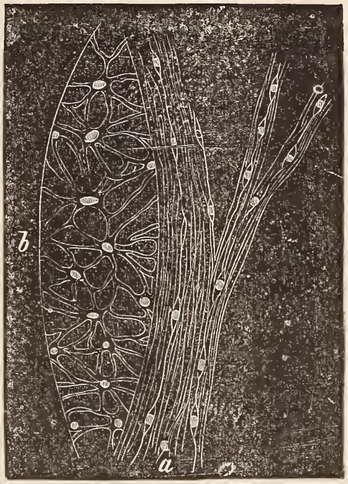


Fig. 36. Section from the semi-lunar cartilage of the knee-joint of a child. *a*. Bands of fibres, with spindle-shaped, parallel and anastomosing cells (seen in longitudinal section). *b*. Cells, forming a network, with broad, branching, and anastomosing canaliculi (seen in transverse section). Treated with acetic acid. 350 diameters.

than in cartilage, to deal with such an arrangement for the supply of nutritive juices, as cannot be under the direct control of the vessels.

For the sake of elucidation, I will merely add that the ultimate elements are seen to consist of very delicate cells, which are prolonged into fine filaments, that in their turn ramify, and look, when cut across, like small points in which a clear centre can be recognised. The filaments can ultimately be very distinctly traced back to the common cell just as in bone. They are extremely fine tubes which are intimately connected with one another, only that here they are in certain spots collected into large groups, by means of which the conveyance of the nutritive juice is principally effected, and that the intercellular substance in no instance becomes infiltrated with lime, but always preserves its character as connective tissue.

LECTURE V.

FEBRUARY 27, 1858.

NUTRITION, AND CONVEYANCE OF THE NUTRITIVE JUICES.

Tendons—Cornea—Umbilical cord.
Elastic tissue—Corium.
Loose connective tissue—Tunica dartos.
Importance of cells in the special distribution of the nutritive juices.

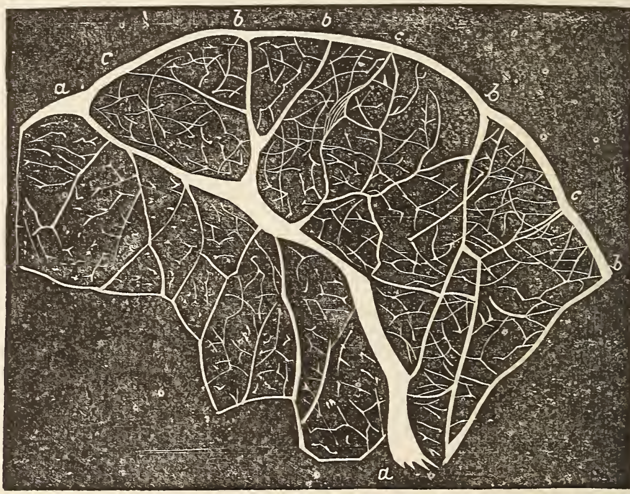
ALLOW me, gentlemen, as a supplement to what we saw and discussed in the preceding lecture, to lay before you a few more preparations in illustration of that peculiar species of nutritive arrangement which we have already seen to exist in various tissues, and which, I hope, will appear to you of very great importance in pathological processes also.

You will remember that the last object of our consideration was a ligamentous disc (Bandscheibe), as it occurs in its most marked form in the knee-joint in the so-called semi-lunar cartilages, which are really no cartilages at all. On the contrary, they possess the qualities of a flat tendon, and the individual structural relations which we found in them, are repeated throughout the whole of the transverse section of a tendon.

We have to-day a series of objects from the tendo Achillis, both of the adult and the child, displaying the different stages of its development; and as this is, moreover a tendon which is of importance in more than one way in an operative point of view, I may, I am sure, be excused for speaking a little more at length concerning it.

On the surface of a tendon we see, as you well know, with the naked eye, a series of parallel, whitish striæ which run pretty close to one another in a longitudinal direction, and give rise to the characteristic glossy appearance. In a microscopical longitudinal section these striæ lie farther apart, so that the tendon presents a

Fig. 37.



somewhat fasciculated appearance and looks less homogeneous than on the surface. This becomes much more evident in a transverse section, in which a series of

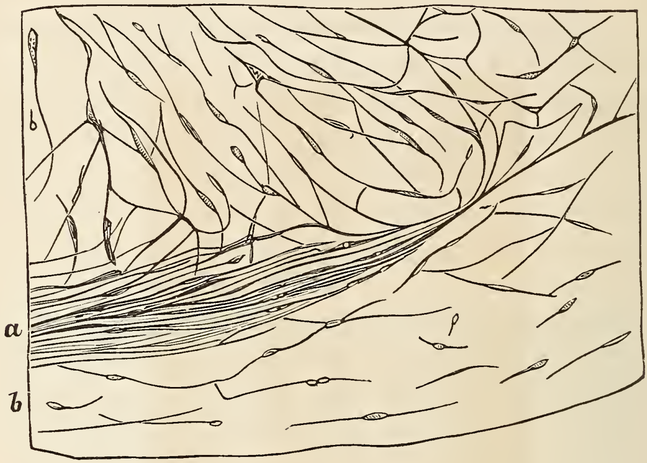
Fig. 37. Transverse section from the tendo Achillis of an adult. From the sheath of the tendon, septa are seen at *a*, *b*, and *c*, running inwardly, and uniting into a network so as to form the boundaries of the primary and secondary fasciculi. The larger ones (*a* and *b*) generally contain vessels, the smaller ones (*c*) do not. Within the secondary fasciculi is seen the delicate network formed by the tendon-corpuscles (reticulating cells—Netzzellen), or the intermediate system of juice-conveying canals (Saftkanalsystem). 80 diameters.

smaller and larger divisions (bundles, fasciculi) are offered to the view.

On magnifying the object, an internal arrangement is shown almost exactly corresponding to that which we have observed in the semi-lunar cartilages. Externally, the tendon is invested in its whole circumference by a fibrous mass, in which the vessels are contained, that are entwined around the tendon. From these at different points vessels proceed into the interior, where they are to be seen in the larger partitions which separate the fasciculi (Fig. 37, *a*); but into the interior of the fasciculi themselves no trace of a vessel enters, any more than it does into the interior of the semi-lunar cartilages; there, on the contrary, we again meet with the network of cells we have been talking about, or, in other words, the peculiar system of juice-conveying canals of which we lately considered the import in bone.

Tendons may therefore in the first place be divided into larger (primary) bundles, and these in their turn into a certain number of smaller (secondary) fasciculi, which are separated by broadish bands of a fibrous substance containing vessels and fibre-cells, so that a transverse section of a tendon presents a meshed appearance. From this intervening substance, which must not, however, be regarded as a tissue of a peculiar description, there pass into the interior of the fasciculi stellate cells (*tendon-corpuscles*) which anastomose with another and establish a communication between the external vascular, and the internal non-vascular, parts of the fasciculi. This relation is, of course, much more evident in the tendons of children than in those of adults. The older the parts become, namely, the larger and finer do the processes of the cells in general become, so that in many sections we do not meet with the real bodies of the cells, but only see minute speck which, by altering the focus, may be traced into filaments—or point-like orifices. The individual cells, therefore, come to be more widely

Fig. 38.



separated, and it becomes more and more difficult to obtain a view of the whole of a cell at once. Besides, we must first obtain a clear notion of the relation between a longitudinal and a transverse section. Where, namely, in a longitudinal section, there are spindle-shaped cells, in a transverse section will be seen stellate ones, and to the network of cells displayed in the transverse section corresponds the regular succession of spindle-shaped corpuscles, arranged in rows which we see in a longitudiual section, entirely in correspondence with the plan which we have shown to be followed in connective tissue. The cells, therefore, are here also only apparently simply spindle-shaped, when an exactly longitudinal section is examined; but if it has been

Fig. 38. Transverse section from the interior of the tendo Achillis of a new-born child. *a*. The intervening mass which separates the secondary fasciculi (corresponding to Fig. 37, *c*), and entirely composed of densely aggregated spindle-shaped cells. Directly anastomosing with these, we see on both sides at *b*, *b*, reticulating and spindle-shaped cells running into the interior of the fasciculi. 300 diameters.

made a little obliquely, the lateral processes are perceived, by means of which the cells of one row communicate with those of another.

Fig. 39.

Up to the present moment the progress of the growth of tendons after birth has not been made the subject of a regular investigation, and it is unknown whether any further multiplication of the cells takes place in them; this much, however, is certain, that the cells in many places afterwards become much elongated, and the intervals between the individual nuclei extremely great. The actual structural relations, however, do not thereby experience any change; the original cells also continue members of the great system of tubes, which in the perfectly developed tendon pervades the whole tissue.

Fig. 39. Longitudinal section from the interior of the tendo Achillis of a newborn child. *a*, *a*, *a*. Intervening bands. *b*, *b*. Fasciculi. In both we see spindle-shaped, nucleated cells, partially anastomosing, with an inter-cellular substance slightly striated in a longitudinal direction, the cells being more crowded in the bands, and less numerous in the fasciculi. *c*. Section of an interstitial blood-vessel. 250 diameters.

Hence we see how, although the tendon contains no vessels in its most internal parts, and, as may be observed in every case of tenotomy, receives but little blood by the external vessels of its sheath, and by the internal vessels of the septa between the larger fasciculi, it is possible, notwithstanding, for a uniform nutrition of the parts to take place. This we cannot imagine to be effected in any other way than by the distribution of nutritive juices in a regular manner throughout the entire substance of the tendon by means of special canals distinguishable from the vessels. The natural divisions of the tendon are, however, nearly entirely symmetrical, so that an equally large quantity of intercellular substance falls to the share of every cellular element, and as the cell-networks in the interior can be directly traced into the dense bundles of cells of the septa, and these in their turn up to the vessels (Figs. 37, 38), we may, I think, unhesitatingly regard these reticulating cells as the channels for the transmission of this intermediate current of nutritive juice, which has no communication by means of orifices with the general circulation.

You have here a fresh instance in support of my view with regard to cell-territories. I would parcel out the whole tendon, not into primary and secondary fasciculi, but rather into certain series of cells connected in a retiform manner; to each series, moreover, I would assign a certain district of tissue, so that in a longitudinal section, for example, about half of each band of basis-substance would belong to one, the other half to another series of cells. What is, therefore, regarded as constituting the proper fasciculi of the tendon, would, according to this view, have really to be split up, and the tendon portioned out into a great number of nutritive districts (Ernährungs-Territorien).

This is the condition which we everywhere find recurring in these tissues, and upon it will at the same time be found to depend, as I hope you will convince yourselves by direct observation, the size of the districts invaded by disease; every disease which essentially depends upon a disturbance in the internal disposition of the tissues is always made up of the sum of the separate changes occurring in such territories. But at the same time the pictures which are here offered to us afford a really æsthetical enjoyment through the delicacy of this arrangement, and I cannot deny that, as often as I look at a section of tendon, it is with a peculiar feeling of satisfaction that I contemplate these reticular arrangements, which effect a union between the exterior and the interior, and, excepting in bone, can in no structure be demonstrated with greater distinctness and clearness than in tendons.

Considering the structure of the *cornea* and the disposition of its parts, it would be most convenient, gentlemen, to proceed at once to the consideration of its history, still I prefer reverting to it hereafter, inasmuch as it is at the same time the most suitable object for the demonstration of pathological changes. I will therefore only observe here, that in the same way that tendons have their peripheral system of vessels, and that their internal parts are nourished by a delicate juice-conveying system of tubes, so also in the cornea only the most minute vessels extend a few lines over its border, so that the central parts are completely destitute of vessels, as indeed they were obliged to be, in order to allow of the transparency of the tissue.

I should like, on the other hand, in connection with the foregoing tissues, to speak of one which has generally met with but little special preference in histology, but is perhaps more likely to have some interest in your eyes, I mean the *umbilical cord.* Its substance (the so-called jelly (gelatina) of Wharton*) is also formed by one of those tissues which certainly contain vessels, but yet really possess none. The vessels which are transmitted through the umbilical cord, do not immediately contribute to its nourishment, at least not in the sense in which we speak of nutrient vessels in other parts. For when we speak of nutrient vessels, we always mean vessels which have capillaries in the parts which are to be nourished. The thoracic aorta is not the nutrient vessel of the thorax, any more than the abdominal aorta, or the vena cava, is that of the abdominal viscera. We should expect, therefore, in the case of the umbilical cord to find umbilical capillaries in addition to the two umbilical arteries and the umbilical vein. But these arteries and this vein run their course to the placenta, without giving off a single small vessel, and it is only when they have reached that body that they begin to ramify. The only capillary vessels which are found in the whole length of the umbilical cord of a somewhat developed fœtus do not extend more than about four or five lines (in rare instances a little farther), beyond the abdominal walls into that part of the cord which remains after birth. The

Fig. 40.

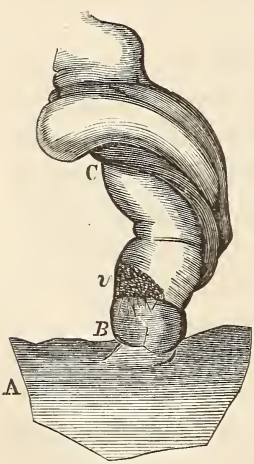


Fig. 40. The abdominal end of the umbilical cord of a nearly full-grown fœtus, injected. *A.* The abdominal wall. *B.* The permanent part of the cord with a congeries of injected vessels along its border. *C.* Its deciduous portion with the convolutions of the umbilical vessels. *v.* The limits of the capillaries.

* Lymphæductus, vel *gelatina, quæ eorum vices gerit,* alterum succum albumini ovorum similorem abducit (a placenta) ad funiculum umbilicalem. (Thom. Whart. Adenographia, Amstelædami, 1659, p. 233.)

farther up this vascular part extends, the greater the development of the navel. When the vascular layer is prolonged but a very short distance the navel is greatly depressed ; when it reaches a long way up, a prominent navel is the result. The capillaries mark the limits of the permanent tissue ; the deciduous portion of the cord has no vessels of its own.

This condition, which seems to be of great importance as regards the theory of nutrition, can be very easily seen with the naked eye in injected fœtuses of five months and upwards, and in new-born children. The vascular layer terminates by a nearly straight line.

Preparations of this sort do not, to be sure, furnish absolute proof, for there might happen to be a few minute vessels proceeding farther up, but invisible to the naked eye. But I formerly made this very point the subject of special investigation, and although I injected a number of umbilical cords, some from the arteries, and others from the veins, I never succeeded in discovering a single collateral vessel, however minute, that passed the limits of the persistent layer. The whole of the deciduous portion of the umbilical cord, that long portion which lies between its cutaneous end and its termination in the placenta, is entirely destitute of capillaries, and there really exist no other vessels in it than the three large trunks. Now these are all of them remarkable for the great thickness of their walls, which, as we have really only known since the investigations of Kölliker, are enormously rich in muscular fibres.

In a transverse section of the umbilical cord it may be observed, that the thick middle coat of the vessels is entirely composed of smooth muscular fibres, lying in immediate contact one with the other, and in such abundance as is scarcely to be seen in any completely developed vessel. This peculiarity explains the extraordinary great contractility of the umbilical vessels, which can be so readily seen in action on a large scale when mechanical stimuli are applied, when the vessels are divided with scissors or are pinched, or after the employment of electrical stimuli. Sometimes, upon the application of external stimuli, they even contract to such a degree that their canal is entirely closed, and thus after birth, even without the application of a ligature, as when, for example, the umbilical cord has been torn asunder, the bleeding may stop of itself. The thickness of the walls of these vessels is, therefore, easily comprehensible, for in addition to the muscular coat, which is of itself so thick, there is an internal, and, though it is certainly not very strongly developed, an external coat; and only after this do we come to the gelatinous, jelly-like tissue (*mucous tissue* (Schleimgewebe)) of the umbilical cord. Through these layers, therefore, nutrition would have to take place, if the umbilical vessels were the nutrient vessels of the cord. Now I certainly can-

FIG. 41.

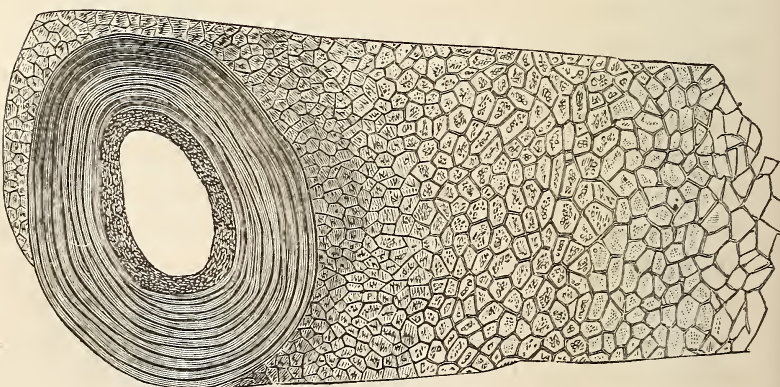
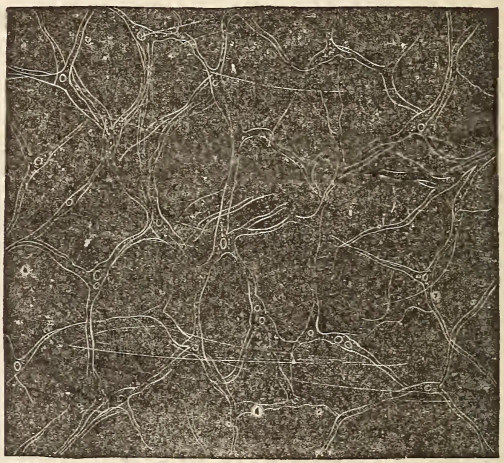


Fig. 41. Transverse section through a part of the umbilical cord. On the left is seen the section of an umbilical artery, with a very thick muscular coat, and to this, as one proceeds outwards, succeeds the gradually widening network of cells of the mucous tissue of the cord. 80 diameters.

not say with certainty whence the tissue of the umbilical cord derives its nourishment; perhaps it receives nutritive matter from the liquor amnii, nor am I inclined to deny the possibility of nutriments passing through the walls of the vessels, or of the onward conveyance of nutritive materials from the small capillaries of the persistent portion. In any case, however, a large extent of tissue lies at a distance from all vessels and from the surface, and is nourished and supported without the presence of any minute system of blood-vessels in it. For a long space of time, indeed, no one troubled himself any further about this tissue, because it was designated by the name of jelly, and thereby summarily ejected from the number of the tissues and thrust into the ambiguous group of mere accumulations of organic materials. I was the first to show that it is really a well-constructed tissue of a typical form, and that what constitutes the jelly in the more restricted sense of the term, is the expressible part of the intercellular substance, after the removal of which there remains a tissue containing a delicate network of anastomosing cellular elements, similar to that which we have seen to exist in tendons and other parts. A section through the external layers of the umbilical cord exhibits a structure bearing great resemblance to the external layers of the cornea; first, an epidermoidal stratum, beneath it a somewhat denser dermoid layer, and then the Whartonian jelly, which corresponds in texture to the subcutaneous cellular tissue, and is in some sort equivalent to it. This has a peculiarly interesting bearing upon the tissues of a more advanced period, inasmuch as, by thus ranking the jelly with subcutaneous tissue, we at the same time establish its very close relationship to the *vitreous body*, which is the only remnant of tissue that, as far as I have until now been able to make out, persists in man in this condition of jelly. It is the last remnant of the embryonic subcutaneous tissue which in the development of the eye is inverted with the lens (which was originally epidermis, p. 38).

The proper substance of the umbilical cord consists of a reticulated tissue, the meshes of which contain mucus (mucin) and a few roundish cells, whilst its trabeculæ are composed of a striated fibrous substance. In this lie stellate corpuscles, and when a good preparation has been obtained by treatment with acetic acid, a symmetrical network of cells is brought to view, which splits up the mass into such regular divisions, that by means of the anastomoses which subsist between these cells throughout the whole of the umbilical cord, a uniform

Fig. 42.



distribution of the nutritive juices throughout the whole of its substance is in this instance also rendered possible.

Fig. 42. Transverse section of the mucous tissue of the umbilical cord, exhibiting the network formed by the stellate corpuscles, after the application of acetic acid and glycerine. 300 diameters.

I have up to the present time, gentlemen, brought to your notice a series of tissues all of which agree in containing either very few capillary vessels, or none at all. In all these cases the conclusion to be drawn seems to be very simple—that, namely, the peculiar cellular, canalicular arrangement which they possess serves for the circulation of juices. It might, however, be supposed that this was an exceptional property, appertaining only to the non- or scantily-vascular and, generally speaking, hard, parts ; and I must therefore add a few words concerning the soft textures which possess a similar structure. All the tissues which we have hitherto considered, belong, in accordance with the classification which I have already given you, to the series of connective tissues ; fibro-cartilage, fibrous or tendinous tissue, mucous tissue, bone and the teeth, must one and all be considered as belonging to the same class. But to the same category belongs also the whole mass of what has usually been included under the name of *cellular tissue* (Zellgewebe), and for which the name proposed by Johannes Müller, *connective tissue* (Bindegewebe) is the most appropriate ; that substance, which fills up the interstices in the most different organs, sometimes in greater, sometimes in less, quantity—which renders the gliding of parts one upon the other possible, and formerly was imagined to enclose considerable spaces (cells in an inexact sense of the word), filled with a gaseous vapor or with moisture.

Of this kind is the peculiar interstitial, or connective, tissue, such as we meet with in the interior of the larger muscles between the several primitive fasciculi and in a still larger quantity between the several parcels, or bundles, of primitive fasciculi. Numerous arteries, veins, and capillaries lie in it ; and the arrangements for its nutrition are the most favorable that can be imagined. Notwithstanding this, however, there exists in it also, in addition to its blood-vessels, a more delicate system of nutrient channels, precisely similar to that with which we have just become acquainted ; only that, wherever it is specially required, in particular parts a peculiar change takes place in the cells, the place of the simple cell-networks and -fibres being gradually occupied by a more compact structure, which originates in a direct transformation of them, namely, the so-called *elastic tissue*.

A few months after I had made known my first observations concerning the systems of tubes existing in the connective tissues, Donders published his concerning the transformation of the cells of connective, into the elements of elastic, tissue—a discovery which has essentially contributed to the completion of the history of connective tissue. If this tissue, namely, be examined at points where it is liable to be much stretched, and where consequently it must be endowed with great power of resistance, the elastic fibres will be found arranged and distributed in it in the same way that the cells and

Fig. 43.

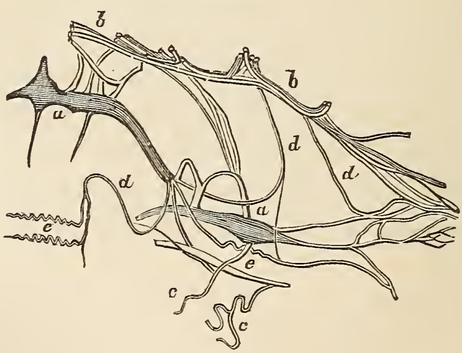


Fig. 43. Elastic networks and fibres from the subcutaneous tissue of the abdomen of a woman. *a*, *a*. Large elastic bodies (cell-bodies), with numerous anastomosing processes. *b*, *b*. Dense elastic bands of fibres, on the border of larger meshes. *c*, *c*. Moderately thick fibres, spirally coiled up at the end. *d*, *d*. Finer elastic fibres, at *e* with more minute spiral coils. 300 diameters.

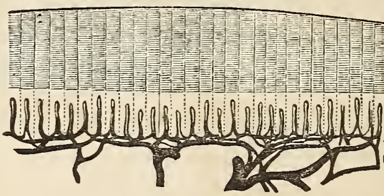
cell-tubules of connective tissue usually are, and the transformation of these latter into the former can gradually be traced with such distinctness, that there remains no doubt, that even the coarser elastic fibres directly result from a chemical change and condensation of the walls of the cells themselves. Where originally there lay a cell, provided with a delicate membrane and elongated processes, there we see the membrane gradually increasing in thickness and refracting the light more strongly, whilst the proper cell-contents continually decrease and finally disappear. The whole structure becomes in this way more homogeneous, and to a certain extent sclerotic, and acquires an incredible power of resisting the influence of reagents, so that it is only after long-continued action that even the strongest caustic substances are able to destroy it, whilst it completely resists the caustic alkalies and acids in the degree of concentration usually employed in microscopical investigations. The farther this change advances, the more does the elasticity of the parts increase, and in sections we usually find these fibres not straight or elongated, but tortuous, curled up, spirally coiled, or forming little zigzags (Fig. 43, *c*, *e*). These are the elements which in virtue of their great elasticity cause retraction in those parts in which they are found in considerable quantity, as, for example, in the arteries. The fine elastic fibres, which are those that possess the greatest extensibility, are usually distinguished from the broader ones which certainly do not present themselves in tortuous forms. As far as regards their origin, however, there seems to be no difference between the two kinds ; both are derived from connective-tissue cells, and their subsequent arrangement is only a reproduction of the original plan. In the place of a tissue, consisting of a basis-substance and anastomosing, reticulated cells, there afterwards arises a tissue with its basis-substance mapped out by large elastic networks with extremely compact and tough fibres.

It has not up to the present time positively been determined, whether in the course of this transformation the condensation (sclerosis) of the walls of the cells proceeds to such a pitch as entirely to obliterate their cavity, and thus completely destroy their powers of conduction, or whether a small cavity remains in their interior. In transverse sections of fine elastic fibres, it looks as if the latter were the case, and there is therefore ground for the supposition, that in the transformation of the corpuscles of connective tissue into elastic fibres, nothing more than a condensation and thickening, and at the same time a chemical metamorphosis of the membrane, takes place, but that ultimately, however, a very small portion of the cell-cavity remains. What sort of a substance it is that constitutes the elastic parts, has not been determined, because it is not possible to accomplish their solution by any means; with a part of the products of the decomposition of this tissue we are, indeed, acquainted, but nothing further is known concerning its chemical constitution. But from this no decision can be arrived at with respect either to its composition, or position in a chemical point of view with regard to other tissues.

This kind of transformation prevails to an extraordinary extent in the skin, especially in the deeper layers of the corium proper, and to it is chiefly owing the extraordinary resistance of this tissue which we so gratefully acknowledge when daily testing it in the soles of our shoes. For the firmness of the individual layers of the skin depends essentially upon the greater or less quantity of elastic fibres contained in them. The most superficial part of the corium immediately beneath the rete mucosum is formed by the papillary portion (Papillarkörper), by which we are to understand not only the papillæ themselves, but also a continuous layer of coriaceous substance running along horizontally beneath them ; it is under this that the coarse elastic networks begin, whilst only fine elastic fibres, and these in a fascicular form, ascend into the papillæ themselves, at the base of which they begin to form fine and close-meshed networks (Figs. 16, *P*, *P;* 83, *A*, *e;* *D*, *c*). These latter are connected inferiorly with the very thick and coarse elastic network which pervades the middle and toughest portion of the skin, the *corium* proper ; below this comes a more coarsely meshed network within the less firm, but nevertheless very solid, undermost layer of the cutis, which passes inferiorly into the adipose or subcutaneous tissue.

In the places where such a transformation into elastic tissue has taken place, there are frequently scarcely any distinct cells to be found. This is the case not merely in the skin, but also especially in certain parts of the middle coat of arteries, and particularly in the aorta. Here the network of elastic fibres attains such a preponderance, that it is only with great care that minute cellular elements can here and there be detected. In the skin, on the other hand, in addition to the elastic fibres, a somewhat greater number of small corpuscles are found, which have retained their cellular nature, though they are certainly so extremely minute that they must be specially sought for. They generally lie in the interstices of the large-meshed networks, where they either form a system with perfect anastomoses and small meshes, or else appear in the shape of more isolated, roundish bodies, in consequence of the individual cells not being very distinctly connected with one another. This is especially the case in the papillary portion of the skin, which both in its continuous layer and in the papillæ contains nucleated cells, in direct contrast with the corium proper, which at the same time is less vascular. But a far greater number of vessels was certainly needed in the former part, inasmuch as they have at the same time to furnish nutritive material for the whole

Fig. 44.



stratum of cuticle which lies above the papillæ ; nevertheless, however, there is left only a small quantity of juice at the disposition of the papillæ as such. Every papillæ, therefore corresponds to a certain (vascular) district of the superjacent cuticle, whilst on the other hand it is itself resolved into as many elementary (histological) districts as there are elements (cells) in it.

In the scrotum the subcutaneous tissue (the *dartos*) presents peculiar interest, from the fact of its being particularly rich in vessels and nerves, quite in accordance with the peculiar import of the part ; and besides from its possessing an enormous quantity of muscular tissue, consisting, in fact, of those little cutaneous muscles, which I lately described to you (p. 58). These are the really active elements of the contractile tunica dartos. In this very part in which formerly a contractile connective substance was considered to exist, the quantity of the little cutaneous muscles is extremely large, and the

Fig. 44. Vertical section from an injected preparation of the skin. *E.* Epidermis. *R.* Rete mucosum. *P.* Papillæ of the skin, with their ascending and descending vessels (loops). *C.* Cutis. 11 diameters.

rugæ of the scrotum are produced solely and exclusively by the contraction of these minute fasciculi, which, especially after they have been coloured with carmine, can very easily be distinguished from the connective tissue.

FIG. 45.

They are of pretty nearly the same breadth, broader for the most part than the bundles of connective tissue ; and in them the individual elements are arranged in the shape of long, smooth fibre-cells. Every muscular fasciculus, after it has been treated with acetic acid, presents at regular intervals those peculiar, long, frequently

Fig. 45. Section from the tunica dartos of the scrotum. Side by side and parallel are seen, an artery (*a*), a vein (*v*), and a nerve (*n*) ; the first two with small branches. On the right and left of them organic muscular fasciculi (*m*, *m*), and in the interspaces soft connective tissue (*c*, *c*), with large anastomosing cells and fine elastic fibres. 300 diameters.

staff-shaped nuclei, and between them is seen a delicate division of the substance into separate cells, the contents of which have a slightly granular appearance. These are the wrinklers of the scrotum (*corrugatores scroti*). Besides, we also find in the extremely soft membrane a certain number of fine elastic elements, and in greater quantity the ordinary, soft, wavy connective tissue, with a great number of relatively voluminous, spindle-shaped and reticulated, granular, nucleated, cells.

These persistent cells of connective tissue had previously been totally overlooked, its fibrils having been regarded as its real elements. If, namely, the individual constituents of connective tissue be separated from one another, little bundles are obtained of a wavy form and streaky, fibrillar appearance. According to Reichert, indeed, this appearance is merely due to the formation of folds, an idea which ought not perhaps to be admitted to the extent in which it was advanced, but which has not been altogether refuted, inasmuch as a complete isolation of the fibrils can never be effected excepting by artificial means. At all events a homogeneous basis-substance, which holds the fasciculi together, must be assumed to exist in addition to the fibrils. This, however, is a question of subordinate importance. On the other hand, it is extremely important to know, that wherever this lax tissue is met with, whether beneath the cutis, in the interspaces of muscle, or in serous membranes, it is pervaded by cells which for the most part anastomose (so as in longitudinal sections to form parallel rows, in transverse ones networks), and separate the bundles of connective tissue from one another, in much the same way that the corpuscles of bone separate its different lamellæ. In addition, the most manifold vascular connections are everywhere met with ; indeed, the vessels are so numerous, that a special nutrient canalicular system in the tissue might even appear altogether unnecessary. But this tissue also, however favourably its capillary channels may be disposed, stands in need of an arrangement of such a nature as to render *a special distribution of the nutritive juices to the separate cellular districts possible.* It is only when we conceive the absorption of nutritive matter to be a consequence of the activity (attraction) of the elements of the tissue themselves, that we are able to comprehend how it is that the individual districts are not exposed every moment to an inundation on the part of the blood, but the proffered material is, on the contrary, taken up into the parts only in accordance with the requirements of the moment, and is conveyed to the individual districts in such a quantity, that in general at least, as long as any possibility of its maintenance exists, one part cannot be essentially defrauded by the others.

LECTURE VI.

MARCH 3, 1858.

NUTRITION AND CIRCULATION.

Arteries—Capillaries—Continuity of their membrane—Its porosity—Hæmorrhage by transudation (per diapedesin)—Veins—Vessels during pregnancy.

Properties of the walls of vessels:

1. Contractility—Rhythmical movement—Active or irritative hyperæmia—Ischæmia—Counter irritants.
2. Elasticity and its importance as regards the rapidity and uniformity of the current of blood—Dilatation of the vessels.
3. Permeability—Diffusion—Specific affinities—Relations between the supply of blood and nutrition—Glandular secretion (liver)—Specific action of the elements of the tissues.

Dyscrasia—Its transitory character and local origin—Dyscrasia of drunkards—Hæmorrhagic diathesis—Syphilis.

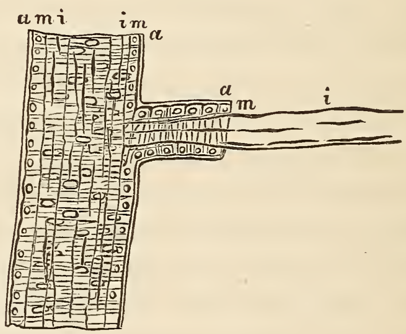
I HAVE endeavoured, gentlemen, in the last two lectures, to present to you a somewhat detailed picture of the more delicate arrangements which prevail in the body for the conveyance of the different currents of nutritive juices, and particularly for the conveyance of those currents in which the juices themselves are more hidden from observation. Allow me to-day to pass on to the consideration of the larger channels and nobler juices, which, according to prevailing opinion, stand more in the foreground.

The distribution of the blood takes place, as is well known, within the vessels in the following manner: The arteries divide into finer and finer branches, and whilst they thus divide, the character of their walls gradually undergoes such alterations, that at last minute canals, the so-called capillary vessels, appear, provided with a membrane as simple as any that is ever met with in the body. The histological appearances which present themselves in these different vessels are as follows:

On isolating an *artery* we find that its walls are relatively very thick, and in those arteries which can be followed with the naked eye, not only the well-known three coats are distinguished with the help of the microscope, but in addition to these, a fine epithelial layer, which invests the internal surface and is not wont to be included in the class of structures usually termed coats The internal and external coats are essentially formations of connective tissue, which in the larger arteries display a continually increasing quantity of elastic fibres; between them lies the relatively thick middle, or circular-fibre, coat, which, as being the seat of the muscular fibres, constitutes what may be almost termed the most important component of the arterial walls. These muscular fibres are found in the greatest abundance in the middle-sized and smaller arteries, whilst in the very large ones, and especially in the aorta, elastic layers form the predominant constituent even of the circular-fibre coat. In small arteries, on microscopical examination, there may be easily observed within this coat (Comp. Figs. 26, *b*, *b*; 45, *a*) little transverse striations, corresponding to the individual fibre-cells, and encircling the vessel in such dense array that we find fibre-cell by the side of fibre-cell without any interruption. The thickness of this layer can be readily estimated in consequence of the well-marked limits set to it upon the in- and out-side by the longitudinal-fibre coats; the only deceptive appearance is presented by certain round bodies, which are to be seen here and there in the substance of the circular-fibre coat, but only at the border of the vessel (Figs. 26, *b*, *b*; 46 ,*m*, *m*), and which look like round cells or nuclei scattered through the tissue. These are fibre-cells seen in apparent transverse section. The layer formed by the middle coat may be most distinctly seen, however, after the addition of acetic acid, which causes the appearance of a great number of oblong nuclei.

It is this layer which, generally speaking, confers upon the arteries their specific character, and distinguishes them most clearly from the veins. There are, indeed, numerous veins in the body which possess considerable layers of muscular tissue—for example, the superficial cutaneous veins ; still, in the case of the smaller vessels, the occurrence of a distinctly marked circular-fibre coat

Fig. 46.



is so peculiarly characteristic of arterial vessels, that, wherever we meet with such a structure, we are at once inclined to assume the vessel to be arterial.

These vessels, which must be included among the

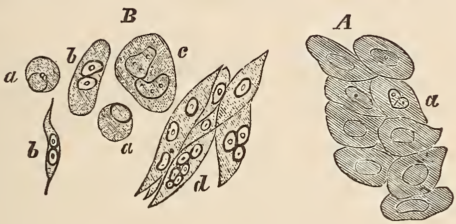
Fig. 46. A minute artery from the sheath of the tendon of one of the extensors of a hand just amputated. *a*, *a*. External coat. *m*, *m*. Middle coat, with well-developed muscular layer. *i*, *i*. Internal coat, partly with longitudinal folds, partly with longitudinal nuclei, in the side-branch brought well into view in consequence of the two external coats having been torn away. 300 diameters.

larger ones, although even when full of blood they only appear to the naked eye like red filaments, pass gradually into smaller ones, and with a power magnifying three hundred diameters, we see them breaking up into branches, into which, even when they are very small, the three coats are at first continued. It is only in the smallest branches that the muscular coat finally disappears, the intervals between the individual transverse fibres becoming wider and wider, and the internal coat (the nuclei of which lie in a longitudinal direction and cross those of the middle coat at right angles (Fig. 26, *D*, *E*,)), at the same time appearing more and more distinctly through it. The external coat also may be followed for a short distance farther (being in many places, as in the brain, rendered more evident by the interspersion of pigment or fat, Fig. 26, *D*, *E*), till at last it also becomes lost to view, and only a simple capillary remains (Fig. 3, *c*). The general supposition, therefore, is that the proper capillary membrane most nearly corresponds to the internal coat of the larger vessels, and it is usually considered that the more complete a vessel becomes, the greater is the number of the coats which develop themselves around it. The real developmental relations which these parts bear to one another have, however, been by no means accurately determined.

Within the true *capillary* region there is nothing further worthy of notice in the vessels than the nuclei I have previously mentioned, which correspond to the longitudinal axis of the vessel, and are so imbedded in its membrane, that it is impossible to discover any traces of a surrounding cell-wall. The capillary membrane is seen to be quite uniform, absolutely homogeneous and continuous (Fig. 3, *c*). Whilst even as lately as twenty years ago, it was a matter of discussion whether there did not exist vessels which were destitute of true walls, and were nothing more than channellings or excavations in the parenchyma of organs, as well as whether vessels could not be produced by the formation of new tracks in communication with the old channels by the forcing asunder of the neighboring parenchyma ; there can, at the present time, be no longer any doubt as to the vascular system's being everywhere continuously closed by membranes. In these it is not possible to descry any porosity. Even the minute pores, which have recently been observed in different parts, have not, up to the present time, met with their counterparts in the capillary membrane, and when the porosity of this membrane is spoken of, the expression can only be admitted in a physical sense, as applying to invisible, really molecular interstices. A film of collodion is not more homogeneous, nor more continuous, than the membrane of a capillary. A series of possibilities, which used to be admitted, as that, for example, the continuity of the capillary membrane did not exist at certain points, simply fall to the ground. A "transudation" or diapedesis of the blood through the walls of vessels without the occurrence of any rupture cannot for an instant be admitted ; and although we cannot in every individual case point out the exact site of the rupture, it is, notwithstanding, quite inconceivable that the blood with its corpuscles should be able to pass through the walls in any other way than through a hole in them. This is such a very natural deduction from ascertained histological facts, that all discussion upon the point is impossible.

After the capillaries have pursued their course for a time, small veins begin gradually to form out of them, and generally run back in the neighbourhood of the arteries (Fig. 45, *v*). In them the characteristic circular-fibre coat of the arteries is in general wanting, or at least it is very much less developed. In its place we find in the middle coat of the larger veins toughish layers, which are not characterized so much by the absence of muscular elements as by the greater abundance of elastic elements which run in a longitudinal direction and are found in greater or less quantity in different localities.

FIG. 47.



In an inward direction there follow next the softer and more delicate layers of connective tissue of the internal

FIG. 48.

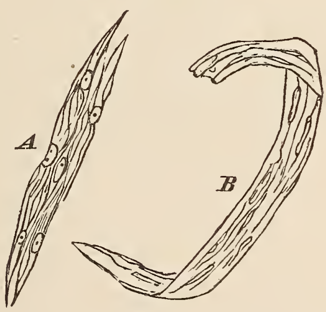


Fig. 47. *A*. Epithelium from the femoral artery ('Archiv f. path. Anat.,' vol. iii., figs. 9 and 12, p. 596). *a*. Division of nucleus.

B. Epithelium from veins of considerable size. *a*, *a*. Largish, granular, round, uni-nuclear cells (colourless blood-corpuscles?) *b*, *b*. Oblong and spindle-shaped cells, with divided nuclei and nucleoli. *c*. Large, flat cells, with two nuclei, of which each has three nucleoli, and is in process of division. *d*. Coherent epithelium, with the nuclei in a state of progressive division, one cell having six nuclei. 320 diameters.

Fig. 48. Epithelium from the vessels of the kidney. *A*. Flat, spindle-shaped cells with longitudinal folds and large nuclei from a new-born child. *B*. Ribbon-like, nearly homogeneous, plate of epithelium with longitudinal nuclei from an adult. 350 diameters.

coat, and lying on this is found, in the last place, a flat, extremely translucent layer of epithelium, which is very prone to protrude out of the cut end of the vessel, and gives the impression of spindle-shaped cells, so that it may easily be mistaken for spindle-shaped muscular cells. The smallest veins likewise possess this epithelium, but, with this exception, are, properly speaking, entirely composed of connective tissue provided with longitudinal nuclei (Fig. 45, *v*).

These relations undergo no essential change even when the individual constituents of the vascular system experience the most extreme enlargement. This is best seen in *pregnancy*, in which not merely in the uterus, but also in the vagina, the Fallopian tubes, the ovaries, and the ligaments of the uturus, both the large and small arteries and veins, as well as the capillaries, exhibit a very high degree of dilatation, so that the rest of the tissue, in spite of its having likewise in no inconsiderable degree become enlarged, is thereby virtually thrust into the background. Nevertheless, however, parts of this puerperal sexual apparatus are extremely well adapted for displaying the relation between the histological elements and the *vascular* (arterial) districts. In the fimbriæ of the Fallopian tubes, for example, every plexus or loop formed towards the borders by the greatly dilated capillaries encloses a certain number of large connective tissue cells, of which only a few lie in immediate contact with the vessels. In the alæ vespertilionum we find, moreover, very beautifully displayed, a condition which is of frequent occurrence in the appendages of the generative organs, and similar to what we lately considered in the scrotum ; the vessels, namely, are accompanied by flat bundles of smooth muscle in considerable quantity which do not belong to them, but only follow the course of the vessels, and in part receive the vessels into them. This is an extremely important feature, inasmuch as the contraction of these ligaments, in which muscular tissue is not generally considered to exist, is by no means solely to be ascribed to the blood-vessels, as James Traer only a short time ago endeavoured to establish; on the contrary, we find thickish, flat bundles of muscle which run through the middle of the ligaments, and during menstrual excitement enable contractions to take place, similar to those which we can follow with such great distinctness in external portions of the genital passages.

If now the question be raised how far the individual elements of the vessels are of importance in the body, it is at once evident that the contractile elements play the most important part in the coarser processes of the circulation, whilst the elastic constituents come next, and the simply permeable, homogeneous membranes last. Let us first consider the import of the *muscular elements*, and more particularly in those vessels which are chiefly provided with them, namely the arteries.

When an artery is acted upon by any influence which causes a contraction of its muscular tissue, it must of course become narrower, inasmuch as the contractile cells lie in rings around the vessel; this contraction may under certain circumstances proceed until the canal is almost entirely obliterated, and the natural consequence then is that less blood penetrates into the corresponding part of the body. When, therefore, an artery is in any way exposed to a pathological irritant, or when it is excited by some physiological stimulus, its proper action cannot be displayed in any other way than by its becoming narrower. Now, indeed, that the muscular elements of the walls of the vessels have become known, the old doctrine might again be taken up, that, namely, the vessels, like the heart, originated a kind of rhythmical pulsating movement, which was capable of directly furthering the onward movement of the blood, so that an arterial hyperæmia would be the result of an increased pulsation in the vessels.

We are indeed acquainted with one isolated fact which is a proof that a real rhythmical movement does take place in the arterial walls ; and this was first observed by Schiff in the ears of rabbits. Its rhythm, however, does not at all correspond with that of the well-known arterial pulsation ; the only counterpart to it exists in the movements which had previously been observed by Wharton Jones in the veins of the wings of bats, and proceed in an extremely slow and quiet manner. I have studied these phenomena in bats, and convinced myself that the rhythm coincindes neither with the cardiac nor the respiratory movements ; it is quite a peculiar, but comparatively not very forcible, movement, and takes place after tolerably long pauses, longer ones than are observed in the case of the circulation and shorter than those which occur in respiration. In the ears of rabbits, also, the contractions of the arteries are far slower than the cardiac and respiratory movements.

After excluding these phenomena, which manifestly ought not to be explained in such a way as to support the old view of the local occurrence of pulsation, the essential fact remains, that the muscular fibres of a vessel contract upon the application of every stimulus which sets them in action, but that this contraction is not propagated in a peristaltic manner, but is confined to the spot irritated, or, at most, extends a little beyond, and continues for a certain length of time at this spot. The more muscular the vessel is, the more lasting and forcible is the contraction and the greater is the obstruction experienced by the current of blood. The smaller the vessels, the more rapidly, on the contrary, do we see the contraction succeeded by a dilatation, which, however, is not in its turn followed by a contraction, as it would have to be to constitute a pulsation, but persists for a longer or shorter time. This dilatation is not of an active, but of a passive nature, and results from the pressure of the blood upon the wall of the vessel which has become fatigued and opposes less resistance.

If we now proceed to examine the phenomena which

Fig. 49.

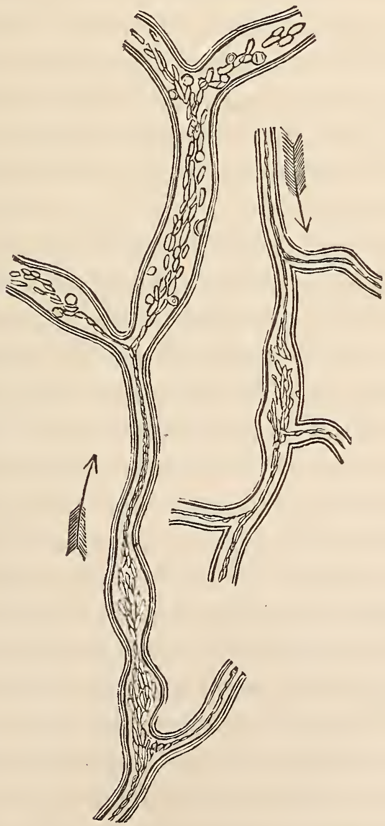


Fig. 49. Irregular contraction of small vessels from the web of a frog's foot after the application of stimuli. Copied from Wharton Jones.

are usually grouped together under the title of active hyperæmia, there can be no doubt but that the muscular tissue of the arteries is generally essentially concerned therein. We very commonly find we have to deal with processes in which the muscular fibres of the vessels have really been stimulated, and the contraction is succeeded by a state of relaxation, such as scarcely ever occurs in an equally marked manner in the rest of the muscles—a state which is manifestly the expression of a kind of fatigue and exhaustion, and is the longer persistent, the more energetic the stimulus which was applied. In small vessels with few muscular fibres, therefore, it often seems as if the stimuli really induced no contraction, in consequence of the extreme rapidity with which a state of relaxation is seen to set in, continuing for a considerable time, and allowing of an increased influx of blood.

This same condition of relaxation we can experimentally most easily produce by cutting the nerves supplying the vessels of a part, whilst the contraction can be effected to a very great extent by submitting these nerves to a very energetic stimulus. That our acquaintance with this kind of contraction is of so late a date, is explained by the fact that the stimuli applied to the nerves must be very powerful, and that, as Claude Bernard has shown, only strong electric currents are sufficient for the purpose. On the other hand, the conditions which ensue upon the section of the nerves are in most parts so complicated, that the dilatation escaped observation, until the lucky spot was discovered also by Bernard, and by the section of the sympathetic nerves in the neck a reliable and convenient field for observation was thrown open to experiment.

We obtain therefore the important fact that, whether the widening of the vessel, or, in other words, the relaxation of its muscular fibres, be produced directly by a paralysis of the nerve or an interruption of the nervous influence, or whether it be the indirect result of a previous stimulation, giving rise to exhaustion—that, I say, in every case we have to deal with a kind of paralysis of the walls of the vessel, and that the process is incorrectly designated active hyperæmia, inasmuch as the condition of the vessels in it is always a completely passive one. All that has been built up upon this assumed activity of the vessels, is, if not exactly built upon sand, still of an extremely ambiguous nature, and all the conclusions that have besides been drawn with regard to the important influence which the activity of the vessels was supposed to have upon the conditions of nutrition of the parts themselves, fall at the same time to the ground.

When an artery is really in action, it gives rise to no hyperæmia; the more powerfully it acts, the more does it occasion anæmia, or, as I have designated it, *ischæmia*, and the less or greater degree of activity in the artery determines the greater or less quantity of blood which in a unit of time can stream into a given part. *The more active the vessel, the less the supply of blood.* If, then, we have to deal with an hyperæmia the result of irritation, the most important point, therapeutically, is just this: to place the vessels in such a state of activity as will enable them to offer resistance to the onward rush of blood. This we can accomplish by means of what is called counter-irritation, a higher degree of irritation in an already irritated part, stimulating the fatigued muscular fibres of the vessel to persistent contraction, and thereby diminishing the supply of blood and leading the way to a regulation of the disturbance. In the very cases in which reaction, that is, regulatory activity, is most called for, the chief point is to overcome that state of passiveness which maintains the (so-called active) hyperæmia.

If we now pass from the muscular to the *elastic* constituents of the vessels, we meet with a property which is of very great importance, on the one hand in the veins, the activity of which is in many cases to be wholly referred to their elastic elements, on the other hand, in the arteries, and particularly in the aorta and its larger branches. In these the elasticity of the walls has the effect of compensating for the loss which the pressure of the blood experiences from the systolic dilatation of the vessels, and of converting the uneven current produced by the jerking movements of the heart into an even one. If the walls of the vessels were not elastic, the stream of the blood would unquestionably be rendered very much slower, and at the same time, pulsation would take place throughout the whole extent of the vascular apparatus as far as the capillaries, for the same jerking movement which is communicated to the blood at the commencement of the aortic system would continue even into the smallest ramifications. But every observation we make in living animals teaches us that within the capillaries the stream is a continuous one. This equable onward movement is effected by the elasticity of the walls of the arteries, in virtue of which they return the impulse which they receive from the in-rushing blood with the same force, and by this means maintain a regular onflow of the blood during the time occupied by the following diastole of the heart.

If the elasticity of the vessel be considerably diminished, without its becoming stiff and immoveable (from calcareous incrustations) in the same degree, the dilatation, which it undergoes from the pressure of the blood, is not again compensated; the vessel remains in a dilated condition, and thus are gradually produced the well-known forms of *ecstasis*, such as we are familiar with in the arteries under the name of aneurysms, and in the veins under that of varices. In these processes, we have not so much, as has been represented of late, to deal with primary disease of the inner coat, as with changes which are situated in the elastic and muscular middle coat.

If therefore it is the muscular elements of the arteries that have the most important influence upon the quantity of blood to be distributed, and the mode of its distribution, in the several organs, and the elastic elements that are chiefly concerned in the production of a rapid and equable stream, they nevertheless exercise only an indirect influence upon the nutrition of the parts which lie outside the vessels themselves, and in this matter, we are obliged to betake ourselves, as a last resource, to the *simple, homogeneous membrane of the capillaries*, without which indeed not even the constituents of the walls of the larger vessels provided with vasa vasorum would be able to maintain themselves for any lengthened period. The difficulty which here presents itself has, as you know, during the last ten years, been chiefly got over by the assumption of the existence of *diffusive currents* (endosmosis and exosmosis) between the contents of the vessels and the fluid in the tissues ; and by regarding the capillary wall as a more or less indifferent membrane, forming merely a partition between two fluids, which enter into a reciprocal relation with one another ; while the nature of this relation would be essentially determined by the state of concentration they are in and their chemical composition, so that, according as the internal or the external fluid was the more concentrated, the diffusive stream would run inwardly or outwardly, and, according to the chemical peculiarities of the individual juices, certain modifications would arise in these currents. Generally speaking, however, the chemical side of this question has been but little regarded.

It cannot be denied that there are certain facts which cannot well be explained in any other manner, especially in cases where essential alterations have taken place in the state of concentration of the juices, for example, in that form of cataract which Kunde has artificially produced in frogs by the introduction of salt into their intestinal canal or subcutaneous cellular tissue. But in proportion as, after a physical study of the phenomena of diffusion, the conviction has been acquired that the membrane which separates the fluids is not an indifferent substance, but that its nature exercises a directly controlling influence upon the permeating powers of the fluids, it becomes impossible that a like influence should be denied the capillary membrane. We must not, however, go so far, as to ascribe to this membrane all the peculiarities observable in the interchange of material, and so explain how it happens, that certain matters which enter into the composition of the blood are not distributed in equal proportion to every part, but leave the vessels at some points in greater, at others in less, quantity, and at others not at all. These peculiarities depend, manifestly, on the one hand, upon the different degrees of pressure to which the column of blood is subjected in certain parts, and, on the other, upon special preperties of the tissues ; and we are irresistibly compelled, both by the consideration of simply pathological, and particularly by that of pharmaco-dynamical, phenomena to admit that there are certain *affinities* existing between definite tissues and definite substances, which must be referred to peculiarities of chemical constitution, in virtue of which certain parts are enabled in a greater degree than others to attract certain substances from the neighbouring blood.

If we consider the possibility of such attraction with a little more attention, it is peculiarly interesting to observe the behaviour of parts, which are at a certain distance from the vessel. If we apply a definite stimulus, for example, a chemical substance, a small quantity of an alkali I will suppose, directly to any part, we see that this shortly afterwards takes up more nutritive matter, so that even in a few hours its size becomes considerably increased, and that, whilst before we were perhaps scarcely able to distinguish anything in its interior, we now find an abundant, relatively opaque material within it, in no wise composed of alkali which had made its way in, but essentially containing substances of an albuminous nature. Observation shows that the process in all vascular parts begins with hyperæmia, so that the idea readily presents itself that the hyperæmia is the essential and determining cause. But if we investigate the matter more minutely, we find it difficult to understand how the blood, which is in the hyperæmic vessels, can contrive only to act just upon the irritated part, whilst other parts lying in the immediate vicinity are not affected in the same manner. In all cases in which the vessels are the immediate originators of disturbances which take place in a tissue, these are most marked in the immediate neighbourhood of the vessels and in the district which they supply (vascular (or vessel-) territory). If we introduce an irritating, as, for example, a decomposing body into a blood-vessel, a fact that has been established by me upon a large scale when tracing out the history of embolia, we by no means see that the parts at a distance from the vessel are the principal seats of active change, but that this is in the first instance manifested in the wall of the vessel itself and then in the adjoining histological elements. But if we apply the stimulus directly to the tissue, the central point of the disturbance will always continue to be that at which the stimulus produced its effect, just the same whether there are vessels in the neighbourhood or not.

We shall hereafter have occasion to return to this subject, and my only object here was to lay this fact before you in its general features, and thus repel the ordinary conclusion, which is as convenient as it is fallacious, that hyperæmia (in itself passive) exercises a directly regulating influence upon the nutrition of tissues.

If a special proof were still required in order to complete the refutation of this assumption, which in an anatomical point of view is utterly untenable, we find a most apposite argument in the experiment above mentioned of the section of the sympathetic. In an animal the sympathetic may be divided in the neck ; thereupon a state of hyperæmia ensues in the whole of that half of the head, the ears become dark red, the vessels greatly dilated, the conjunctiva and nasal mucous membrane turgidly injected. This may continue for days, weeks, or months, without the least appreciable nutritive disturbance necessarily arising therefrom; the parts, although gorged with blood, are yet, as far at least as we are at present able to judge of this, in the same state of nutrition as before. If we apply stimuli sufficient to produce inflammation to these parts, the only thing that we remark is, that the inflammation runs its course more quickly, without exhibiting either in itself or in the nature of its products anything essentially unusual.

The greater or less quantity of blood, therefore, which flows through a part is not to be regarded as the only cause of the changes in its nutrition. There is, I suppose, no doubt that, when a part, which is in a state of irritation, receives more blood than usual, it is also able to attract a larger quantity of material from the blood with greater readiness than it otherwise would have done, or than it would be able to do, if the vessels were in a state of contraction or less filled with blood. If, therefore, it were to be objected to my view that in such conditions the most favorable effects are often produced by local abstractions of blood, this would be no proof of its incorrectness. If we cut off or diminish the supply of nutritive matter, we must, of course, prevent the part from absorbing more than its wont, but, *vice versâ*, we cannot by offering it a larger quantity of nutritive material straightway compel it to take up more than it did; these are two entirely independent cases. However apt one may be to conclude (and however much I may be disposed to allow, that at the first glance there is something very plausible in such a conclusion) that, from the favourable effect which the cutting off of the supply of blood has in putting a stop to a process which arose from an increase of it, the process depended upon this increased supply, yet I am of opinion that the practical fact cannot be interpreted in this way. It is not so much an increase of quantity, either in the blood as a whole or in that portion of it contained in an individual part, which is required in order that a like increase should forthwith take place in the nutrition of that part, or of the whole body, as that, in my opinion, particular conditions should obtain in the tissues (irritation) altering the nature of their attraction for the constituents of the blood, or that particular matters should be present in the blood (specific substances), upon which definite parts of the tissues are able to exercise a particular attraction.

If you apply this doctrine to the humoro-pathological conception of the processes, you will be able to deduce from it that I am far from contesting the correctness of the humoral explanations in general, and that I rather cherish the conviction that particular substances which find their way into the blood are able to induce particular changes in individual parts of the body by their being taken up into them in virtue of the specific attraction of individual parts for individual substances. We know, for example, that a number of substances are introduced into the body which possess special affinities for the nervous system, and that among this number again there are some which stand in a closer connection with certain very definite parts of the nervous system, as for instance with the brain, the spinal cord or sympathetic ganglia, and others again with particular parts of the brain, spinal cord, etc. On the other hand, we see that certain materials have some special relation to definite secreting organs; that they penetrate and pervade them by a kind of elective affinity; that they are excreted by them; and that, when there is a too abundant supply of such materials, a state of irritation is produced in these organs. But an essential condition in all these cases is, that the parts which are believed to have a particular elective affinity for particular matters, should really exist, for a kidney which loses its epithelium is thereby deprived of its secreting power. Another condition is that the parts should possess a relation of affinity, for neither a diseased, nor a dead, kidney has any longer the affinity for particular substances which the gland, when living and healthy, possessed. The power of attracting and transforming definite substances can be maintained at most for a short time in an organ, which no longer continues in a really living condition. We are therefore, in the end, always compelled to regard the individual elements as the active agents in these attractions. An hepatic cell can attract certain substances from the blood which flows through the nearest capillary vessel, but it must in the first place exist, and in the next be in the ejoyment of its special properties, in order to exercise this attraction. If the living element become altered, if a disease set in which causes changes in its molecular, physical, or chemical peculiarities, then its power of exercising this special attraction will at the same time also be impaired.

Let us consider this example with still greater attention. The hepatic cells are almost in direct contact with the walls of the capillaries, from which they are only separated by a thin layer of delicate connective tissue. If now we were to imagine that the peculiar property possessed by the liver of secreting bile, merely consisted in a particular disposition of the vessels of the organ, we should indeed in no wise be justified in doing so. Similar networks of vessels, in a great measure of a venous nature, are found in several other places, for example, in the lungs. But the peculiarity of the secretion of bile manifestly depends upon the liver-cells, and only so long as the blood flows past in the immediate neighbourhood of the hepatic cells, does the particular attraction of matter continue which characterizes the action of the liver.

When the blood contains free fat, we see that after a time the hepatic cells take it up in minute particles, and that if the supply continues, the fat becomes more abundant and is gradually separated in the form of largish drops within the hepatic cells (Fig. 27, *B*, *b*). That which we see in the case of fat in a more palpable form, we must conceive to occur in the case of many other substances in a state of more minute division. Thus for the due performance of secretion it will always be essential that the cells exist in a certain, special condition ; if they become diseased, if a condition be developed in them connected with some important chemical change in their contents, for example, an atrophy, ultimately causing the destruction of the parts, then the power possessed by the organ of forming bile will at the same time continually become more limited. We cannot conceive a liver without liver-cells ; they are, as far as we know, the really active elements, since even in cases in which the supply of blood has become limited owing to obstruction in the portal vein, the hepatic cells are able to produce bile, although perhaps not in the same quantity.

This fact derives peculiar value from its occurrence in the liver, because the matters which constitute the bile do not, as is well known, exist pre-formed in the blood, and we must therefore suppose the constituents of the bile to arise not by a process of simple secretion, but by one of actual formation in the liver. This question has, as you are aware, recently become invested with a still greater degree of interest in consequence of the observation of Bernard that the property of producing sugar is also inherent in these elements, whereby the blood is supplied upon so gigantic a scale with a substance which has the most decided influence upon the internal metamorphic processes and upon the production of heat. If, therefore, we speak of the action of the liver, we can, both in regard to the formation of sugar as well as that of bile, mean nothing but the action of its individual elements (cells), an action which consists in their attracting matters from the passing current of blood, in their effecting within their cavity a transmutation of these matters, and returning them in this transmuted form either to the blood, or yielding them up to the bile-ducts in the shape of bile.

Now I demand for cellular pathology nothing more than that this view, which must be admitted to be true in the case of the large secreting organs, be extended also to the smaller organs and smaller elements ; and that, for example, an epidermis-cell, a lens-fibre or a cartilage-cell be, to a certain extent, admitted to possess the power of deriving from the vessels nearest to them (not always indeed directly, but often by transmission from a dis tance), in accordance with their several special requirements, certain quantities of material; and again that, after they have taken this material up, they be held to be capable of subjecting it to further changes within themselves, and this in such a manner that they either derive therefrom new matter for their own development; or that the substances accumulate in their interior, without their reaping any immediate benefit from it; or finally that, after this imbibition of material, even decay may arise in their structure and their dissolution ensue. At all events it seems necessary to me that great prominence should be assigned to this *specific action of the elements of tissues*, in opposition to the specific action of the vessels, and that in studying local processes we should principally devote ourselves to the investigation of processes of this nature.

It will now, I think, be most suitable for us next to enter a little more in detail upon the consideration of the facts which form the basis of the humoro-pathological system—upon the study of the so-called *nobler juices.* If the blood be considered in its normal influence upon nutrition, the most important point is not its movement, nor the greater or less afflux of it, but its intimate composition. When the quantity of blood is great, but its composition does not correspond to the natural requirements of the parts, nutrition may suffer; when the quantity is small, nutrition may proceed in a comparatively very favourable manner, if every single particle of the blood contain its ingredients mixed in the most favorable proportions.

If the blood be considered as a whole in contradistinction to other parts, the most dangerous thing we can do is to assume what has at all times created the greatest confusion, namely, that we have in it to deal with a fluid in itself independent, but upon which the great mass of tissues more or less depend. The greater number of the humoro-pathological doctrines are based upon the supposition, that certain changes which have taken place in the blood are more or less persistent ; and just in the very instance where these doctrines have practically exercised the greatest influence, in the theory, namely, of chronic dyscrasiæ, it is usually conceived that the change is continuous, and that by inheritance peculiar alterations in the blood may be transmitted from generation to generation, and be perpetuated.

This is, I think, the fundamental mistake of the humoralists, the real hinge upon which their errors turn. Not that I doubt at all that a change in the composition of the blood may pertinaciously continue, or that it may propagate itself from generation to generation, but I do not believe that it can be propagated *in the blood itself* and there persist, and that the blood is the real seat of the dyscrasia.

My cellulo-pathological views differ from the humoro-pathological ones essentially in this, that I do not regard the blood as a permanent tissue, in itself independent, regenerating and propagating itself out of itself, but as in a state of constant dependence upon other parts. We need only apply the same conclusions which are universally admitted to be true as regards the dependence of the blood upon the absorption of new nutritive matters from the stomach, to the tissues of the body themselves also. When the drunkard's dyscrasia is spoken of, nobody of course imagines that every one who has once been drunk labours under a permanent alcoholic dyscrasia, but the common opinion is, that, when continually fresh quantities of alcohol are ingested, continually fresh changes also declare themselves in the blood, so that its altered state must continue as long as the supply of fresh noxious matters takes place, or as, in consequence of a previous supply, individual organs remain in a diseased condition. If no more alcohol be ingested, if the organs which had been injured by the previous indulgence in it be restored to their normal condition, there is no doubt but that the dyscrasia will therewith terminate. This example, applied to the history of all the remaining dyscrasiæ, elucidates in a very simple manner the proposition, that *every dyscrasia is dependent upon a permanent supply of noxious ingredients from certain sources.* As a continual ingestion of injurious articles of food is capable of producing a permanently faulty composition of the blood, in like manner persistent disease in a definite organ is able to furnish the blood with a continual supply of morbid materials.

The essential point, therefore, is to search for the *local origins* of the different dyscrasiæ, to discover the definite tissues or organs from which this derangement in the constitution of the blood proceeds. Now I am quite willing to confess that it has not in many cases hitherto been possible to find out these tissues or organs. In many cases, however, success has been obtained, although it cannot be said in every instance in what way the blood has become changed. Thus we have that remarkable condition, which may very well be referred to a dyscrasia, the scorbutic condition, purpura, and the petechial dyscrasia. In vain will you look around for decisive information as to the nature of this dyscrasia, and as to the kind of change experienced by the blood when purpura or scurvy show themselves. What has been found by one has been contradicted by another, and it has even been shown that sometimes no change had taken place in the proportions of the grosser constituents of the blood. There remains in this case, therefore, a *quid ignotum*, and you will, I am sure, deem it excusable, if we are unable to say whence a dyscrasia proceeds, of which we are altogether unacquainted with the nature. However, the knowledge of the nature of the change in the blood does not involve an insight into the requisite conditions for the dyscrasia, and just as little is the reverse the case. In the case of the hæmorrhagic diathesis, also, it must at all events be regarded as an important step in advance, that we are in a number of instances able to point to a definite organ as its source, as, for example, to the spleen or liver. The chief point now is to determine what influence the spleen or the liver exercises upon the special composition of the blood. If we were acquainted with the nature of the changes effected in the blood by the influence of these organs, it might not perhaps be difficult from our knowledge of the diseased organ also at once to infer what kind of change the blood would experience. But it is nevertheless an important fact that we have got beyond the mere study of the changes in the blood, and have been able to ascertain that there are definite organs in which the dyscrasia has its root.

In conformity herewith we must conclude that, if there is a syphilitic dyscrasia in which a virulent substance circulates in the blood, this cannot be permanently present there, but that its existence must be due to the persistence of local depots (Heerde), whence new quantities of noxious matter are continually being introduced into the blood. By following this track we arrive at the conclusion which we have already mentioned, and which is of extreme importance in a practical point of view, that, namely, every permanent change which takes place in the condition of the circulating juices, must be derived from definite points in the body, from individual organs or tissues ; and this fact, moreover, is educed, that certain organs and tissues exercise a more marked influence upon the composition of the blood than others ; that some bear a necessary relation to this fluid, others only an accidental one.

LECTURE VII.

MARCH 6, 1858.

THE BLOOD.

Fibrine—Its fibrillæ—Compared with mucus, and connective tissue—Homogeneous condition.

Red blood-corpuscles—Their nucleus and contents—Changes of form—Blood-crystals (Hæmatoidine, Hæmine, Hæmatocrystalline).

Colourless blood-corpuscles—Numerical proportion—Structure—Compared with pus-corpuscles—Their viscosity and agglutination—Specific gravity—Crusta granulosa—Diagnosis between pus-, and colourless blood-corpuscles.

I INTEND to lay before you to-day, gentlemen, some further particulars with regard to the history of the blood.

I concluded my last lecture by impressing upon you the necessity of localizing the different dyscrasiæ ; employing the term localize, not in its ordinary sense, as the dyscrasiæ have heretofore been considered as localized, but rather in a genetical meaning, in accordance with which we constantly refer the dyscrasiæ to a pre-existing local affection, and regard some one tissue as the source of the persistent changes in the blood.

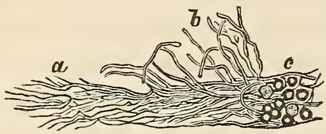
If now we consider the different dyscrasiæ with regard to their importance and their source, two great categories of dyscrasic conditions may at the very outset be distinguished, according namely as the morphological elements of the blood become changed, or the deviation is more of a chemical one, and seated in the fluid constituents.

Among these latter, it is the *fibrine*, which, in consequence of its coagulability, first, and that very soon after the blood has been removed from the living body, assumes a visible form, and which for this reason has frequently passed for a morphological constituent of the blood. This notion concerning it has of late been maintained in many quarters, and has indeed always had a traditional existence in medicine, inasmuch as from ancient times fibrine was constantly brought forward in addition to the red constituents of the blood as a special element, and it was the custom to estimate the quality of the blood, not only from the number of the blood-corpuscles, but frequently in a much more positive manner from the amount of fibrine.

This dissociation of fibrine from the other fluid constituents of the blood is, to a certain extent, of real value, because fibrine, like the blood-corpuscles, is quite a peculiar substance, and so exclusively confined to the blood and the most closely allied juices, that it really may be viewed as connected rather with the blood-corpuscles than with the mere fluids which circulate as serum. If we consider the blood in its really specific constituents, in those, by means of which it becomes blood, and is distinguished from other fluids, it cannot be denied that, on the one hand, the corpuscles with their hæmatine, and, on the other, the fibrine of the liquor sanguinis are the elements in which the specific differences must be sought for.

If now we next proceed to consider these constituents a little more closely, the morphological description of fibrine is comparatively rapidly made. On examining it, as it appears in blood-coagula, it is nearly always found in the form described by Malpighi, the fibrillar. Its fibres generally form extremely fine interlacements, delicate networks, in which they usually cross and join one another in a somewhat tortuous form. The greatest variations exhibited by these fibres when forming out of the blood have reference to their size and breadth; these are peculiarities concerning which it has not hitherto been possible to form any certain judgment. I meet with these variations pretty frequently, but without being in a position to assign the causes which determine them. The extremely fine and delicate fibres are those usually met with; but sometimes we find far broader, and almost ribbon-like fibres, which are much smoother, but in other respects, cross and interlace in pretty nearly the same manner. Essentially, therefore, there is always present in a clot a network composed of fibres, in the meshes of which the blood-corpuscles are enclosed. If a drop of blood be allowed to coagulate, fine filaments of fibrine can be seen everywhere shooting up between the blood-corpuscles.

Fig. 50.



With regard to the nature of these fibres, we may observe that there are only two other kinds which, histologically speaking, bear at all a near resemblance to them. The one kind occurs in a substance which, singularly enough, effects an approximation between the most ancient, perfectly antique, craseological ideas and the modern ones, namely in mucus. In the old Hippocratical system of medicine the whole mass of fibrine is, as is well known, included under the terms *phlegma*, *mucus*, and when we compare mucus with fibrine, we are obliged to confess that there does indeed exist a great similarity between them in the form they assume upon coagulation. In a similar manner to fibrine,

Fig. 50. Coagulated fibrine from human blood. *a*, Fine, *b*, coarser and broader fibrils. *c*, Red and colourless blood-corpuscles enclosed in the coagulum. 280 diameters.

mucus also forms into fibres, which frequently become isolated and then coalesce, so as to give rise to certain figures. The other substance which belongs here is the intercellular, or, if you will, the gelatine-yielding substance of connective tissue, the collagen (gluten of earlier writers). The fibrils of connective tissue only differ in that they are not usually reticulated, but run a parallel course, whilst in other respects they resemble those of fibrine in a high degree. The intercellular substance of connective tissue presents another point of resemblance with fibrine in the great analogy of its behaviour with reagents. When we expose it to the action of diluted acids, especially the ordinary vegetable acids, or also weak mineral acids, the fibres swell up and disappear before our eyes, so that we are no longer able to say where they are. The mass swells up, every interspace disappears, and it looks as if the whole were composed of a perfectly homogeneous substance. If we slowly wash it and again remove the acid, a fibrous tissue may, if the action have not been too violent, once more be obtained, after which the previous condition can be produced afresh, and changed again at pleasure. This behaviour has hitherto remained unexplained, and for this very reason Reichert's view, which I have already mentioned, that the substance of connective tissue, is really homogeneous and the fibres are only an artificial product, or an optical delusion, has something alluring in it. In fibrine, however, the individual fibres can, much more distinctly than is the case with connective tissue, be so completely isolated, that I cannot help saying that I regard the separation into single fibres as really taking place, and not merely as an artificial one, or as a delusion on the part of the observer.

But it is very interesting to observe that this fibrillar stage of fibrine is invariably preceded by a homogeneous one, just as connective tissue originally wears the form of a homogeneous intercellular substance (mucus) from which fibres are only by degrees, if I may so express myself, excreted, or, to employ the usual term, differentiated. So fibrine, too, which is first of all gelatinous, becomes differentiated into a fibrillar mass. And indeed in the case of inorganic substances also we find certain analogous appearances. From deposits of calcareous salts or silicic acid, which were originally perfectly gelatinous and amorphous, solid granules and crystals are gradually separated.

The name fibrils may therefore still be retained to designate the usual form in which fibrine presents itself, but at the same time it must be borne in mind, that this substance originally existed in a homogeneous, amorphous, gelatinous condition, and can again be reduced to it. This reduction can not only be effected artificially, but takes place also naturally in the body itself, so that where we have previously found fibrils, we may afterwards meet with the fibrine in a homogeneous condition, as, for example, in the vessels, where aneurysmal coagula, and others, are gradually converted into a homogeneous mass of cartilaginous density.

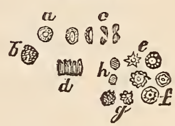
Now, with reference to the second portion of the blood, the *blood-corpuscles*, I may express myself briefly, as they are well-known elements. I have already remarked that nearly all the histologists of the present time are agreed that the coloured corpuscles of the blood of man and the higher mammalia contain no nuclei, but that they are simple vesicles,

Fig. 51.

Fig. 51. Nucleated blood-corpuscles from a human fœtus, six weeks old. *a.* Homogeneous cells varying in size, with simple, relatively large nuclei, of which

concerning the cellular nature of which doubts might be permitted, if we did not happen to know that, at certain periods of the development of the embryo, they do contain nuclei. An ordinary red blood-corpuscle must therefore be considered as composed of a closed membrane, containing a tolerably tough mass, which is the seat of the colour. Now, in man the blood-corpuscles are, as is well known, flat, disc- or plate-shaped bodies, with a central depression on each surface, and, when regular in form, constitute, as it were, a ring, in the centre of which the colour is fainter from the diminished thickness. The contents are generally somewhat summarily regarded as consisting of hæmatine, or the colouring matter of the blood. They are, however, unquestionably very complex, and what is called hæmatine forms merely a part of them; how great a part it has not been hitherto possible to determine. Whatever other matters are contained within the blood-corpuscle belong entirely to its chemistry. Certain changes produced by the action of external media constitute all that can be seen of them. We observe that the blood-corpuscles, according as they imbibe oxygen, or contain carbonic acid, appear light or dark, whilst they alter their form a little. We know, further, that

Fig. 52.



a few are slightly granular, but the greater number more homogeneous; at * a colourless corpuscle. *b*. Cells with extremely small, but well defined nuclei, and distinctly red contents. *c*. After the addition of acetic acid the nuclei are seen in some instances shrivelled and jagged, in several, double; at * a granular corpuscle. 280 diameters.

Fig. 52. Human blood-corpuscles from an adult. *a*. An ordinary disc-shaped, red blood-corpuscle; *b*, a colourless one; *c*, red corpuscles seen in profile, and standing upon their rims. *d*. Red corpuscles arranged in the form of rouleaux of money. *e*. Red corpuscles which have become irregular in outline, and shrivelled through loss of water (exosmosis). *f*. Shrivelled red corpuscles, with tuberculated margins, and a projection, like that produced by a nucleus, upon the flat surface of the disc. *g*. A still more shrivelled state. *h*. The highest degree of shrivelling (melanic corpuscles). Magnified 280 diameters.

by the action of chemical fluids, certain quantities of water are abstracted from the corpuscles, and that they then shrivel up and experience peculiar changes in form, which might very easily give rise to errors. These are not unimportant conditions, and I will therefore now add a few words concerning them.

When a blood-corpuscle is exposed to a loss of water by the action of a strongly concentrated liquid upon it, the first thing we observe is that, as fast as fluid exudes, little prominences arise on the surface of the corpuscle, at first very much scattered, sometimes at the border, sometimes more towards the middle, and in the latter case, occasionally bearing a deceptive resemblance to a nucleus (Fig. 52, *e*, *f*). This has been the source of the erroneous assumption of nuclei, which have been so much described. If a blood-corpuscle be watched for a considerable time whilst under the action of concentrated media, more and more protuberances are seen to arise, and the surface of the corpuscle becomes less in diameter. At the same time, little folds and knobs form with continually increasing distinctness on the surface, and the cell becomes jagged, stellate, and angular (Fig. 52, *g*). Jagged bodies of this sort are to be seen every moment on examining blood which has been for some time exposed to the air. Even mere evaporation will produce this change. We can effect it with great rapidity by altering the composition of the serum by the addition of salt or sugar. If the abstraction of water continue, the corpuscle grows smaller still, and ultimately becomes smooth again, and at the same time globular (Fig. 52, *h*), or even perfectly spherical, whilst its colour appears much more intense, and the contained mass assumes quite a deep blackish-red hue. Hence we are able to draw the not uninteresting conclusion, that this exosmosis consists essentially in a withdrawal of water, during which perhaps one or more other matters pass out. as, for example, salt, but the essential constituents remain behind. The hæmatine does not follow the water; the membrane of the blood-corpuscles keeps it back, so that when a large quantity of fluid is lost, the hæmatine in the interior must of course become proportionately increased in density.

The reverse is the case when we employ diluted fluids. The more diluted the fluid, the more does the blood-corpuscles enlarge; it swells up and becomes paler. On treating blood-corpuscles, which have become smaller from the action of concentrated fluids, with water, we see them pass back from the globular into the angular form, and from this into the discoidal one; after which they continually become more and more globular, often assume very peculiar shapes, and again grow paler. This process may, if the dilution of the blood be effected with great precaution, be continued until the blood-corpuscles scarcely seem to retain a trace of colour, though they still remain visible. In ordinary cases, when much liquid is added at once, such a violent revolution is produced in the economy of the blood-corpuscle, that an escape of the hæmatine immediately ensues. We then obtain a red solution, in which the colouring matter is free and dissolved in the fluid. I call your attention to this peculiarity, because it is continually occurring in the course of investigations, and because it explains one of the most important phenomena in the formation of pathological deposits of pigment, in which we meet with a precisely similar escape of hæmatine from the blood-corpuscles (Fig. 54, *a*). The expression generally made use of under such circumstances is, that the blood-corpuscles are dissolved, but it has long been a well-known fact that, as was first shown by Carl Heinrich Schultz, although there apparently no longer exist any cells, yet their membranes may, by means of an aqueous solution of iodine, again be rendered visible, whence it is evident that it was only the high degree of distension and the extraordinary thinness of the membranes which prevented the corpuscles from being seen. Indeed, very violent action on the part of substances chemically different is required, in order to effect a real destruction of the blood-corpuscles. If, immediately after they have been treated with a very concentrated solution of salt, water be added in large quantity, we may succeed in bringing things to such a pass that the contents of the corpuscles are abstracted without their swelling up, and their membranes remain behind visible. This was the reason why Denis and Lecanu asserted that the blood-corpuscles contained fibrine; for they believed that, by treating them first with salt and then with water, they were able to demonstrate its presence in them. This so-called fibrine is, however, as I have shown, nothing more than the membranes of the blood-corpuscles; real fibrine is not contained in them, although their walls are certainly composed of a substance which has more or less affinity to albuminous matters, and may, when obtained in large masses, present appearances reminding one of fibrine.

Now with regard to the substances contained in the blood-corpuscles, they happen quite recently to have become invested with great interest in consequence of the more morphological products which have been observed to arise out of them, and which have produced a kind of revolution in the whole theory of the nature of organic matters. I refer here to the peculiar forms of coloured crystals, which can, under certain circumstances, be obtained from the colouring matter of the blood, and which have acquired not only on their own account great chemical, but also very considerable practical, interest.

We have already become acquainted with three different kinds of *crystals*, of which hæmatine seems to be the common origin.

To the first form, with which I at one time busied myself much, I have given the name of *Hæmatoidine.* This is one of the most frequent of metamorphic products, and is spontaneously formed in the body out of hæmatine, and that indeed often in such large quantities that its excretion can be perceived with the naked eye. This substance in its perfect form presents itself in the shape of oblique rhombic columns, and is of a beatiful yellowish-red, or frequently, when in thicker pieces, deep ruby-red, colour, and forms one of the most beautiful crystals we are acquainted with. In little plates too it is not uncommonly met with, and frequently bears a considerable resemblance to the crystalline forms of uric acid. In the majority of cases the crystals are very small, not merely microscopical, but even somewhat difficult of observation with the microscope. A man must either be a very keen observer, or provided with special preparatory knowledge, else he will frequently discover in the spots where the hæmatoidine is lying nothing more than little streaks, or an apparently shapeless mass. But, upon more accurate inspection, the streaks resolve themselves into minute rhombic columns, the mass into an aggregation of crystals. This substance may be considered as the regular, typical, ultimate form into which hæmatine is converted in any part of the body where large masses of blood continue to lie for any length of time. An apoplectic effusion in the brain, for example, cannot be repaired by any other process than by a large portion of the blood undergoing this form of crystalliza-

Fig. 53.

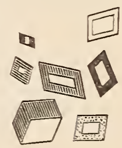
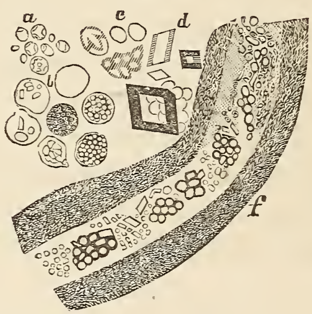


Fig. 53. Crystals of Hæmatoidine in different forms (Comp. 'Archiv. f. path. Anat.,' vol. i, p. 391, plate iii, fig. 11). Magnified 300 diameters.

tion, and if we afterwards find a coloured cicatrix at the spot, we may feel perfectly assured that the colour is dependent upon the presence of hæmatoidine. When a young woman menstruates, and the cavity of the Graafian vesicle, from which the ovum has been extruded, becomes filled with coagulated blood, the hæmatine is gradually converted into hæmatoidine, and we afterwards find at the spot where the ovum had lain, the beautiful deep-red colour of the hæmatoidine crystals, which remain as the last memorials of this episode. In this manner we can count the number of apoplectic attacks, or calculate how often a young girl has menstruated. Every extravasation may leave behind its little contingent of hæmatoidine crystals, and these, once formed,

Fig. 54.



remain in the interior of the organ, in the shape of compact bodies endowed with the greatest powers of resistance.

With respect to the peculiarities of hæmatoidine, it has, in a theoretical point of view, another special claim to

Fig. 54. Pigment from an apoplectic cicatrix in the brain ('Archiv,' vol. i, pp. 401, 454, plate iii, fig. 7). *a.* Blood-corpuscles which have become granular and are in process of decolorization. *b.* Cells from the neuroglia, some of them provided with granular and crystalline pigment. *c.* Pigment-granules. *d.* Crystals of Hæmatoidine. *f.* Obliterated vessel with its former channel filled with granular and crystalline red pigment. 300 diameters.

our interest, from its presenting to us a series of properties, which render it conspicuous as the only substance in the body, at least, that we are as yet acquainted with, which is allied to the colouring matter of the bile (Cholepyrrhine). By the direct action of mineral acids, or after previous treatment and preparation by means of alkalies, the same, or precisely similar, colour-tests are obtained, which are yielded by the colouring matter of the bile when treated with mineral acids, and it seems also from other facts, that we have here a body before us, which is very intimately connected with the colouring matter of the bile. This circumstance derives its especial interest from its being supposed, for other reasons also, that the coloured constituents of the bile are products of the decomposition of the red colouring matter of the blood. In the interior of extravasations there really does arise a yellowish red substance which may be designated as a newly formed kind of biliary colouring matter.

The second kind of crystals which arise out of hematine was discovered later; they are very similar to the preceding ones, but differ from them in that they do not occur as a spontaneous product in the body, but must be artificially produced. They are more of a dark brownish

Fig. 55.

colour and usually form flat rhombic plates with more acute angles; they are in an extraordinary degree capable of resisting tests, and also do not, when acted upon

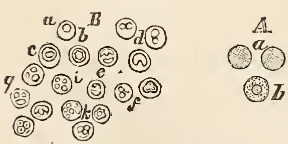
Fig. 55. Crystals of Hæmine, artificially procured from human blood. 300 diameters.

by the mineral acids, exhibit the peculiar play of colours afforded by hæmatoidine. This second kind of crystals has received the name of *Hæmine* from their discoverer Teichmann. Quite recently Teichmann has himself begun to entertain doubts as to whether it is not really a sort of hæmatine. These forms do not present as yet the slightest pathological interest, but, on the other hand, they have proved of very great importance in forensic medicine on account of their having been recently employed as one of the surest tests for the examination of blood-stains. I myself have been in a position to make experiments of this sort in forensic cases. For this purpose the best mode of proceeding is to mix dried blood in as compact a form as possible with dry, crystallized, powdered common salt, and then to add to this mixture glacial acetic acid, and evaporate at a boiling heat. When this has been done, crystals of hæmine are found where the blood-corpuscles or the substance previously lay, in which the presence of hæmatine was doubtful. This is a reaction which must be ranked among the most certain and reliable ones with which we are acquainted. There is no other substance in which we know such a transformation to take place, but hæmatine. This test is extremely important, because it is applicable in the case of extremely minute quantities, only they must not be spread over too large a surface. It would therefore not be easy of application in a case where we had to deal with a cloth which had been dipped into a thin, watery, fluid coloured with blood. Yet I was able, in the case of a murdered man, on the sleeve of whose coat blood had spurted, and where some of the drops were only a line in diameter, from these minute specks to produce innumerable crystals of hæmine, though of course microscopical ones. In cases in which the ordinary chemical tests would necessarily absolutely fail on account of the smallness of the quantity, we are still able to obtain hæmine. When the mass of blood is so very small, the size of the crystals is certainly also extremely minute, and we then find, as in the case of hæmatoidine, small needles of an intensely brown colour and provided with acute angles.

The third substance which belongs to this series, is the so-called *Hæmato-crystalline*, a substance about the discovery of which the learned still dispute, for the simple reason that it was found out piecemeal. The first observation concerning it was made by Reichert in extravasations in the uterus of the guinea-pig, in a preparation which, I think, had already lain for some little time in spirits. This observation of his acquired especial significance because he showed that these crystals in certain respects behaved like organic substances, inasmuch as they became larger through the action of certain agencies, and smaller through that of others, without any change of form, a phenomenon which, up to that time, had not been known to take place in crystals. Afterwards these crystals were again discovered by Kölliker, but Funke, Kunde, and especially Lehmann, have examined them more closely. The result has been that they are very different in different classes of animals, but hitherto it has not been possible to discover any definite reason for their existence, or to obtain any insight into the nature of the substance itself. In man the crystals are tolerably large. At first it was believed that they only occurred in the blood of certain organs, but it has since turned out that they occur everywhere, though they are obtained with greater readiness in certain morbid conditions. In a few very rare cases it happens that they are found already formed in the blood of the dead bodies of animals. These crystals are very easily destructible ; both when they dry up and when they become moist, or are brought into contact with any fluid medium, they perish, and they are therefore only observed in certain transitional stages, which must be exactly hit upon, in the destruction of blood-corpuscles. The well-developed forms in man are perfectly rectangular bodies; but very frequently they are extremely small, and nothing is seen but simple spicules which shoot up into the object at certain spots in large masses. There is besides this peculiarity about them, that they retain the property which hæmatine itself has of becoming bright red with oxygen and dark red with carbonic acid. It is still, however, a frequent subject of discussion whether their whole substance is composed of colouring matter, or whether in this case also the crystals are really colourless and merely impregnated with pigment; this much, however, may be regarded as certain, that the colour has something very characteristic about it, and that the existence of a close connection between it and the ordinary colouring matter of the blood cannot be doubted.

If we now revert to the natural morphological elements of the blood, we meet with the *colourless corpuscles* as its third constituent. They are present in comparatively small quantity in the blood of a healthy man. To three hundred red corpuscles we reckon about one colourless one. As they generally present themselves in the blood, they are spherical corpuscles, which are sometimes a little larger, sometimes a little smaller than, or of the same size as, ordinary red blood-corpuscles, from which they are, however, strikingly distinguished by the want of all colour and by their perfectly spherical form.

Fig. 56.



In a drop of blood which has become quiet, the red cor-

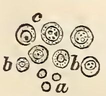
Fig. 56. Colourless blood-corpuscles from a vein of the pia-mater of a lunatic. *A*. Examined when fresh; *a* in their natural fluid, *b* in water. *B*. After the addi-

puscles are usually found aggregated in rows, presenting the familiar form of rouleaux of money, with their flat discs one against the other (Fig. 52, *d*) ; in the interspaces may be observed here and there one of these pale, spherical bodies, in which in the first instance, when the blood is quite fresh, nothing more can be distinguished than an occasionally slightly granular-looking surface. If water be added, the colourless corpuscles are seen to swell up, and in proportion as they absorb the water, a membrane first becomes distinct; then granular contents gradually come into view with more and more clearness, and at last some indication is perceived of the presence of one or several nuclei. The apparently homogeneous globule is gradually transformed into a structure with delicate walls, and often so fragile, that when water is incautiously added, the external parts begin to fall to pieces, and in the interior a somewhat granular mass displays itself, which becomes looser and looser, and discloses within it a nucleus generally in process of division, or several nuclei. These may be made to display themselves with much greater rapidity, by treating the object with acetic acid, which renders the membrane translucent, dissolves the nebulous contents, and causes the nucleus to coagulate and shrivel up. The nuclei then are seen to be dark bodies with sharply defined outlines, and one or more in number according to circumstances. In short, we obtain in this way in the majority of cases the view of an object which presents the peculiar appearance that one of our *confrères* now present, Dr. Güterbock, first proclaimed to be the special characteristic of pus-corpuscles. The question concerning the resemblance or want of re-

tion of acetic acid: *a—c*, cells with a single, granular nucleus, which becomes progressively larger, and is finally provided with a nucleolus. *d.* Simple division of the nuclei. *e.* A more advanced stage of the division. *f—h.* Gradual division of the nuclei into three parts. *i—k.* Four and more nuclei. 280 diameters.

semblance between the colourless cells of the blood and pus-corpuscles still continues to occupy the attention of observers, and it will probably still require a number of years before the views entertained with regard to the connection between the colourless corpuscles and pyæmia have been rendered so clear that relapses on one side or the other will not now and then recur. There is namely this source of error, that upon examining a number of persons, in the blood of several among them corpuscles will be found which have only a single nucleus, and that a very large one and not unfrequently provided with a nucleolus, whilst in the blood of others no corpuscles will be seen which do not contain several nuclei. Now, since these latter bear a great resemblance to pus-corpuscles, those observers, who had previously chanced to meet with nothing but uni-nuclear corpuscles in normal blood, cannot be blamed for believing, in another case in which they see multi-nuclear ones, that they have something essentially different before them, namely, pus-corpuscles in the blood, and that the case is one of pyæmia. But, strange to say, the corpuscles with one nucleus form the exception, and you may look for a long time without finding blood in which all the cells have only one nucleus. Oddly enough to-day, while occupied in preparing the microscopical objects, I stumbled upon a specimen of blood, in which scarcely anything but cells with one nucleus are to be met with, and these in extremely large number ; it was taken from a man who died of smallpox, and in whom a very highly remarkable acute hyperplasia of the bronchial glands existed.

Fig. 57.



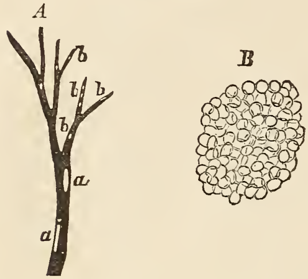
Now, one might be inclined to believe that these are

Fig. 57. Colourless blood-corpuscles in variolous leucocytosis. *a*. Free or naked nuclei. *b*, *b*. Colourless cells with small, simple nuclei. *c*. Larger, colourless cells, with large nuclei and nucleoli. 300 diameters.

different qualities of blood. But in opposition to such an idea it must be remarked, that, although in the cases in which the one or the other kind of corpuscles exist in large quantities, we have to deal with a pathological phenomenon, yet that, when we do not find such large quantities, we have before us only an earlier or a later stage of the development of the elements. For one and the same blood-corpuscle may, in the course of its life, have one or several nuclei, the one belonging to an earlier, the several to a later, stage of its existence. You must always bear in mind, that the change is seen to take place in the same individual in a short time, indeed often in the course of a few hours, so that in blood which had previously only contained one sort, afterwards quite a different one may be found—a proof of the rapidity of the change to which these bodies are subjected.

Allow me, gentlemen, to add a few words with regard to the more palpable relations which the individual constituents of the blood present towards one another. It is, as you well know, generally assumed that of the morphological constituents only two are accessible to the grosser perception of the naked eye, namely, the red corpuscles in the clot, and the masses of fibrine, which under certain circumstances form a buffy coat, but that, on the other hand, the colourless cells are not to be perceived by the unaided sight. This is a notion which I consider myself bound to correct. The colourless corpuscles, whenever they are present in considerable numbers, become very distinctly manifest to the more practised eye during the separation of the constituents of the blood, and especially when the coagulation is accompanied by movement; and they then exhibit a peculiarity, with which it is as well that one should be acquainted when one is required to pass judgment upon specimens derived from post-mortem examinations, and the ignorance of which has led to great errors. The colourless corpuscles possess namely, as was brought to light in the discussion which Herr Ascherson, now here present, had some time ago with E. H. Weber, the peculiar property of being sticky, so that they readily adhere to one another, and under certain circumstances also cling fast to other parts, when the red corpuscles do not present this phenomenon. This tendency to adhere to other parts is particularly evident when several of the corpuscles are at the same time placed in a position which enables them to stick together. Thus, in blood in which there is an actual increase in the number of colourless cells, it is extremely common for agglutinations to take place among them, as soon as the pressure, under which the blood flows, is diminished ; in every vessel, in which the stream becomes slower, and the pressure weaker, an agglutination of the corpuscles may take place.

Fig. 58.



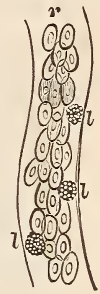
The adhesiveness (viscosity) of the colourless blood-corpuscles produces besides this effect, that, as has been shown by Herr Ascherson, when the blood is flowing as usual through the capillary vessels, the colourless corpuscles generally float rather more slowly than the red, and that, whilst these move along more in the centre of the vessel in a continuous stream, a comparatively large vacuity is left at the circumference, within which the

Fig. 58. *A*. Fibrine clot from the pulmonary artery, and corresponding to its terminal branches; at *a*, *a* beset with largish patches, composed of heaps of white cells; at *b*, *b*, *b* with specks of an analogous nature. Natural size.

B. A portion of one of these specks or heaps, composed of thickly crowded, colourless blood-corpuscles. Magnified 280 diameters.

colourless corpuscles move, and that indeed often with such constancy, that Weber came to the conclusion that every capillary lay within a lymphatic vessel, in the inside of which the colourless blood- or lymph-corpuscles floated. But there cannot be the least doubt but that the canals in question are single ones, in which the colourless corpuscles float along closer to the walls than the red ones ; and it is in this peripheral space that, whilst the corpuscles move on, we see one here and there stick fast for a moment, then tear itself away and again move on slowly, so that the name of the *sluggish layer* (träge Schicht), applied to this part of the stream, has been universally adopted.

Fig. 59.



These two peculiarities, first, that, when the current becomes weaker, the corpuscles here and there cling to the walls of the vessel, and in some measure adhere to them, and, secondly, that they gather together and become conglomerated into largish masses, combine to produce this effect, that, when there exists a large number of colourless corpuscles in the blood, and death occurs, as it does in ordinary cases, after a gradual weakening of the propelling force, the colourless corpuscles collect in vessels of every description, into small heaps, and generally lie upon the outside of the later formed blood-clot.

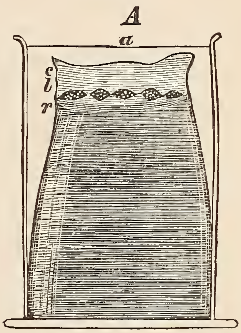
If, for example, we pull out of the pulmonary artery the generally very tough clot of blood which fills it, minute granules will perchance be found upon its surface (Fig. 58, *A*), little beads of a white colour, which look like specks of pus, or are connected several of them together in the form of a string of pearls. This appearance

Fig. 59. Capillary vessel from the web of a frog's foot. *r*. The central stream of red corpuscles. *l*, *l*, *l*. The sluggish, peripheral layer of the stream with the colourless corpuscles. Magnified 280 diameters.

most frequently presents itself at those points where the number of the bodies is normally the largest, namely in the interval between the orifice of the thoracic duct, and the capillaries of the lungs. The naked eye can with tolerable ease detect in these clots the greater or less quantity of colourless corpuscles. Under circumstances inducing the presence of a very large number of them, whole heaps of them may be seen, investing different parts of the coagulum like a sheath, and if one of these heaps be placed under the microscope, many thousands of colourless corpuscles are seen crowded together.

If the coagulation of the blood takes place, when it is more at rest, another appearance is presented with great distinctness, as may be seen in the vessels used to receive the blood after venæsection. When the fibrine does not coagulate very quickly, as is the case in inflammatory blood, the blood-corpuscles begin, in consequence of their greater specific gravity, to sink through the fluid. This subsidence proceeds, as is well known, to such a pitch, that, after the fibrine has been removed by stirring, the serum becomes perfectly clear, in consequence of the corpuscles' falling to the bottom. On defibrinating blood rich in colourless corpuscles, and allowing it to stand, a double sediment forms, a red and a white one. The red one constitutes the deeper, the white one the more superficial stratum, and the latter looks exactly as if a layer of pus were lying upon the blood. When the blood has not been deprived of its fibrine, yet coagulates slowly, the subsidence of the corpuscles does not take place so completely, but only the highest part of the liquor sanguinis becomes free from corpuscles ; and when after this the fibrine coagulates, we obtain the well-known *crusta phlogistica*, the *buffy coat*, and on looking for the colourless corpuscles, we find them forming a separate layer at the lower border of the buffy coat. This peculiarity is simply explained by the different specific gravity of the two kinds of blood-corpuscles. The colourless ones are always light, poor in solid matter and very delicate in structure, whilst the red ones are as heavy as lead in comparison, owing to their richness in hæmatine. They therefore reach the bottom with comparatively great rapidity, whilst the colourless ones are still engaged in falling. If two bodies of different specific gravities be allowed to fall from a sufficient height in the open air, the lighter one will, you know, in a similar manner, reach the ground after the other, owing to the resistance of the air.

Fig. 60.



In the coagulation which takes place in blood derived from venæsection, this white clot does not usually form a continuous, but an interrupted, layer, composed of little heaps or nodules adhering to the under side of the buffy coat. Hence Piorry, who was the first to observe this appearance, but completely misinterpreted it, seeing that he referred it to an inflammation of the blood itself (Hæmitis) and established the doctrine of Pyæmia, upon it, termed this form of buffy coat *crusta granulosa.* It really consists of nothing more than large accumulations of colourless corpuscles.

Under all circumstances this layer resembles pus in appearance, and since, as we have already seen, the colourless blood-cells individually are constituted like pus-corpuscles, you see that we are liable not only in the case of a healthy person to take colourless blood-cells for

Fig. 60. Diagram of a bleeding-glass with coagulated hyperinotic blood. *a.* The level of the liquor sanguinis. *c.* The cup-shaped buffy coat. *l.* The layer of lymph (Cruor lymphaticus, Crusta granulosa), with the granular and mulberry-like accumulations of colourless corpuscles. *r.* The red clot.

pus-corpuscles, but still more so in pathological conditions when the blood or other parts are full of these elements. You can imagine how apt the question is to present itself, which has already been seriously raised by Addison and Zimmermann, whether pus-corpuscles are not merely extravasated colourless blood-cells, or *vice versâ*, whether the colourless blood-cells found within the vessels are not pus-corpuscles which have been admitted into them from the exterior. We are here called upon for the first time to make the practical application of the principles which I laid down with regard to the specific nature and heterology of elements (p. 92.) A pus-corpuscle can be distinguished from a colourless blood-cell by nothing else than its mode of origin. If you do not know whence it has come, you cannot say what it is; you may conceive the greatest doubt as to whether you are to regard a body of the kind as a pus- or a colourless blood-corpuscle. In every case of the sort the points to be considered are, where the body belongs to, and where its home is. If this prove to be external to the blood, you may safely conclude that it is pus; but if this is not the case, you have to do with blood-cells.

LECTURE VIII.

MARCH 10, 1858.

BLOOD AND LYMPH.

Change and replacement of the constituents of the blood—*Fibrine*—Lymph and its coagulation—Lymphatic exudation—Fibrinogenous substance—Formation of the buffy coat—Lymphatic blood, hyperinosis, phlogistic crasis—Local formation of fibrine—Transudation of fibrine—Formation of fibrine in the blood.

Colourless blood-corpuscles (lymph-corpuscles)—Their increase in hyperinosis and hypinosis (Erysipelas, pseudo-erysipelas, typhoid fever)—Leucocytosis and leukæmia—Splenic and lymphatic leukæmia.

The spleen and lymphatic glands as blood-making organs—Structure of lymphatic glands.

The last time, gentlemen, I introduced to your notice the individual morphological elements of the blood, and endeavored to portray their special peculiarities. Allow me to begin to-day with a few words concerning their origin.

From the facts which have been ascertained with regard to the first development of the elements of the blood, important conclusions may be drawn respecting the nature of the changes which take place in the mass of the blood in deceased conditions. Formerly the blood was regarded more as a juice shut up by itself, which was indeed to a certain extent connected with the parts external to it, but yet was in itself endowed with real durability, and it was assumed that it could retain peculiar properties for lengthened periods, nay, that these might cling to it for many years. Of course it was impossible at the same time to entertain the opinion, that the constituents of the blood were of a perishable nature, and that new elements were added to it, to replace the old ones. For the durability of a part as such presupposes either that all its individual particles are durable, or that these individual particles are continually producing fresh ones within the part which bear impressed upon them all the peculiarities of the old ones. In the case of the blood, therefore, one would have to assume that its constituents really did subsist for years, and could for years present the same changes, or one would have to imagine that the blood transmitted something from one particle to another, and that from a parent blood-cell to its progeny something hereditary was handed down. Of these possibilities the former has, I believe, at the present time been pretty generally discarded. No one, I think, now imagines that the individual constituents of the blood last on for years. On the other hand, the possibility that the corpuscles of the blood are renewed by propagation, and that certain peculiarities which are introduced into the blood at a certain time, are transmitted from corpuscle to corpuscle, cannot straightway be rejected. But the only phenomena pointing to such a propagation of the blood, concerning which we possess any positive information, belong to an early period of embryonic life. There it appears from observations which were only the other day again confirmed by Remak, the existing blood-corpuscles undergo direct division, the process being that, in a corpuscle which during the early stages of its development had displayed itself as a nucleated cell, first of all a partition of the nucleus takes place (Fig. 51, *c*); and that then the whole cell becomes constricted in the middle, and gradually is really seen to pass into a state of complete division. At this early period it is therefore certainly allowable to regard a blood-corpuscle as endowed with qualities which are propagated from the first series of cells to the second, and from this to the third, and so on.

In the blood of a fully developed human being, nay even in that of a fœtus in the later months of pregnancy, these phenomena of partition are no longer known, and not a single one of the facts which can be adduced from the history of development speaks in favour of an increase of the cellular elements taking place in fully developed blood by means of direct division, or any other formative process taking its rise in the blood itself. As long as the possibility was regarded as demonstrated, that cells might arise out of simple cytoblastema by means of the direct precipitation of different substances, so long was it possible to conceive new precipitates as forming in the liquor sanguinis from which cells were produced. But this view also has been abandoned. All the morphological elements of the blood, whatever may be their nature, are at present considered to be derived from sources external to the blood. On all hands recourse is had to organs which do not communicate with the blood directly, but rather by the means of intermediate channels. The principal organs which here come into play are the lymphatic glands. *Lymph* is the fluid which, whilst it conveys certain substances to the blood which come from the tissues, at the same time brings along with it the corpuscular elements out of which the blood-cells continually recruit their numbers.

With regard to two of the constituents of the blood, there can, I think, be scarcely any doubt but that this is the view which is perfectly warranted, I mean with regard to the fibrine and the colourless corpuscles. As for the fibrine, the properties of which I brought to your notice last time, it is a very essential and important fact that the fibrine which circulates in lymph differs in certain respects from that contained in the blood, which we see on examining different extravasations, or blood drawn from a vein. The fibrine of lymph has this special peculiarity, that under ordinary circumstances it coagulates within the lymphatic vessel neither during life nor after death, whilst blood in many instances coagulates even during life, and regularly does so after death, so that coagulative power is attributed to blood as being one of its regular properties. In the lymphatics of a dead animal or human corpse, no coagulated lymph is met with, yet the coagulation takes place directly the lymph is brought into contact with the air, or has changes imparted to it by some diseased organ.

The explanation of this peculiarity has been attempted in very different ways. For my own part I must still adhere to the view that there is, properly speaking, no perfectly developed fibrine contained in lymph, but that it becomes perfect either by contact with the atmospheric air, or in abnormal conditions by the introduction into it of altered matters. Normal lymph contains a substance which is very readily converted into fibrine, and is, when it has once coagulated, scarcely to be distinguished from fibrine, but which, as long as it continues to circulate with the ordinary stream of lymph, cannot be regarded as really perfect fibrine. This is a substance, of which I had demonstrated the presence in various exudations, especially in pleuritic fluids, long before my attention had been drawn to its occurrence in lymph.

In many forms of pleurisy the exudation long remains fluid, and a number of years ago a peculiar case came under my notice, in which on puncturiug the thorax a liquid was evacuated which was perfectly clear and fluid, but in a short time after its evacuation had its whole mass pervaded by a coagulum, as is often enough the case with fluids from the abdominal cavity. After I had removed this coagulum from the liquid by stirring it, in order to convince myself of its identity with ordinary fibrine, the next day a fresh coagulum displayed itself, and this took place also on the following days. This coagulative power lasted fourteen days, although the operation had been performed in the midst of the heat of summer. This therefore was a phenomenon essentially differing from the ordinary coagulation of the blood, and somewhat difficult to explain upon the supposition that real fibrine existed completely developed in the fluid, but it seemed to indicate that it was only under the influence of the atmospheric air that the fibrine was produced from a substance which must indeed have been nearly related to fibrine, but yet could not be real fibrine. I therefore propose to give it the distinctive name of *fibrinogenous* substance, and when I afterwards had come to the conclusion that it was the same substance which we find in lymph, I was enabled to extend my view so as to include the proposition, that in lymph also fibrine is not contained in a perfect form.

This same substance, which is distinguished from ordinary fibrine by its requiring to be a longer or shorter time in contact with atmospheric air before it can become coagulable, is also found under certain circumstances in the blood of the peripheral veins, so that even by an ordinary venæsection performed on the arm blood may be obtained, distinguished from ordinary blood by the slowness of its coagulation. Polli named this coagulative substance *brady-fibrine.* Such cases occur especially in inflammatory diseases of the respiratory organs, and most frequently give rise to the formation of a *buffy coat* (crusta pleuritica, crusta phlogistica). You all know that the ordinary crusta phlogistica forms in the blood of pneumonia or pleurisy the more readily the greater the wateriness of the liquor sanguinis, and the poorer the blood is in solid constituents, but it is an essential requisite that the fibrine should coagulate slowly. If the duration of the process be noted watch in hand, the conviction will soon be acquired that a very much longer time passes than is requisite for ordinary coagulation. From this frequent phenomenon, as it is met with in the ordinary formation of a crust upon the surface of inflamed blood, gradual transitions are observed to a greatly increased prolongation of the period during which fluidity is retained.

The most extreme instance of this kind as yet known occurred in a case observed by Polli. In a vigorous man, suffering from pneumonia, who came under treatment in the summer, at a time which does not offer the external conditions most favourable to slowness of coagulation, the blood, which flowed from the opened vein, took a week before it began to coagulate, and not until the end of a fortnight was the coagulation complete. In this case, too, occurred the other phenomenon which I had observed in the pleuritic exudations, namely, that decomposition (putrefaction) took place in the blood at an unusally late period in proportion to this lateness of coagulation.

Now since phenomena of this kind are observed to occur with especial frequency in chest affections, a frequency so especial indeed that the buffy coat was long since designated *Crusta pleuritica*, there would seem to be some grounds for inferring from this, that the function of respiration has a definite influence upon the occurrence or non-occurrence of the fibrinogenous substance in the blood. At all events, the peculiarity possessed by the lymph is under certain circumstances transmitted to the blood, so that either the whole of the blood partakes of it, and that in a higher degree, the greater the disturbance under which the respiration labours; or, in addition to the ordinary, quickly coagulating matter, a second which coagulates more slowly is found. It frequently happens, namely, that two sorts of coagulation subsist side by side in the same blood, one early and the other late, especially in the cases in which direct analysis shows an increase of fibrine, a *hyperinosis*. These hyperinotic conditions appear therefore to indicate that in them an increased supply of lymphatic fluid is introduced into the blood, and that the matters which are afterwards found in the blood are not the products of an internal transformation of its constituents, and that therefore the original source of the fibrine must not be sought for in the blood itself, but in those parts from which the lymphatic vessels convey the increased supply of fibrine.

In explanation of these phenomena, I have ventured to advance the hypothesis, somewhat bold perhaps, though I consider it perfectly able to sustain discussion, namely, that *fibrine generally, wherever it occurs in the body external to the blood, is not to be regarded as an excretion from the blood, but as a local production;* and I have endeavored to introduce an important change in the views entertained with regard to the so-called phlogistic crasis in relation to its localization. Whilst it had previously been the custom to regard the altered composition of the blood in inflammation as a condition existing from the very outset, and especially denoted by a primary increase in the fibrine, I on the contrary have shown the crasis to be an occurrence dependent upon the local inflammation. Certain organs and tissues have inherent in them in a higher degree the power of producing fibrine and of favouring the occurrence of large quantities of fibrine in the blood, whilst other organs are by far less adapted for its production.

I have, moreover, pointed out the fact, that those organs which with especial frequency exhibit this peculiar combination of a so-called phlogistic state of the blood with a local inflammation are generally abundantly provided with lymphatic vessels and connected with large masses of lymphatic glands, whilst all those organs which either contain very few lymphatics, or in which these vessels are scarcely known to exist, do not exercise any influence worth naming upon the amount of fibrine in the blood. Former observers had already remarked that there were inflammations occurring in very important organs, as for example, in the brain, in which the phlogistic crasis was, properly speaking, not at all met with. Now it is precisely in the brain that we have scarcely any evidence of the existence of lymphatics. In those cases, on the contrary, in which the composition of the blood is earliest altered, namely, in diseases of the respiratory organs, we find an unusually abundant network of lymphatics. Not merely the lungs are pervaded by, and covered with, them, but the pleura also has extremely numerous connections with the lymphatic system, and the bronchial glands constitute almost the greatest accumulations of lymphatic-gland substance possessed by an organ in the whole body.

On the other hand, we are acquainted with no fact which shows it to be possible that, in consequence of a simple increase of the pressure of the blood, or of a simple change in the conditions which influence its circulation, an exudation of fibrinous fluids could in any organ take place into its parenchyma, or upon its surface, from the blood. It is certainly generally imagined that, when the current of the blood attains a certain strength, fibrine begins to appear in the exudation, but this has never been proved by experiment. Nobody has ever been able, by the production of a mere change in the force of the current of the blood, to induce the fibrine to transude directly as it is wont to do in certain inflammatory processes; for this some irritation is always required. The greatest obstructions may be induced in the circulation, exudations of serous fluids may be experimentally produced upon the largest scale, but that peculiar fibrinous exudation which the irritation of certain tissues provokes with so much ease, never ensues upon these occasions.

That the fibrine in the blood itself is produced by a transformation of the albumen, is a chemical theory, which has no other evidence in its favour than the fact that albumen and fibrine have a strong chemical resemblance, and that, on comparing the questionable formula for fibrine with the equally questionable one for albumen, it is very easy to imagine how, by the abstraction of a couple of atoms, the transition from albumen to fibrine might be effected. But our being able in this manner to deduce one of the formulæ from the other does not afford the slightest proof that an analogous transformation occurs in the blood. It may possibly take place in the body, but even then it would at any rate be more probable that it was accomplished in the tissues, and that from them the fibrine was conveyed away into the blood by means of the lymph. This is, however, the more doubtful, because rational formulæ for the chemical composition of albumen and fibrine have not yet been determined, and the incredibly high atomic numbers in the empirical formulæ point to a very complex grouping of the atoms.

Let us therefore hold fast the well-ascertained fact that fibrine can only be made to exude upon any surface by the occurrence of some irritation, that is, local change, in addition to the disturbance in the circulation. This local change, however, is, as results from experiment, alone sufficient to cause the exudation of fibrine, even when no obstruction arises in the circulation. Such obstruction is not therefore in any way needed in order that the production of fibrine may commence at any given point. On the contrary, we see that the cause of the greatest differences in the nature of exudations is to be found in the special constitution of the irritated parts. On the simple application of an irritating substance to the surface of the skin, there arises, when the irritation, whether chemical or mechanical in its nature, is only slight in degree, a vesicle, a serous exudation. If the irritation is more violent, a liquid exudes, which in the vesicle appears quite fluid, but coagulates after its evacuation. If the fluid from a blister raised by a cantharides-plaster be received into a watch-glass and exposed to the air, a coagulum forms, showing that there is fibrinogenous substance in the fluid. But we sometimes meet with conditions of the body, in which an external stimulus is sufficient for the production of blisters containing a fluid which directly coagulates. I had, last winter, a patient in my wards, whose feet had remained in a state of anæsthesia ever since they had been frozen, and I employed as a remedy, amongst other things, local baths containing aqua regia. After a certain number of these baths, blisters, which varied in diameter up to two inches, and were found, when opened, to be filled with large, jelly-like masses of coagulum, formed upon every occasion on the anæsthetic part of the soles of the feet. In other persons probably ordinary blisters would have formed, containing a fluid, which would not have coagulated until after its evacuation. Such a difference manifestly depends upon a difference, not in the composition of the blood, but in the disposition of the part affected. The difference between that form of pleurisy, which from its very commencement furnishes coagulable and coagulating fluids, and that in which the exudation is coagulable, but not coagulating, certainly points to peculiarities in the local irritation.

I do not think therefore that we are entitled to conclude that in a person who has an excess of fibrine in his blood, there is on that account also a greater tendency to fibrinous transudation ; on the contrary, I should rather expect that in a patient who produces at a certain point a large quantity of fibrine-forming substance, much of it would pass from that point into the lymph and finally into the blood. The exudation may therefore in such cases be regarded as the surplus of the fibrine formed *in loco*, for the removal of which the lymphatic circulation did not suffice. As long as the current of lymph does suffice, all the foreign matters which are formed in the irritated part are conveyed into the blood ; but, as soon as the local production becomes excessive, the products accumulate, and in addition to the hyperinosis, a local accumulation of fibrinous exudation will also take place. On account of the shortness of the time which is allotted to us, we cannot follow up this subject in its whole extent, but still I hope that you will at least completely grasp the fundamental idea which has guided me. Here, too, we have another example of that dependence of a dyscrasia upon a local disease to which I but a short time ago called your attention as being the most important result of all our investigations concerning the blood.

Now it is a very remarkable fact, and one which adds weight to this very view of mine, that it is *very rarely that a considerable increase of fibrine takes place without a simultaneous increase in the colourless blood-corpuscles*, and that therefore the two essential constituents which we find in the lymph we again meet with in the blood. In every case of hyperinosis we may rely upon discovering an increase in the colourless corpuscles, or, in other words, every irritation of a part, which is abundantly provided with lymphatics, and freely connected with lymphatic glands, occasions also the introduction of large numbers of colourless cells (lymph-corpuscles) into the blood.

This fact is especially interesting, inasmuch as you will perceive from it, that not only organs richly provided with lymphatic vessels can occasion this increase, but that certain processes also are more calculated than others to lead to the introduction of considerable quantities of these elements into the blood, namely all those which are early conjoined with serious disease in the lymphatic system. If you compare an erysipelatous, or a diffuse phlegmonous (according to Rust pseudo-erysipelatous), inflammation in its effects upon the blood with a simple superficial inflammation of the skin, such as occurs in the course of the ordinary acute exanthemata, or after traumatic or chemical irritation, you will at once see how great the difference is. Every erysipelatous or diffuse phlegmonous inflammation has the peculiarity of early affecting the lymphatic vessels and producing swellings in the lymphatic glands. In such a case we may feel assured that an increase in the number of the colourless corpuscles is taking place. Further, we find the significant fact, that there are certain processes which simultaneously cause an increase of fibrine and colourless corpuscles, and others again which only occasion an increased production of the latter. To this latter category belong the whole series of simple diffuse inflammations of the skin, in which also no considerable formation of fibrine takes place in the diseased parts. On the other hand, a number of conditions belong to it, which with regard to the quantity of fibrine may be designated as *hypinotical*, all the processes namely which belong to the typhoid class, and agree in producing considerable swelling now of one, and now of another, kind in the lymphatic glands, but do not produce any local exudation of fibrine. Thus typhoid fever causes these changes not only in the spleen, but also in the mesenteric glands.

The condition in which the increased proportion of colourless corpuscles in the blood appears to be dependent upon an affection of the lymphatic glands, I have designated by the name of *Leucocytosis.* Now you know that another matter has long been the subject of my studies, the affection named by me *Leukæmia*, and our next business must be to determine how far genuine leukæmia differs from these leucocytotical conditions. In the very first cases of leukæmia which came before me, a very essential property was discovered to exist, namely, that there was no essential variation in the proportion of fibrine in the blood. Afterwards it was found out that the proportion of fibrine might, according to the particular circumstances of the case, be greater or less than, or the same as, usual, but that a continually augmenting increase of the colourless blood-corpuscles invariably took place ; and that the coincidence of this increase with a diminution in the number of the coloured (red) corpuscles became more and more marked, so that as a final result a condition was attained, in which the number of the colourless corpuscles was almost equal to that of the red ones, and striking phenomena were displayed, even when the coarser modes of observation were employed. Whilst in ordinary blood we can seldom count more than one colourless corpuscle to about three hundred coloured ones, there are cases of leukæmia in which the increase of the colourless ones reaches such a height, that to every three red corpuscles there is one colourless one, or even two ; or in which indeed the greater numbers are in favour of the colourless corpuscles.

In dead bodies the increase in the colourless corpuscles generally appears more considerable than it really is, from reasons which I but a short time ago pointed out to you (p. 184); for these corpuscles possess extraordinary adhesiveness and accumulate in considerable masses wherever there is a retardation in the stream of blood, so that in the dead body the greatest number is always found in the right heart. Once, before I left Berlin, this singular case occurred to me, that, when I punctured the right auricle, the physician who had treated the case cried out, astonished, "Why, there's an abscess there!" So like pus did the blood appear. This puriform condition of the blood does not indeed pervade the entire circulating stream; the whole of the blood never looks like pus, because a comparatively large number of red corpuscles always continues to exist; still it sometimes happens that blood flowing from a vein even during life exhibits whitish streaks, and that, when the fibrine has been removed by stirring, and the defibrinated blood is allowed to stand, a voluntary separation at once takes place, the whole of the blood-corpuscles, red and colourless, gradually sinking to the bottom of the vessel, and there forming a double sediment, a lower red stratum, covered by an upper, white and puriform one. This is explained by the difference in the specific gravity of the two kinds of corpuscles and the time they take to sink (p. 186). In this way too we are enabled very readily to distinguish leukæmic from chylous (lipæmic) blood in which a milky appearance of the liquor sanguinis is produced by the admixture of fat, for, if the fibrine be removed, after some time there forms not a white sediment, but a cream-like layer on the surface.

In the histories of all the known cases of leukæmia we only find it once as yet recorded that the patient, after he had been for some time the subject of medical treatment, left the hospital considerably improved in health.

In all the other cases the result was death. I do not wish by any means to infer from this that the disease in question is absolutely incurable ; I hope on the contrary that for it too remedies will at length be discovered ; but it is certainly a very important fact that we have in it, much, as in the progressive atrophy of muscles, to deal with conditions, which, when abandoned to themselves, or subjected to any one of the hitherto known methods of treatment, continually grow worse and ultimately lead to death. These cases possess, in addition, the remarkable peculiarity that, usually towards the close of life, a genuine *hæmorrhagic diathesis* is developed and hæmorrhages ensue, which occur with especial frequency in the nasal cavity (under the form of exhausting epistaxis) but may also, under certain circumstances, take place in other parts of the body, as for example on a very large scale in the form of apoplectic clots in the brain, or of melæna in the intestinal canal.

Now, upon investigating whence this curious change in the blood takes its origin, we find in the great majority of cases that it is a certain, definite organ which presents itself over and over again with convincing constancy as the one essentially diseased, an organ which frequently, even at the outset of the malady, forms the chief object of the complaints and distress of the patients, namely, the *spleen.* In addition, a number of lymphatic glands are very frequently diseased, but the affection of the spleen stands in the foreground. Only in a few cases have I found the change in the spleen the less and that in the lymphatic glands the more prominent, and in these, matters had proceeded to such a pitch, that lymphatic glands, at other times scarcely observable, had developed themselves into lumps the size of walnuts, and that indeed in some few places there appeared to be scarcely anything else than glandular substance. Of the glands which lie between the inguinal and lumbar glands we are wont to hear but little, nor have they indeed even a suitable name. Some of them lie in the course of the iliac vessels, and some in the real pelvis. But in two of these cases of leukæmia I found them so enlarged that the whole cavity of the pelvis proper was, as at were, stuffed full of glandular substance, between which the rectum and the bladder only just dipped in.

I have therefore distingushed two forms of leukæmia, namely, the *ordinary splenic*, and the *lymphatic*, *form*, which are certainly not unfrequently combined. The distinction rests not only upon the circumstance, that in the one case the spleen, in the other the lymphatic glands, constitute the starting point of the disease, but also upon the fact that the characteristic morphological elements which are found in the blood are not precisely similar. Whilst namely in the splenic forms these elements are generally comparatively large and perfectly developed cells with one or more nuclei, and in many cases bear a particularly great resemblance to the cells of the spleen, we notice in the well-marked lymphatic forms that the cells are small, the nuclei large in proportion and single, usually sharply defined, with dark outlines and somewhat granular, whilst the cell-wall is frequently in such close apposition to them that an interval can scarcely be demonstrated. In many instances it looks as if perfectly free nuclei were contained in the blood. In these (the lymphatic) cases, therefore, it seems that the enlargement of the glands alone, which is accompanied in its progress by a real increase in the number of their elements (hyperplasia), also conveys a larger number of cellular elements into the lymph and through this into the blood, and that, just in proportion to the predominance of these elements, the formation of the red cells suffers obstruction. This is in a few words the history of these processes. Leukæmia is thus a sort of permanent, progressive leucocytosis, whilst this on the other hand in its simple forms constitutes a transitory process, connected with fluctuating conditions in certain organs.

You see therefore that there are at least three different conditions here, bordering one upon the other : hyperinosis, leucocytosis and leukæmia, between which and the lymphatic fluids there exists an intimate connection. The one series, that namely which is distinguished by an increase in the quantity of fibrine, is rather to be referred to the accidental condition of the organs from which the lymphatic fluids are derived, whilst those states which are induced by an increase in the number of cellular elements are rather regulated by the condition of the glands through which these fluids have flowed. These facts can hardly, I think, be interpreted in any other manner than by supposing that the spleen and lymphatic glands are really intimately concerned in the development of the blood. This has become still more probable since we have succeeded in obtaining chemical evidence also in support of it. Herr Scherer upon two occasions examined leukæmic blood which I had submitted to him, in order to compare it with the matters he had discovered in the spleen, and the result was that hypoxanthine, leucine, uric, lactic, and formic, acid, were found there. In one case of leukæmia a liver which I had kept for several days became entirely covered with granules of tyrosine ; in another, leucine and tyrosine crystallized in large masses out of the contents of the intestines. In short, everything points to an increased action in the spleen, which normally contains these substances in considerable quantity.

A good many years elapsed (after 1845) during which I found myself pretty nearly alone in my views. It has only been by degrees and indeed, as I am sorry to be obliged to confess, in consequence rather of physiological than pathological considerations, that people have come round to these ideas of mine, and only gradually have their minds proved accessible to the notion, that in the ordinary course of things the lymphatic glands and the spleen are really immediately concerned in the production of the formed elements of the blood; and that in particular the corpuscular constituents of this fluid are really descendants of the cellular bodies of the lymphatic glands and the spleen which have been set free in their interior and conveyed into the current of the blood. And let this serve as an introduction to the consideration of the question of the origin of the blood-corpuscles themselves.

You will probably recollect, gentlemen, from the time of your studies, that the lymphatic glands used to be regarded as coils of lymphatic vessels. The afferent lymphatics may, as is well known, even with the naked eye be seen breaking up into smaller branches, disappearing within the glands, and finally again emerging from them. From the results of the mercurial injections which even in the last century were made with such great care, the only inference to be drawn appeared to be, that the afferent lymphatic vessel formed a number of convolutions, which interlaced in various ways and were finally continued into the efferent vessel, so that the gland was composed of nothing else than the thickly crowded coils of the afferent vessels. The whole attention of modern histologists has been directed to the task of confirming this tortuous transit of the lymphatic vessels through the gland, but after many years of labour spent in vain, the attempt was at length abandoned.

At the present moment there is, I should suppose, scarcely an histologist who believes in the perfect continuity of the lymphatic vessels throughout the gland, but

Kölliker's view is generally adopted, that the lymphatic glands interrupt the current of the lymph, the afferent vessel resolving itself into the parenchyma of the gland and reconstituting itself out of it. This condition we cannot well compare with anything else than a kind of filtering apparatus, something like our ordinary sand or charcoal filters.

When a gland is cut across, a structure is frequently brought to view resembling that of a kidney. At those points where the afferent vessels break up, a firmer substance is seen to lie, half surrounded by which a kind of hilus marks the spot at which the lymphatic vessels again forsake the gland. Here there is found a reticular tissue with an often distinctly areolar or cavernous structure, into which, besides the efferent lymphatic vessels, blood-vessels also enter on their way into the proper substance of the gland. Kölliker has accordingly distinguished a cortical and a medullary substance ; but the so-called medullary substance scarcely retains the character of glandular tissue. This is found chiefly in the cortical substance, which is of greater or less thickness, and it is therefore best to call the medullary substance simply the hilus, since afferent and efferent vessels lie there in close contact, just as in the hilus of the kidneys the ureters and veins emerge, whilst the arteries enter. The essential part of the gland is therefore the periphery, the often kidney-like cortical substance.

In this can be distinguished, whenever the gland is at all well developed (and in some cases of pathological enlargement it is extremely distinct) even with the naked eye, little, roundish, white or grey granules lying side by side. When the part is moderately well filled with blood, around each granule may be pretty nearly always discerned a red circle of vessels. These granules have long been called *follicles*, but it was doubtful whether they were distinct formations or mere convolutions of the lymphatic vessel protruding on the surface. Upon more delicate microscopical examination, the proper (glandular) substance of the follicles can easily be distinguished from the fibrous meshwork (stroma) which bounds them on all sides, and is externally continuous with the connective tissue of the capsule. The internal substance is chiefly composed of little cellular elements, which lie pretty loosely, being merely enclosed in a fine network of star-shaped, often nucleated trabeculæ. If we attempt to search for the lymphatic vessels in the cortical substance, but very little can be discovered of them in the stroma, and if a gland be injected, the injection penetrates right into the middle of the follicles. If a mesenteric gland be examined during chylification, that is perhaps three or four hours after a meal at which fat has been taken in abundance, its whole substance appears white and perfectly milky, and on examining individual parts of it microscopically, the minute fat-drops of the chyle may be detected every where lying between the cellular elements of the follicles. It seems, therefore, that the current of lymph forces its way between these elements, and

Fig. 61.

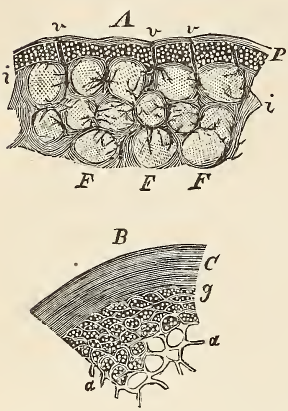


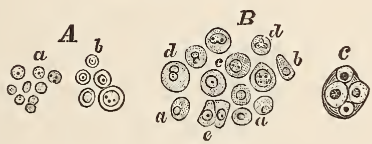
Fig. 61. Sections through the cortical substance of human mesenteric glands. *A*. View of the whole cortical substance slightly magnified: *P*, investing adipose tissue and capsule, through which blood-vessels *v*, *v*, *v* enter. *F*, *F*, *F*. Follicles of the gland, into which the blood-vessels in part plunge, at *i*, *i* the interstitial tissue separating the follicles (stroma).

B. More highly magnified (280 times). *C*. The tissue of the capsule with parallel fibrils. *a*, *a*. The reticulum, partly empty, partly filled with the nucleated contents. The whole corresponds to the outer part of a follicle.

that no really free channel for it exists, seeing that the elements lie crowded together like the particles in a charcoal filter, so that the lymph trickles out again on the other side in a more or less purified state. The follicles should accordingly be regarded as spaces filled with cellular elements but variously intersected by a trabecular network, and thus they can no longer be held to be convolutions or dilatations of the lymphatics, but must be viewed as interposing themselves in the course of these vessels after they have broken up into a series of ramifications continually increasing in minuteness.

Of the minute elements contained in the follicles, the cells of the parenchyma, some appear to become separated

FIG. 62.



and afterwards to mingle with the blood as colourless blood- or lymph-corpuscles. The more the glands become enlarged, the more numerous are the cellular elements which pass into the blood, and the larger and more perfectly developed are the individual colourless cells of the blood wont to be.

The same condition seems to prevail in the spleen. Originally we all imagined that the veins were the chan-

Fig. 62. Lymph-corpuscles from the interior of the follicles of a lymphatic gland. *A*. As usually seen; *a*, free nuclei, with and without nucleoli, simple and divided. *b*. Cells with smaller and larger nuclei, which are closely invested by the cell-wall. *B*. Enlarged cells from a hyperplastic bronchial gland in a case of variolous pneumonia (comp. in Fig. 57 the colourless blood-corpuscles from the same source). *a*. Largish cells with granules, and single nuclei. *b*. Club-shaped cells. *c*. Larger cells with larger nuclei and nucleoli. *d*. Division of nuclei. *e*. Club-shaped cells in close apposition (cell-division ?). *C*. Cells with an endogenous brood. 300 diameters.

nels by which the colourless corpuscles were conveyed away from the spleen; but in this instance also I have come to the conclusion that their removal is in all probability effected by means of the lymphatic vessels.

LECTURE IX.

MARCH 13, 1858.

PYÆMIA AND LEUCOCYTOSIS.

Comparison between colourless blood- and pus-corpuscles—Physiological re-absorption of pus; incomplete (inspissation, cheesy transformation), and complete (fatty metamorphosis, or milky transformation). Intravasation of pus.

Pus in the lymphatic vessels—Retention of matters in the lymphatic glands—Mechanical separation (filtration)—Coloration by tattooing—Chemical separation (attraction): Cancer, Syphilis—Irritation of lymphatic glands, and its relation to leucocytosis.

Digestive and puerperal (physiological) leucocytosis—Pathological leucocytosis (Scrofulosis, typhoid fever, cancer, erysipelas).

Lymphoid apparatuses: solitary and Peyerian follicles in the intestines—Tonsils and follicles of the tongue—Thymus—Spleen.

Complete rejection of pyæmia as a dyscrasia susceptible of demonstration morphologically.

In a practical point of view the question of *pyæmia* forcibly intrudes itself upon us in connection with the changes which we have last considered, and as this must still be reckoned among the most controvertible of subjects, you will, I hope, allow me to enter a little more particularly into its details.

What is to be understood by pyæmia? It has generally been conceived to be a condition, in which the blood contains pus, and as pus is essentially characterized by its morphological constituents, what is meant of course is, that pus-corpuscles are to be seen in the blood. Now that we have found out, however, that the colourless corpuscles of the blood as they usually appear and are to be observed in people in the best state of health, resemble pus-corpuscles in every respect (p. 180), one essential point in the question is thus at the very outset got rid of. In order, however, to render the subject to some extent perspicuous, it is necessary to enter into the consideration of the different points of view which are here involved a little more in detail.

Colourless blood-cells are so like pus-corpuscles as easily to be mistaken for them, so that if in any specimen we meet with such elements, we can never say with certainty off-hand whether we have to deal with colourless blood-, or pus-corpuscles. Formerly, and to some extent even up to our own times, the view was very generally entertained that the constituents of pus pre-existed in the blood; that pus was only a kind of secretion from the blood, in somewhat the same way that urine is; and that it could also like a simple fluid return into the blood. This view explains, you see, the conception which has been so long preserved in the doctrine of the so called *physiological reabsorption of pus.*

It was imagined that the pus might be again taken up into the blood from the different points at which it had been deposited, and that a favourable turn was thereby effected in the disease, inasmuch as the reabsorbed pus was thus at last removed from the body. The tale went that in the case of a patient with pus in the cavity of the pleura the disease might terminate in the evacuation of purulent urine or purulent fæces, without the pus having previously made its way directly from the pleura into the urinary passages or the intestinal canal. It is therefore admitted to be possible that pus may be reabsorbed and conveyed away in substance. Afterwards, when the doctrine of pyæmia had more and more gained ground, these cases were distinguished by the name of physiological reabsorption of pus, from that which was considered to be pathological, and the only question that remained was, in what way the first process with its favourable and the second with its malignant issue could be accounted for. This matter finds its simple solution in the fact that *pus as pus is never reabsorbed.* There is no form, by which pus in substance can disappear by the way of reabsorption; it is always the fluid part of the pus which is taken up, and therefore what is called the reabsorption of pus may be referred to the two following possibilities.

In the first case, the pus with its corpuscles is at the time of the reabsorption still more or less intact. Then the pus becomes of course thicker in proportion as the fluid disappears. This constitutes the long known *thickening* (*inspissation*) of pus, whereby is produced what the French term "pus concret," which consists of a thick mass, containing the pus-corpuscles in a shrivelled condition, when not only the fluid between the pus-corpuscles (pus-serum) but a part also of that present in them has disappeared.

Fig. 63.

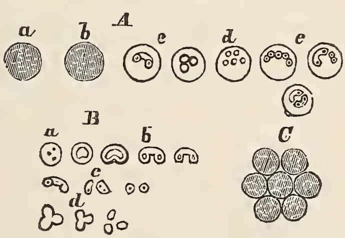
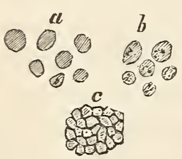


Fig. 63. *A*. Pus-corpuscles, *a* fresh, *b* after the addition of a little water, *c*—*e* after treatment with acetic acid, the contents cleared up, the nuclei which were in process of division, or already divided, visible, at *e* with a slight depression on their surface. *B*. Nuclei of pus-corpuscles in gonorrhœa; *a* simple nucleus with nucleoli, *b* incipient division, with depressions* on the surface of the nuclei, *c* progressive bi-partition, *d* tri-partition. *C*. Pus-corpuscles in their natural position with regard to one another. 500 diameters.

* By many held to be nucleoli.

Pus consists essentially of cells, which in their ordinary condition lie close to one another (Fig. 63, *C*, and between which a small quantity of intercellular fluid (*pus-serum*) exists. Within the pus-corpuscles themselves lies a substance which is likewise provided with a great quantity of water ; for nearly every specimen of pus, although it may look very thick when fresh, contains such a large amount of water that it loses a great deal more by evaporation than a corresponding quantity of blood. The latter only gives the impression of being more watery because it contains a great deal of free (intercellular), but relatively little intracellular, fluid, whilst in pus on the contrary there is a greater quantity of water in the cells, and less without them. When then reabsorption takes place, the greatest part of the intercellular fluid first disappears, and the pus-corpuscles draw nearer to one another ; soon, however, a part of the fluid from the cells themselves also vanishes, and in proportion as this is the case, they become smaller, more irregular, angular, and uneven, they assume the most singular forms, lie closely pressed together, refract the light more strongly on account of their containing a greater quantity of solid matter, and present a more homogeneous appearance.

Fig. 64.



This kind of inspissation is by no means so rare a process as it is often assumed to be, but on the contrary of extremely frequent occurrence, and almost even more important than frequent. This is namely one of the processes which lead to the formation of the much discussed

Fig. 64. Inspissated, cheesy pus. *a.* Shrivelled pus-corpuscles, diminished in size, somewhat distorted, and looking more homogeneous and solid than usual. *b.* Similar corpuscles with fat granules. *c.* Their natural position with regard to one another. 300 diameters.

cheesy products which have recently been all included under the term tubercle, and concerning which it has been shown, especially by Reinhardt, that they must to a very considerable extent really be referred to pus as their origin, and therefore be regarded as inflammatory products. Hereafter, we shall see that these observations have been employed for the deduction of false conclusions concerning tubercle itself; but that by inspissation inflammatory products can be converted into things which are called tubercles, is indubitable. It is precisely in the history of pulmonary tuberculosis that this operation plays a very prominent part. You have only to imagine shrivelled-up cells like these inclosed within the alveoli of the lungs and undergoing inspissation of their contents in one alveolus after another, and you will at length obtain a cheesy hepatization such as is usually described under the name of *tubercular infiltration*.

This imperfect reabsorption, in which only the fluid constituents are reabsorbed, leaves the mass of solid constituents lying in the part as a *caput mortuum*, as a mass deprived of vitality and no longer capable of life. This is the kind of inspissation which we see occur on a large scale in the case of imperfect reabsorption of pleuritic exudations, when very large layers of a crumbling substance remain behind in the sac of the pleura; and also round about the vertebral column in caries of the verte-

Fig. 65.

Fig. 65. Inspissated hæmorrhagic pus from a case of empyema, some of it in process of disintegration. *a*. The natural mass, containing granular débris, shrivelled pus- and blood-corpuscles. *b*. The same mass treated with water; a few granular, decolorized blood-corpuscles have become evident. *c* and *d*. After the addition of acetic acid. 300 diameters, and at *d* 520.

bræ (Spondylarthocace), cold abscesses, etc. In all these cases the reabsorption is at an end as soon as the fluid has disappeared. Herein consists the evil import of these processes. For the solid parts which are not reabsorbed, either remain lying in the part as such, or they may afterwards soften, in which case, however, they do not usually undergo reabsorption, but for the most part give rise to ulceration. At all events what is reabsorbed is not pus, but a simple fluid composed in great part of water, a few salts, and a very small quantity of albuminous matter, and there can be no question but that we have here presented to us one of the most incomplete forms of reabsorption.

The second form of purulent reabsorption is that which constitutes the most favourable case, when the pus really disappears and no essential part of it need remain behind. But here too the pus is not reabsorbed as pus, but first undergoes a fatty metamorphosis ; every single cell sets fatty particles free within it, breaks up and at last nothing further remains than fatty granules and intervening fluid. Then therefore there exist no longer either cells or pus ; and their place is occupied by an emulsive mass, a kind of milk, composed of water, some albuminous matter and fat, and in which even sugar has on various occasions been demonstrated, whereby a still greater analogy with real milk is brought about. It is this *pathological milk* which afterwards comes to be reabsorbed—once more therefore not pus, but fat, water, and salts. These are the processes which may be denominated "physiolo-

Fig. 66.

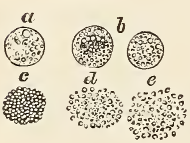


Fig. 66. Pus engaged in retrograde fatty metamorphosis (fatty degeneration). *a.* Commencement of the change. *b.* Fat-granule cells with nuclei still distinct. *c.* Granule-globule (inflammatory globule). *d.* Disintegration of the globule. *e.* Emulsion, milky débris. 350 diameters.

gical reabsorption of pus;" a reabsorption, in which pus is not reabsorbed as such, but either only its fluid constituents, or its solid ones after they have been considerably altered by an internal transformation.

There is however certainly one case in which pus in substance may become the object, not exactly of a reabsorption, but at any rate of an *intravasation*, and where this intravasated pus may circulate within the vessels; I mean the case in which a vessel receives a wound or is perforated and pus passes through the opening into its interior. An abscess may lie close to a vein, burst through the walls, and evacuate its contents into the vessel. Still more easily can such a transit be effected in lymphatic vessels which run into open abscesses. The only question therefore is how far we are entitled to consider this case as a frequent one. As far as the veins are concerned, the possibility of such an occurrence has been for the last twenty years confined within somewhat narrow limits, and the notion of the reabsorption of pus in substance through the medium of the veins has been more and more abandoned; but about its taking place by means of the lymphatics people still pretty frequently talk, and indeed they have frequently occasion to do so.

But it is almost a matter of indifference whether the pus really finds its way into lymphatic vessels from the outside, or, whether, as others assume to be the case, it owes its origin to inflammation in the lymphatic vessels; ultimately, the question is always this, how far a lymphatic vessel filled with pus is capable of effecting an evacuation of its contents into the circulating stream of blood, and producing a genuine pyæmia. The possibility of such an occurrence must as a rule be denied, and indeed for a very simple reason. All the lymphatic vessels which are in a condition to take up pus in this way are peripheral ones, whether they arise from external or internal parts, and only after a somewhat lengthened course do they gradually reach the blood-vessels. In all, interruptions are formed by the lymphatic glands, and since we know that the lymphatic vessels do not pass through the glands as wide, tortuous, and interlacing canals (p. 208), but that, after they have broken up into fine branches, they enter into spaces which are filled with cellular elements, it is manifest, that no pus-corpuscle can pass a gland.

This is a very important point of view which curiously enough is generally overlooked, although it meets with the best possible confirmation in the daily experience of the practical physician. In proof of the inevitable obstruction to the passage of solid particles through the lymphatic glands, a very pretty experiment is afforded by a custom prevalent amongst the lower classes of our population, the well-known practice of tattooing the arms and occasionally other parts. When a workman or a soldier has a number of punctures made upon his arm, and arranged so as to represent letters, signs, or figures, nearly always, in consequence of the great number of punctures, some of the superficial lymphatic vessels are injured. It could not indeed well happen otherwise than that, when whole regions of skin are circumscribed by the pricks of a needle, at least some few lymphatic vessels should be hit upon. Afterwards a substance is rubbed in which is insoluble in the fluids of the body, such as cinnabar, gunpowder, or the like, and which, remaining in the parts, causes a permanent coloration of them. But in the rubbing in a certain number of the particles find their way into lymphatic vessels, are carried along in spite of their heaviness by the current of lymph, and reach the nearest lymphatic glands, where they are separated by filtration. We never find that any particles are conveyed beyond the lymphatic glands and make their way to more distant points, or that they deposit themselves in any way in the parenchyma of internal organs. No, the mass always settles in the nearest group of glands. On examining the infiltrated glands it is easy to convince oneself that the size of the deposited particles is less than that even of the smallest pus-corpuscle.

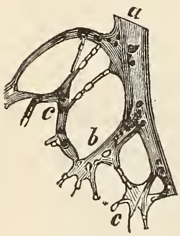
Fig. 67.

In the object which I place before you (Fig. 67) the spot has accidentally been hit upon, at which the lymphatic vessel enters into the gland, and whence, enclosed within the trabeculæ of connective tissue which are prolonged from the capsules between the follicles, it proceeds in a spiral form, and finally breaks up into its branches. Where these pass into the neighbouring follicles, which are here

Fig. 67. Section through the cortical substance of an axillary gland from an arm, the skin of which had been tattooed. A large lymphatic vessel is seen entering from the cortical substance, gently winding and breaking up into fine branches. Round about are follicles, for the most part filled with connective tissue. The dark, finely granular mass represents the deposit of cinnabar. 80 diameters.

indeed in great part filled with connective tissue, they have poured out the whole mass of cinnabar, so that in part it still lies within the intervening trabeculæ, but yet in part has penetrated into the follicles themselves. The preparation comes from the arm of a soldier who had the figures rubbed in in 1809, so that the mass has remained nearly fifty years in the same place. None of it has penetrated farther than this spot; even the next layer of follicles does not contain any. The particles are however so small, and the majority of them so minute in comparison with the cells of the gland, that they cannot at all be compared to pus-corpuscles. Now when such molecules as these are unable to pass, when such extremely minute particles cause an obstruction, it would be somewhat bold to imagine that pus-corpuscles, which are relatively large, could effect a passage.

Fig. 68.



This arrangement, gentlemen, by means of which the free current of fluid is interrupted in the lymphatic glands, and the coarser particles are retained there in quite a mechanical manner, admits, as may readily be conceived, of no other kind of reabsorption from the periphery through the medium of the lymphatic vessels than that of simple fluids. We should indeed be mistaken, if we were to consider the whole action of the lymphatic glands to consist merely in their being interposed like filters between the different portions of the lymphatic vessels. They have manifestly another part to play, inasmuch as the substance of the glands indubitably takes up

Fig. 68. Reticulum of an axillary gland filled with cinnabar, from an arm which had been tattooed (Fig. 67). *a.* Part of an inter-follicular trabecula with a lymphatic vessel; *b* one of its larger branches entering into a follicle; *c*, *c* the anastomosing, nucleated networks of the reticulum; the dark granules are particles of cinnabar. 300 diameters.

into itself certain ingredients from the fluid mass of the lymph, retains them, and thereby also alters the chemical constitution of the fluid, so that it quits the gland all the more altered because it must at the same time be assumed that the gland yields up certain constituents to the lymph, which did not previously exist in it.

I will not here enter into minute details, since the history of every *malignant tumour* affords the best examples in support of this position. When an axillary gland becomes cancerous, after previous cancerous disease of the mamma, and when during a long period only the axillary gland remains diseased without the group of glands next in succession or any other organs becoming affected with cancer, we can account for this upon no other supposition than that the gland collects the hurtful ingredients absorbed from the breast, and thereby for a time affords protection to the body, but at length proves insufficient, nay, perhaps at a later period itself becomes a new source of independent infection to the body, inasmuch as a further propagation of the poisonous matter may take place from the diseased parts of the gland. Equally instructive examples are afforded by the history of *syphilis*, in which a bubo may for a time become the depository of the poison, so that the rest of the economy is affected in a comparatively trifling degree. As Ricord has shown, it is precisely in the interior of the real substance of the gland that the virulent matter is found, whilst the pus at the circumference of the bubo is free from it; only so far as the parts come into contact with the lymph conveyed from the diseased part, do they absorb the virulent matter.

If we apply these facts to the reabsorption of pus, we are not, even in the case when it has really made its way into lymphatic vessels, at all entitled to conclude that as an immediate consequence of this irruption the blood becomes infected with the constituents of pus ; on the contrary a retention of the pus-corpuscles will probably take place within the glands, and even the fluids which succeed in passing them, will during that passage lose a great part of their noxious properties. Secondary glandular swellings show themselves in various forms after peripheral infection. How can they be explained otherwise than upon the supposition, that every contaminating (miasmatic) substance, which is to be regarded as essentially foreign or, if I may so express myself, hostile, to the body, by penetrating into the substance of the gland, produces in it a state of more or less marked irritation which very frequently increases to a real inflammation of the gland ? I shall hereafter revert to the subject of irritation and enter a little more fully into the consideration of the meaning which should be attached to it, and I will therefore here only make this remark, that according to my investigations the irritation of a gland consists in its falling into a state in which there is an increased formation of cells in it—its follicles becoming enlarged, and after a time exhibiting a much greater number of cells than before. In proportion to the extent of these processes we then see the colourless elements of the blood also increase. Every considerable irritation of a gland is followed by an increase in the proportion of lymph-corpuscles in the blood, and every process therefore which is accompanied by glandular irritation, will also have the effect of supplying the blood with larger quantities of colourless blood-corpuscles, or, in other words, of producing a leucocytotic condition. If then the opinion be entertained that pus has been absorbed, and that pus is the cause of the disturbances which have declared themselves, nothing is easier than to demonstrate the presence of cells in the blood which have the appearance of pus-corpuscles and are often present in such large quantities as to form accumulations (Fig. 58) which may be seen, in the dead body, with the naked eye, looking like minute spots of pus; or as to constitute large, continuous or granular layers on the inferior surface of the buffy coat of blood taken from a vein (Fig. 60). Apparently the proof is as plausible as possible. The observer starts with the supposition that pus has found its way into the blood; he examines the blood and really discovers elements, having all the appearance of pus-corpuscles, and in very great numbers. Even if it be admitted that colourless blood-cells may look like pus-corpuscles, still the conclusion which has been repeatedly arrived at in cases of pyæmia, is very seductive, namely, that on account of the great multitude, they cannot possibly be colourless blood-, but must be pus-corpuscles. This was the conclusion arrived at years ago by Bouchut on the occasion of an epidemic of puerperal fever which he then took to be pyæmia, but has very recently, founding his opinion upon the same observations, declared to have been acute leukæmia. It is moreover the same conclusion which Bennett came to in the much-discussed matter of priority between us, when he observed a case of indubitable leukæmia some months before I saw my first case, and inferred from the presence of colourless corpuscles in larger numbers than in any instance upon record, that it was a case of "suppuration of the blood." This conclusion of his indeed was not original, but was based upon the hæmitis of Piorry of which I lately spoke (p. 187), this physician having conceived the blood itself to become inflamed and engender pus, a state which was afterwards denominated spontaneous pyæmia by the Vienna school.

Now all these errors proceeded from the circumstance that such an enormously great number of colourless corpuscles were found in the blood. Now-a-days their occurrence can be just as simply explained according to our theory of hæmatopoiesis, as it previously seemed explicable only according to that of pyæmia. Irritation of the lymphatic glands explains without any difficulty the increase in the colourless, pus-like cells in the blood, and that too in all cases—not only in those where pyæmia was expected to be found, but also in those where it was not expected, but where the blood, notwithstanding, exhibited the same quantity of colourless corpuscles as in genuine pyæmia answering to our clinical notions of the disease

Thus it has been shown that every meal produces a certain state of irritation in the mesenteric glands, inasmuch as the constituents of the chyle which are conveyed to these bodies, act as a physiological stimulus to them. The milk which we drink, the fatty matters in our soups, the various kinds of fat distributed in a state of minute division throughout the more solid articles of our food, find their way in the form of extremely minute globules into the lacteals and diffuse themselves there just like the cinnabar in the glands; but the smallest of the fatty molecules after a time force their way through the gland. For such minute bodies therefore there still exists a real permeability in the channels of the gland, but even they are for a time retained, and it always takes a long time before the mesenteric glands after a meal again become entirely free from fat, and the propulsion of this substance through them is manifestly effected by a proportionately strong pressure. At the same time we observe an enlargement of the gland, and likewise after every meal an increase in the number of colourless corpuscles in the blood—a *physiological leucocytosis*, but no pyæmia.

In proportion as *pregnancy* advances, as the lymphatic vessels in the uterus dilate, and the interchange of material in the organ increases with the development of the fœtus, the lymphatic glands in the inguinal and lumbar regions become considerably enlarged, and that sometimes to such an extent, that, if we were to find them in a similar state at any other time, we should regard them as inflamed. This enlargement conveys into the blood an increased quantity of fresh particles of a cellular nature, and thus from month to month the number of colourless corpuscles augments. At the time of birth we may see in the defibrinated blood of nearly every puerperal woman, whether suffering from pyæmia or not, the colourless corpuscles forming a pus-like sediment. This too is a physiological form which is far from being a pyæmic one. But if care be taken to select a puerperal woman, offering symptoms of disease which correspond with those usually presented by pyæmia, nothing is easier than to find these numerous colourless multi-nuclear cells, which are precisely such as are supposed to corroborate the presence of pyæmia. These are fallacious conclusions which result from imperfect knowledge of the normal conditions of life and development. As long as we are exclusively bent upon proving the presence of pyæmia, all this may have the appearance of being a great and new occurrence, and we may, when we examine the blood of a woman in child-bed, consider ourselves justified in concluding that she has pyæmia even before its symptoms declare themselves. But we may examine when we will, we shall always find some traces of leucocytosis, just as it has already long been known that it is very common for a buffy coat to form in the case of pregnant women, because their blood generally has conveyed into it a larger quantity than usual of a more slowly contracting fibrine (hyperinosis). This is accounted for by the increased nutrition of the uterus, and by the changes, so nearly allied to inflammatory processes, which are going on in the uterine system, and are associated with a certain amount of irritation in the lymphatic glands immediately in connection with it.

If we proceed a step farther and consider pathological cases, we meet with these leucocytotic conditions in the whole of that series of diseases which are complicated with glandular irritation, and in which the irritation does not lead to a destruction of the glandular substance. During the progress of an attack of scrofula, in which, if the disease run a somewhat unfavourable course, the glands are destroyed, either by ulceration, or cheesy thickening, calcification, etc., an increased introduction of corpuscles into the blood can only take place as long as the irritated gland is still in some degree capable of performing its functions, or still continues to exist ; as soon however as the gland is withered or destroyed, the formation of lymph-cells likewise ceases and with it the leucocytosis. In all cases, on the other hand, in which a more acute form of disturbance prevails, connected with inflammatory tumefaction of the glands, an increase in the colourless corpuscles always takes place in the blood. So it is in typhoid fever, in which we observe such extensive medullary (markige) swellings of the abdominal glands ; so it is in cancer patients, when irritation of the lymphatic glands manifests itself ; so, lastly is it in the course of the processes which come under the denomination of malignant erysipelas and are so early wont to be accompanied by glandular swellings. Such is the meaning of this increase in the colourless elements which ultimately always refers us to an increased development of lymph-corpuscles within the irritated glands.

It is now of importance that I should point out to you, that at present our conceptions concerning lymphatic glands are much more comprehensive than they were a short time ago. The most recent histological investigations have shown that. in addition to the ordinary well-known lymphatic glands, which are of a certain size, a great number of smaller apparatuses exist in the body which possess precisely the same structure, but do not exhibit such a complex arrangement as we find in a lymphatic gland. To this class belong above all the *follicles of the intestines*, both the solitary and the Peyerian. A Peyer's patch is nothing more than a lymphatic gland spread out as it were upon the surface; the individual follicles of the patch, just as the solitary follicles of the digestive tract, correspond to the individual follicles of a lymphatic gland, only that the former, in man at least, are disposed in a single layer, the latter in several. The solitary and Peyerian glands have therefore nothing at all in common with the ordinary glands which pour their secretions into the intestinal canal; on the contrary, they rather hold the position, and manifestly also fulfil the functions, of lymphatic glands.

To the same category belong in all probability also the analogous apparatuses which we find grouped together in such large masses in the upper part of the digestive tract, where they form the *tonsils* and the *follicles of the root of the tongue.* Whilst in the intestine the follicles lie spread out on an even surface, in these parts the surface is inverted and the individual follicles lie around the involuted membrane.

To the same category belongs moreover the *thymus gland*, which in its interior exhibits no other differences of structure excepting that the aggregation of the follicles reaches a still higher degree than in the lymphatic glands. Whilst in most of the lymphatic glands we have a hilus, where there are no follicles, this ceases to be the case in the thymus gland which has no hilus.

Finally, to the same class belongs also a very essential constituent of the *spleen*, namely, the *Malpighian or white bodies*, which in different persons are distributed in just as different numbers throughout the parenchyma of the spleen, as the solitary and Peyerian follicles in the intestine. In a section through the spleen we see the trabeculæ radiating from the hilus towards the capsule and enclosing certain districts of glandular substance, within which the red spleen pulp lies, interrupted here and there by a sometimes greater, sometimes less, number of white bodies (follicles) of larger or smaller size, single or in groups, and sometimes almost clustered. The structure of these follicles agrees exactly with that of the follicles of lymphatic glands.

We may therefore regard this whole series of apparatuses as nearly equivalent to the lymphatic glands properly so called, and a swelling of the spleen will, under certain circumstances, furnish just as abundant a supply of colourless blood-corpuscles, as is the case when a lymphatic gland enlarges. This possibility explains how it is that, for example, in cholera, where the change in the solitary glands and Peyer's patches forms the chief part of the disease, and where the swelling of the other lymphatic glands is much less marked, we meet at an extremely early period with a considerable increase in the colourless corpuscles. Hereby is explained moreover why, in such cases of pneumonia as are connected with great swelling of the bronchial glands, an increase in the number of colourless blood-corpuscles likewise takes place, which is generally wanting in those forms of pneumonia which are not connected with such swelling. The more the irritation extends from the lung to the lymphatic glands, the more abundantly noxious fluids are conveyed from the lung to the glands—the more manifestly does the blood undergo this change.

Upon examining these different pathological processes in this manner one by one, it is really impossible to discover anything at all, which in a morphological point of view, could even in a remote degree justify the assumption of a condition such as might be called pyæmia. In the extremely rare cases, in which pus breaks through into veins, purulent ingredients may, without doubt, be conveyed into the blood, but in such instances the introduction of pus occurs for the most part but once. The abscess empties itself, and if it be large, an extravasation of blood is more apt to ensue than the establishment of a persistent pyæmia. Perhaps we shall at some future time succeed, in the course of such a process, in discovering pus-corpuscles with well-defined characters in the blood ; at present, however, the matter stands thus, that it can most positively be maintained that nobody has hitherto succeeded in demonstrating, by arguments capable of supporting even gentle criticism, the existence of a morphological pyæmia. This name therefore must, as designating a definite change in the blood, be entirely abandoned.

LECTURE X.

MARCH 17, 1858.

METASTATICAL DYSCRASIÆ.

Pyæmia and phlebitis—Thrombosis—Puriform softening of thrombi—True and false phlebitis—Purulent cysts of the heart.

Embolia—Import of prolonged thrombi—Pulmonary metastases—Crumbling away of the emboli—Varying character of the metastases—Endocarditis and capillary embolia—Latent pyæmia.

Infectant fluids—Diseases of the lymphatic apparatuses and secreting organs—Chemical substances in the blood; salts of silver—Arthritis—Calcareous metastases—Diffuse metastatic processes—Ichorrhæmia—Pyæmia as a collective name.

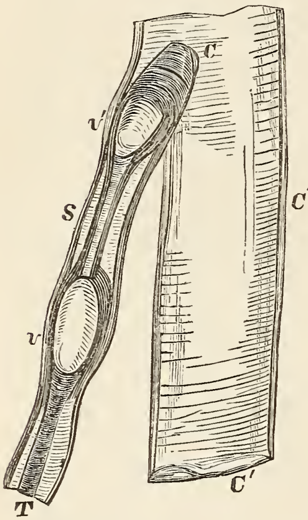
Chemical dyscrasiæ—Malignant tumours, especially cancer—Diffusion by means of contagious parenchymatous juices.

Gentlemen,—I was interrupted the last time in my description of pyæmia by the termination of the lecture, just as I was about to discuss the nature of the connection between this disease and certain affections of the vessels.

As soon as it was found necessary to abandon the original view, in accordance with which the mass of pus which was believed to be seen in a vein, was considered to have made its way in (been absorbed) through an opening in its walls, or through its yawning extremity, recourse was had to the doctrine of phlebitis, which is still the one most current. It was imagined that the pus which was regarded as the really noxious matter, was furnished as a product of secretion by the wall of the vessel (John Hunter). This doctrine, however, presented some difficulty, because it was soon pretty generally allowed that a primary purulent inflammation of the veins did not occur, but that, as was first distinctly shown by Cruveilhier, at the commencement a clot of blood is always present. Cruveilhier himself was so greatly surprised at this observation of his, that he connected a theory with it which was beyond all medical comprehension. He concluded namely from the impossibility of explaining why inflammations of the veins began with coagulation of the blood, that inflammation in every case whatever consisted in a coagulation of the blood. The impossibility of explaining phlebitis seemed to him to be got over by raising coagulation into a general law, and by referring every inflammation to a phlebitis on a small scale (capillary phlebitis). Cruveilhier was the more induced to assert this in consequence of his entertaining similar views with regard to other morbid processes, and believing that cysts, tubercles, cancer, and in short all important processes, accompanied by changes susceptible of anatomical demonstration, really ran their course within special, minute veins imagined by him. This manner of thinking, however, continued so entirely alien to that of the great majority of learned and unlearned physicians, that the separate conclusions propounded by Cruveilhier, which were adopted in medical science in part as drawn up by him, were altogether misunderstood.

Cruveilhier was right in this point, as indeed has since been more and more acknowledged, namely, that the so-called pus in the veins in the first instance never lies against the wall of the vein, but always first appears in the centre of the previously existing clot of blood which marks the outset of the process. He imagined that the pus was secreted from the wall of the vessel, but that it did not remain there, but by means of " capillary attraction" made its way to the centre of the clot. This was a very singular theory, which can only be approximatively comprehended by assuming, as it was still the custom to do in Cruveilhier's time, pus to be a simple fluid. But apart from these extremely obscure interpretations, the fact remains constant, against which even now no argument can be advanced, that before a trace of inflammation is visible, we find a clot, and that shortly afterwards in the middle of this clot a mass displays itself, which differs in appearance from the clot, whilst on the other hand it exhibits a greater or less resemblance to pus.

Fig. 69.



With this observation as my starting point, I have endeavoured to clear up the doctrine of phlebitis, as far as lies in my power, by substituting for the mysticism which pervaded Cruveilhier's interpretation, merely a statement of the real facts. We do not know that inflammation as such has any necessary connection with coagula ; on the contrary, it has turned out that the doctrine of stasis rests upon manifold misinterpretations. Inflammation may unquestionably exist when the current of blood within the vessels of the affected part is perfectly free and unobstructed. If we therefore leave inflammation on one side and confine our attention simply to the coagulation

Fig. 69. Thrombosis of the saphenous vein. *S.* Saphenous vein. *T.* Thrombus: *v*, *v′* thrombi seated on the valves (valvular) in process of softening, and connected by more recent and thinner portions of coagulum. *C.* Prolongation of the plug, projecting beyond the mouth of the vessel into the femoral vein *C′*.

of the blood, to the formation of the clot (thrombus), it seems most convenient to comprehend the whole of this process under the term *Thrombosis.* I have proposed to substitute this term for the different names, phlebitis, arteritis, etc., inasmuch as the affection essentially consists in a real coagulation of the blood *at a certain fixed spot.*

Upon investigating the history of these thrombi, we find that the puriform mass which is met with in their interior does not originate in the wall, but is produced by a direct transformation of the central layers of the clots themselves, a transformation indeed which is of a chemical nature, and during which, with a result similar to that which can be artificially obtained by the slow digestion of coagulated fibrine, the fibrine breaks up into a finely granular substance and the whole mass becomes converted into *débris.* This is a kind of softening and retrograde metamorphosis of the organic substance, in the course of which from the very commencement a number of extremely minute particles become visible ; the large threads of fibrine crumble into pieces, these again into smaller ones, and so on until after a certain time has elapsed the chief part of the mass is found to be composed of small, fine, pale granules (Fig. 70, *A*). In cases in which the fibrine is comparatively very pure, we frequently see scarcely anything else than these granules.

Fig. 70.

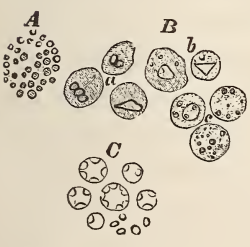


Fig. 70. Puriform mass of débris from softened thrombi. *A.* The granules seen in disintegrating fibrine, varying in size, and pale. *B.* The colourless blood-corpuscles set free by the softening, some of them in process of retrograde metamorphosis; *a*, with multiple nuclei, *b*, with simple, angular nuclei and a few fat-granules, *c*, non-nucleated (pyoid) corpuscles, in a state of fatty metamorphosis. *C.* Red blood-corpuscles undergoing decolorization and disorganization. 350 diameters.

You see, gentlemen, the microscope solves the difficulties in a very simple manner, by demonstrating that this mass, which looks like pus, is not pus. For we understand by pus a fluid essentially provided with cellular elements. Just as little as we can imagine blood without blood-corpuscles, just as little can pus exist without pus corpuscles. But when, as in the present instance, we find a fluid which is nothing more than a mass pervaded by granules, this may indeed, as far as external appearance goes, look like pus, but never ought to be regarded as real pus. *It is a puriform, but not a purulent substance.*

But now we frequently see that in addition to these granules a certain proportion of other structures show themselves, for example, really cellular elements (Fig. 70, *B*), which are round (spherical), or angular, present one, two, or more nuclei, frequently lie tolerably close to one another, and in reality exhibit a great similarity to pus-corpuscles, the distinction at most being that very often fat-granules occur in them, indicating that a process of disintegration is going on. Whilst therefore in individual cases there can, on account of the often very greatly preponderating mass of débris, exist no doubt as to what the observer has before him, in others considerable doubts may exist as to whether real pus is not present. These doubts cannot be removed in any other way than by an examination into the history of the development of the puriform mass. Now that we have already seen that colourless blood- and pus-corpuscles perfectly agree with one another in form, so that it is impossible to draw a real distinction between them, the question which suggests itself in cases where we find round, colourless cells in a clot of blood, whether these cells are colourless blood- or pus-corpuscles, can only be decided by determining whether the corpuscles were present in the thrombus from its very commencement, or only sprang up in it afterwards, or found their way into it in some other manner. Now upon accurately following up the different stages of the process, the very positive result is obtained that the corpuscles pre-exist, and that they do not arise within the clot, and are not forced into it. Even when quite recent thrombi are examined, the corpuscles are found in many places heaped up in great masses, so that, when the fibrine breaks up, they are set free in such numbers, that the débris are nearly as rich in cells as pus. It is with this process just as when water which is thoroughly impregnated with solid particles is frozen and then exposed to a higher temperature; when the ice melts the enclosed particles must of course again come to light.

To this view of the matter one objection may be raised, to wit, that we do not see the red blood-corpuscles set free in a similar manner. The red corpuscles, however, perish very early; they are soon seen to grow pale; they lose a portion of their colouring matter and become smaller, whilst numerous dark granules appear at their circumference (Figs. 54, *a;* 70, *C*), and in the majority of cases they entirely disappear, nothing but these granules at last remaining. Still there are also cases in which the red corpuscles retain their integrity within the softening mass. As a rule they certainly perish, and it is precisely upon this that depends the peculiarity of the transformation, by means of which a yellowish white fluid arises bearing the external appearance of pus. And for it too an explanation may be found without any particular difficulty, if it be borne in mind how very trifling is the power possessed by the red blood-corpuscles of resisting the most various reagents. If to a drop of blood you add a drop of water, you see the red corpuscles disappear before your eyes while the colourless ones remain behind.

That therefore, which according to the ordinary nomenclature is called suppurative phlebitis, is neither suppurative, nor yet phlebitis, but a process which begins with a coagulation, with the formation of a thrombus in the blood, and afterwards presents a stage in which the thrombi soften, so that the whole history of the process is contained in the history of the thrombus. But here I must impress upon you that I do not, as has been said of me in different quarters, deny the possibility of a real phlebitis, and that I have not in any way discovered that there is no such thing as phlebitis. *No! phlebitis certainly does exist.* But it is an inflammation which really affects the walls, and not the contents of a vessel. In the larger vessels the most different layers of their walls may become inflamed and enter upon every possible phase of inflammation, and yet all the while their channel remain entirely unaltered. In accordance with the views generally entertained the internal coat of the vessels was thought to be like a serous membrane, and as this readily furnishes fibrinous exudations or purulent masses, the same was supposed to be the case with the internal coat. Concerning this point a series of investigations was years ago set on foot, and I too have occupied myself at various times with it, but hitherto no experimenter, who carefully prevented the blood from streaming into the vessels, has succeeded in producing an exudation, which was deposited in their cavity. On the contrary, when the wall is inflamed, the "exuded matter" (Exsudatmasse) passes into the wall, which becomes thicker, cloudy, and subsequently begins to suppurate. Nay, even abscesses may form, which cause the wall to bulge on both sides like a variolous pustule, without any coagulation of the blood ensuing in the cavity of the vessel. At other times, certainly, phlebitis, properly so called (and in like manner arteritis and endocarditis), is the cause of thrombosis, in consequence of the formation of inequalities, elevations, depressions, and even ulcerations upon the inner wall which favour the production of the thrombus. Still, wherever phlebitis, in the usual sense of the word, takes place, the alteration in the coat of the vessel is almost always a secondary one, and indeed occurs at a comparatively late period.

The process runs its course in such a way that the most recent parts of the thrombus always consist of the blood which has most lately coagulated. The softening, the partial liquefaction, generally commences in the centre, in the oldest layers, so that, when the thrombus has attained a certain size, there exists in the midst of it a cavity of larger or smaller dimensions, which gradually enlarges and keeps approaching more and more closely to the wall of the vessel. But in general this cavity is shut off in an upward and downward direction by means of a more recent and tougher portion of the clot which, after the manner of a cap, takes care that, as Cruveilhier expresses himself, the "pus" remains sequestered, and all contact between the *débris* and the circulating blood is prevented. Only sideways does the softening extend until it at last reaches the wall of the vessel itself; this becomes altered, it begins to grow thicker and at the same time cloudy, and ultimately even suppuration takes place within the walls.

The same thing which we have hitherto considered in the veins occurs also in the heart. In the right ventricle especially we not unfrequently see what are called purulent cysts between the trabeculæ of its wall. They project into the cavity like small rounded knobs, and form little pouches which, when cut open, contain a soft pulp that may present a completely pus-like appearance.

People have plagued themselves to an indefinite extent about these purulent cysts and invented all possible theories to account for them, until at length the simple fact came out, that their contents are frequently nothing more than a finely granular pulp of an albuminous substance, which does not offer even the slightest resemblance in its more intimate structure to pus. This was so far tranquillizing, as there is no observation as yet on record of the death of any patient from pyæmia who had sacs of this description even in pretty considerable number, but it ought to have struck those who are so much inclined to establish a connection between peripheral thromboses, which are however just the same thing, and pyæmia.

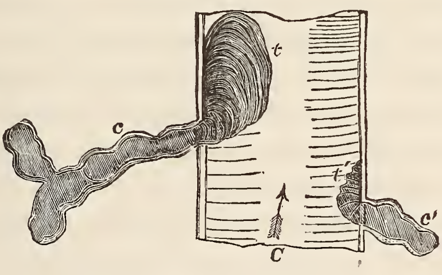
For the question naturally arises how far particular disturbances that can be designated by the name of pyæmia may, in consequence of the softening of the thrombi, be evoked in the body. To this in the first place we may answer that secondary disturbances certainly are very frequently occasioned, but not so much by the immediate introduction of the softened masses as fast as they become liquid into the blood, as by the detachment of larger or smaller fragments from the end of the softening thrombus which are carried along by the current of blood and driven into remote vessels. This gives rise to the very frequent process upon which I have bestowed the name of *Embolia*.

This is an occurrence which we can here only briefly touch upon. In the peripheral veins the danger proceeds chiefly from the small branches. By no means rarely do these become quite filled with masses of coagulum. As long however as the thrombus is confined to the branch itself, so long the body is not exposed to any particular danger; the worst that can happen is that, in consequence of a peri- or meso-phlebitis,* an abscess

* See the Author's "Gesammelte Abhandl.," p. 484.

may form and open externally. Only the greater number of the thrombi in the small branches do not content themselves with advancing up to the level of the main trunk, but pretty constantly new masses of coagulum deposit themselves from the blood upon the end of the thrombus layer after layer, the thrombus is prolonged beyond the mouth of the branch into the trunk in the direction of the current of the blood, shoots out in the form of a thick cylinder farther and farther, and becomes continually larger and larger. Soon this *prolonged* thrombus (Fig. 71, *t*) no longer bears any proportion to the original (*autochthonous*) thrombus (Fig. 71, *c*), from which it proceeded. The prolonged thrombus may have the thickness of a thumb, the original one that of a knitting-needle. From a lumbar vein, for example, a plug may extend into the vena cava as thick as the last phalanx of the thumb.

FIG. 71.



It is these prolonged plugs that constitute the source of real danger; it is in them that ensues the crumbling away which leads to secondary occlusions in remote vessels. They are the parts from which larger or smaller

Fig. 71. Autochthonous and prolonged thrombi. *c*, *c'*. Smallish, varicose, lateral branches (circumflex veins of the thigh), filled with autochthonous thrombi which project beyond the orifices into the trunk of the femoral vein. *t*. Prolonged thrombus produced by concentrically apposed deposits from the blood. *t'*. Prolonged thrombus, as it appears after fragments (emboli) have become detached from it.

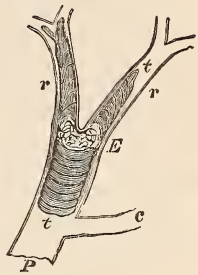
particles are torn away by the blood as it streams by (Fig. 71, *t'*).

Through the vessel originally occluded no blood at all flows ; in it the circulation is entirely interrupted : but in the larger trunk through which the blood still continues its course, and into which only at intervals the thrombus-plugs project, the stream of blood may detach minute particles, hurry them away with it, and wedge them tightly into the nearest system of arteries or capillaries.

Thus we see, that as a rule all the thrombi at the periphery of the body produce secondary obstructions and metastatic deposits in the lungs. I long entertained doubts whether I ought to consider the metastatic inflammations of the lungs one and all as embolical, because it is very difficult to examine the vessels in the small metastatic deposits, but I am continually becoming more and more convinced of the necessity of regarding this mode of origin as the rule. When a considerable number of cases are compared statistically, the result obtained is that every time metastatic deposits occur, thrombosis is also present in certain vessels. Quite recently, for example, we have had a tolerably severe epidemic of puerperal fever, and in this it was found that, however manifold the forms the disease assumed, yet all those cases which were accompanied by metastases in the lungs, were also attended with thrombosis in the region of the pelvis or in the lower extremities, whilst in the inflammations of lymphatic vessels the pulmonary metastases were wanting. Such statistical results carry with them a certain amount of compulsory conviction, even where strict anatomical proof is wanting.

Into the pulmonary artery the introduced fragments of thrombus of course penetrate to different depths according to their size. Usually a fragment of the kind sticks fast where a division of the vessel takes place (Fig. 72, *E*), because the diverging vessels are too small to admit it. In the case of very large fragments even the principal trunks of the pulmonary artery are blocked up, and instantaneous asphyxia ensues; other fragments again penetrate into the most minute arteries and there give rise to very minute, and sometimes miliary inflammations of the parenchyma. In explanation of these small and often very numerous deposits, I must mention a conjecture which only occurred to me whilst engaged in my more recent observations, but which I do not scruple to declare to be a necessary inference. I believe namely that, when a considerable fragment of a thrombus becomes wedged at a certain point in an artery, it may in its turn crumble away through the onward pressure of the blood, and thus the minute particles to which this crumbling of the larger plug gives rise be conveyed into the small branches into which the vessel breaks up. Thus alone does it seem to me that the fact can be explained, that in the district supplied by an artery of considerable size a number of little deposits of the same sort are often found.

Fig. 72.



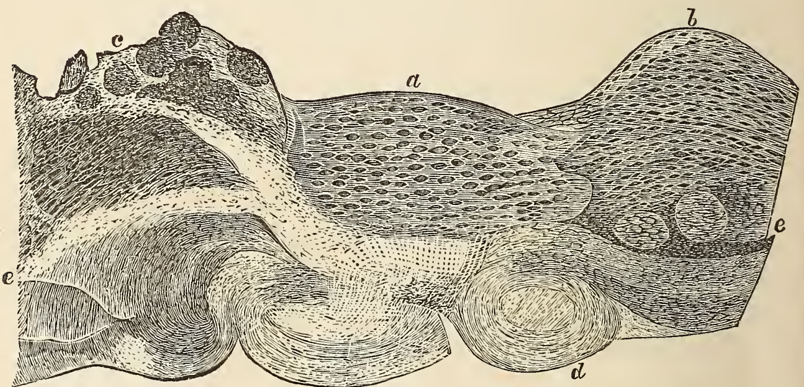
This whole series of cases has nothing whatever to do with the question, whether there is pus in the blood or not. We have in them to deal with bodies of quite a different nature, with fragments of coagula in a more or less altered condition, and according as this alteration has assumed this or that character, the nature of the pro-

Fig. 72. Embolia of the pulmonary artery. *P.* Moderately large branch of the pulmonary artery. *E.* The embolus, astride upon the angle (spur—Sporn), formed by the division of the artery. *t*, *t'*. The capsulating (secondary) thrombus: *t*, the portion in front of the embolus reaching to the next highest collateral vessel *c*; *t'*, the portion behind the embolus, in a great measure filling up the diverging branches *r*, *r'*, and ultimately terminating in the form of a cone.

cesses which arise in consequence of the obstruction may also be very different. If, for example, a gangrenous softening has taken place at the original site of the coagulum, the metastatic deposit will also assume a gangrenous character, just as this would be the case if gangrenous matter were inoculated. So, *vice versâ*, it also happens that the secondary disturbances, like those at the spot whence the fragments were detached, run a very favourable course, the embolus like the thrombus becoming converted into pigment and connective tissue, and at the same time growing smaller.

This group of processes must be separated from those ordinarily occurring in pyæmia all the more, because the same processes are also met with on the other side of the

Fig. 73.



lungs in the regions belonging to the left side of the circulation, where they often run the same course and pre-

Fig. 73. Ulcerative endocarditis affecting the mitral valve. *a*. The free, smooth surface of the mitral valve, beneath which the connective-tissue-corpuscles are enlarged and clouded, whilst the intervening tissue is denser than usual. *b*. A considerable hilly swelling caused by increasing enlargement and cloudiness of the tissue. *c*. A swollen part which has already begun to soften and break up. *d*, *d*. The tissue at the lower part of the valves which is stil but little altered, with numerous corpuscles, the results of proliferation. *e*, *e*. The commencement of the enlargement, cloudiness, and proliferation of the corpuscles. 80 diameters.

sent the same results, but are still less dependent upon an original phlebitis. Thus, for example, *endocarditis* by no means seldom forms the starting point of such metastases. Ulceration takes place in one of the valves of the heart, not by means of the formation of pus, but in consequence of an acute or chronic softening ; crumbling fragments of the surface of the valve are borne away by the stream of blood and reach with it far distant points. The kind of obstruction which these masses produce is altogether similar to that which the thrombi in the veins give rise to, but they present a different chemical constitution. Their minuteness also and their friability favour their penetration into the smallest vessels in a high degree. Therefore we do not so very unfrequently find the obstructing mass in minute microscopical vessels

Fig. 74.

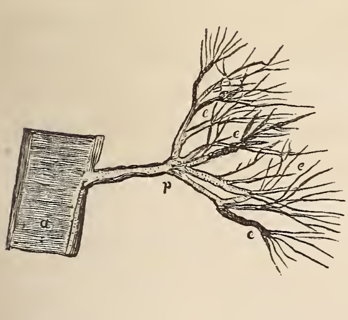


Fig. 75.

Fig. 74—75. Capillary embolia in the tufts (penicilli) of the splenic artery after endocarditis (Cf. Gesammelte Abhandlungen zur wiss. Medicin. 1856, p. 716). 74. Vessels of a tuft magnified 10 times, in order to show the position of the occluding emboli in the arterial district. 75. An artery filled a little before its division, and in the branches into which it next divides, with fragments of the finely granular embolic mass (Cf. Fig. 73, *c*). 300 diameters.

which are no longer to be followed with the naked eye, and in them it usually extends as far down as a point of division and somewhat beyond. This mass constantly presents a finely granular appearance, and does not consist of the coarse débris that we find in the veins, but of a very fine, yet at the same time dense, granular matter; chemically, it possesses the extremely convenient quality for examination of being remarkably resistant to the ordinary tests, and thus readily distinguished from other matters. This is *capillary embolia* properly so called, one of the most important forms of metastasis, which frequently gives rise to minute deposits in the kidney, the spleen, and the substance of the heart itself; in certain cases occasions sudden occlusions in the vessels of the eye or brain, and according to circumstancs produces metastatic deposits or sudden functional disturbances (amaurosis, apoplexy). Here too one can clearly convince oneself that in recent cases the wall of the vessel is quite unaltered at the seat of the affection; nay here indeed the doctrine of phlebitis would no longer suffice, since these are not vessels which possess vasa vasorum, and concerning which it might be assumed that a secretion proceeded from the wall inwards. In these cases it is impossible to regard the occluding mass in any other light than as one primarily existing in the vessel, and in no wise dependent upon the condition of its wall.

Perhaps this description has convinced you, gentlemen, that two essential errors have existed in the doctrine of pyæmia; the one, that people thought they had found pus-corpuscles in the blood, when only colourless blood-corpuscles were really present; the second, that they thought they had found pus in vessels in which nothing more than the products of the softening of fibrine existed. Yet we have ascertained that this last class of cases certainly furnishes the most important source of genuine metastatic deposits. But in my opinion, the history of the processes which have been called pyæmia is not confined to these conditions. When the process runs its course free from all complication, so that from the original seat of the disease (thrombosis in a vein, endocarditis, etc.), only *solid* masses in an undecomposed state are detached and cause obstructions, the real process is in many cases brought to notice only in consequence of the metastasis. There are cases which run their course so latently that all the earlier stages of the affection are entirely overlooked, and that the first rigors which declare themselves announce that the development of the metastatic processes has already set in. Usually, however, another condition must be taken into consideration, which is not directly accessible either to the coarser or more delicate modes of anatomical investigation ; I mean certain *fluids*, which in themselves bear no immediate and necessary relation to pus as such, but manifestly differ very much from one another in their nature and origin.

Whilst I was engaged in the consideration of the changes which lymph undergoes, I pointed out to you (p. 220), that fluids which were taken up by lymphatic vessels were not only freed in the filters of the lymphatic glands from corpuscular elements, but were also in part attracted and retained by the substance of the glands, so as to display some activity within them. Similar effects appear to take place also elsewhere than in the glands. Where the reabsorption was primarily effected by the veins, this must, of course, always be the case. There is namely a series of peculiar phenomena which pervade all infectious processes as a constant element. These are on the one hand the changes which the lymphatic and lymphoid glands may undergo not so much at the seat of the primary affection as rather in the body generally, and on the other hand the changes which the secreting organs offer, through which the matters have to be excreted.

It was for some time believed that *tumefaction of the spleen* was characteristic of typhoid fever, inasmuch as it formed a parallel to the swellings of the mesenteric glands occurring in that disease. But more accurate observation has shown that a great number of feverish conditions which follow a more or less typhoid course, and affect the nervous system in such a manner that a state of depression is brought about in its most important central organs, set in with swelling of the spleen. The spleen is a remarkably sensitive organ, which swells not only in intermittent and typhoid fever, but also in most other processes in which noxious, infectant matters have been freely taken up into the blood. No doubt the spleen must always be considered in its near relationship to the lymphatic system, but its diseases in addition usually bear a very direct relation to analogous diseases of the important glands in its vicinity, especially the liver and the kidneys. In most cases of infection do these three organs exhibit corresponding enlargement connected with real changes in their interior; but since these changes do not, even on microscopical examination, apparently present anything remarkable, the attention of the observer is chiefly attracted by the result which is obvious to the naked eye, namely, the great swelling. On careful comparison, however, a good deal is discovered, so that we can affirm with certainty that the gland-cells quickly become changed, and that disturbances early show themselves in the elements by means of which the secretion is to be accomplished. I shall revert to this subject hereafter. Allow me now, in elucidation of these conditions, in the first place to advert to one or two more obvious examples which are accessible to direct observation.

We know that when any one takes *salts of silver*, they penetrate into the different tissues of his body; and if we do not employ them in a really corrosive and destructive manner, the silver penetrates into the elements of the tissues in a state of combination, the nature of which has not yet been satisfactorily made out, and, when it has been made use of long enough, produces a change of colour at the point of application. A patient who had in Dr. Von Graefe's out-patient room on the 10th November received a solution of nitrate of silver as a lotion, very conscientiously employed the remedy up to the present time (17th March); the result of which was that his conjunctiva assumed an intensely brown, nearly black appearance. The examination of a piece cut out of it showed that silver had been taken up into the parenchyma, and indeed in such a manner that the whole of the connective tissue had a slightly yellowish brown hue upon the surface, whilst in the deeper parts the deposition had only taken place in the fine elastic fibres of the connective tissue, the intervening parts, the proper basis-substance, being perfectly free. But deposits of an entirely similar nature take place also in more remote organs. Our collection contains a very rare preparation from the kidneys of a person who on account of epilepsy had long taken nitrate of silver internally. In it may be seen the Malpighian bodies, in which the real secretion takes place, a blackish blue colouring of the whole of the membrane of the coils of the vessels, limited to this part in the cortex, and appearing again, in a similar, though less marked form, only in the intertubular stroma of the medullary substance. In the whole kidney, therefore, besides the parts which constitute the real seat of their secretion, those only are altered which correspond to the ultimate system of capillaries in the medullary substance.

Of the well-known discoloration of the skin by silver I need not speak here.

Another instance is afforded us by *gout*. If we examine the concretions (tophi) in the joints of a gouty person, we find they are composed of very delicate, needle-shaped, crystalline deposits of all possible sizes, and consisting of urate of soda, with at most here and there a pus- or blood-corpuscle lying between them. We have here therefore also, as when silver has been employed, to deal with a material substance which is usually excreted by the kidneys, and that indeed not rarely in such large quantities, that deposits form even within the kidney itself and large crystals of urate of soda accumulate, especially in the uriniferous tubules of the medullary portion, so as sometimes to lead even to an occlusion of the tubules. If, however, this secretion does not proceed in a regular manner, the immediate result is an accumulation of urates in the blood, as has been shown in a very able manner by Garrod. Then at last deposits begin to form at other points, not throughout the whole body, nor uniformly in all parts, but at certain definite points and in accordance with certain rules.

Here we have to do with very different forms of metastasis from those with which we became acquainted whilst considering the nature of embolia. That the changes which ensue in the substance of the kidney, in consequence of the absorption of silver from the stomach, accord with what has in pathology since times of old been termed metastasis is unquestionable. This consists in a transferrence of matter from one spot to another, so that the same substance which had previously been present in the first comes and lodges in the second, and the secreting organ takes up minute particles of the matter into its own tissue. This is what we find constantly recurring in the history of all metastatic deposits of this kind, in which only matters in solution and not particles of a visible and mechanical nature are present in the blood. The urate of soda cannot be directly seen in the blood of the gouty person, unless it have previously been collected by the help of chemical processes ; and just as little the salts of silver.

I have moreover described a new form of metastasis which is certainly more rare but yet belongs to the same category. When calcareous salts are reabsorbed from the bones in large quantity, the bone-earth is generally excreted by the kidneys, likewise in large quantity, so that sediments form in the urine, the knowledge of which has straggled down to us in the history of osteomalacia [mollities ossium], from the notorious Mme. Supiot in the last century. But this regular excretion of the calcareous salts is not unfrequently impaired by disturbances in the functions of the kidneys, in the same way as in arthritis the excretion of urate of soda ; then there also arise metastatic deposits of bone-earth, but at other points, namely the lungs and the stomach. Considerable portions of the lungs sometimes become calcified without any injury to the permeability of the respiratory passages ; the diseased parts look like fine bathing sponge. The mucous membrane of the stomach becomes filled in like manner with calcareous salts, so that it feels like a rasp and grates under the knife without the glands of the stomach becoming directly implicated ; they are merely imbedded in a stiffened mass, and possibly even thus secretion might take place from them.

To these kinds of metastasis in which definite substances, though not in a palpable form, but in solution, find their way into the mass of the blood, careful attention must at all events be paid when we endeavour to unravel the complex mass of conditions which are comprehended under the term pyæmia. I see at least no other possible way of explaining certain more diffuse processes, which do not present themselves in the form of the ordinary circumscribed metastatic deposits. To this class belongs that metastatic pleurisy which develops itself without any metastatic abscesses in the lungs—that seemingly rheumatic articular affection, in which no distinct deposit is found in the joints—that diffuse gangrenous inflammation of the subcutaneous connective tissue which cannot well be accounted for unless we suppose a more chemical mode of infection. Here we have, as may be seen in cases of variolous and cadaveric infection, to deal with a transferrence of *corrupted, ichorous juices* into the body ; and we must admit the existence of a dyscrasia (*ichorous infection*) in which this ichorous substance which has made its way into the body, displays its effects in an acute form in the organs which have a special predilection for such matters.

Now it may possibly happen that in the course of the same case of illness the three different changes which we have considered may coexist. An increase in the number of the colourless corpuscles (leucocytosis) may take place to such an extent as to tempt one to believe in the presence of a morphological pyæmia. This will at all events always be the case when the process has been connected with extensive irritation of the lymphatic glands. The formation of thrombi, moreover, and embolia with metastatic deposits may occur. And finally there may at the same time be taking place an absorption of ichorous or putrid juices (ichorrhæmia, septhæmia). These three different conditions may present themselves as complications one of the other, but do not necessarily coincide. If it be wished therefore to retain the term pyæmia, let it be reserved for such complications as these, only we must not *seek for a common central point in a* *purulent infection of the blood*, but the term must be regarded as a collective name for several processes dissimilar in their nature.

I hope, gentlemen, that what I have now imparted to you will be sufficient to put you in possession of the chief bearings of the subject. Of course no real demonstration can be afforded without reference to distinct cases. You will, however, yourselves have sufficient opportunity for testing the exactitude of this description of mine, and I shall be glad if you find that important data have thereby also been furnished, by which clearer conceptions with regard to the really practical, and especially the therapeutical, questions arising out of the subject, may be obtained.

Now that we have become acquainted not only with corporeal particles, but also with certain chemical substances as the originators of dyscrasia, lasting for a longer or shorter time according as the supply of these particles and substances continues for a longer or shorter period, we may briefly revert to the question, whether, in addition to these forms, a kind of dyscrasia can be shown to exist in which the blood is the permanent seat of definite changes. We must answer this question in the negative. The more marked a really demonstrable contamination of the blood with certain matters is, the more manifest is the relatively acute course of the process. Just the very forms* in which medical men are most apt to console themselves—especially for the shortcomings of the therapeutical results, with the reflection that they have to do with the deeply rooted and incurable chronic dyscrasia—just these forms depend, I imagine, least of all upon an original change in the blood ; for these are pre-

* Tubercle, cancer, purpura, syphilis, etc.

cisely the cases, in the majority of which extensive alterations are discovered in certain organs or in individual parts. I cannot assert that investigation has in this matter in any way been pushed to its utmost limits, I can only say that every resource afforded by microscopical or chemical analysis has hitherto been fruitlessly employed in investigating the part played by the blood in these processes ; and that, on the other hand, we are in most of them able to demonstrate important changes in larger or smaller groups of the ultimate constituents of organs ; and that on the whole the probability that the dyscrasia should in these instances also be regarded as secondary, and as derived from definite points in organs, becomes stronger every day. I shall have to examine this question a little more closely when I come to consider the theory of the propagation of malignant tumours, in the case of which recourse is, you know, so often had to the supposition that the malignancy has its root in the blood which gives rise to the local affections. And yet it is precisely in the course of these processes that it is comparatively most easy to show the mode of propagation, both in the immediate neighbourhood of the diseased part, and in remote organs ; and it is in them we find, that there is one circumstance which especially favours the extension of such processes, namely the *abundance of parenchymatous juices* in the pathological formation. The drier a new formation is, the less in general are its powers of infecting, both nearer and more distant parts. The mode of propagation itself commonly entirely agrees with what we have already said ; first of all, a conveyance of the morbid matter though the lymphatic channels, and then an affection of the lymphatic glands, takes place, and it is only by degrees that processes of a similar nature declare themselves in more remote organs. Or the process may here too in the first instance encroach upon the walls of the veins, so that they become really cancerous, and after a certain time the cancer either grows directly through the walls into the vessel and there continues its course, or a thrombus forms at the point, which invests the cancerous plug in a greater or less degree and into which the mass of cancer grows. Here, therefore, we see a diffusion of the disease may possibly take place in two different manners, but the diffusion of corpuscular elements only in one, when, namely, an irruption ensues into the veins. An absorption of cancer-cells by means of the lymphatics cannot indeed in itself be ranked amongst impossibilities, but at all events this much is certain, that no propagation of the disease can take place until the lymphatic glands have in their turn undergone a complete cancerous transformation, and similar masses of cancer push on their growth from them into their efferent vessels. In no case can a peripheral lymphatic vessel sweep along into the blood the cells of the cancer so simply as it does the fluid parts ; this is only conceivable and possible in the case of the veins. But even in that case there is not the slightest probability that noxious matters are frequently diffused by their means, and for the simple reason that the metastases of cancer very frequently do not correspond with those with which we have become acquainted as occurring in embolia. The usual form of metastatic diffusion in cancer follows rather the direction of the secreting organs. The lungs, as is well known, are much more rarely invaded by cancerous disease than the liver, not only after gastric and uterine, but also after mammary cancer which would necessarily rather produce cancer in the lungs, if it were anything corpuscular which was conveyed away, became stagnant and gave rise to a new eruption of the disease. The manner in which the metastatic diffusion takes place seems, on the contrary, to render it probable that the transferrence takes place by means of certain fluids, and that these possess the power of producing an infection which disposes different parts to a reproduction of a mass of the same nature as the one which originally existed. We need only imagine a process similar to that which we see upon a large scale in small pox. The pus of small pox when directly inoculated does indeed induce the disease, but the contagium* is also volatile, and a person may have pustules over his skin after merely breathing air of a certain character. A similar state of things seems to prevail in cases, in which, in the course of heteroplastic processes, dyscrasiæ occur which do not burst out afresh at points which, according to the direction of the current of blood or lymph, would be most directly exposed to them, but at remote spots. As the salts of silver do not deposit themselves in the lungs, but pass through them to be precipitated only when they reach the kidneys or the skin, so an ichorous juice may pass from a cancerous tumour through the lungs without producing any change in them, and yet at a more remote point, as for example in the bones of a far distant part, excite changes of a malignant nature.

* *i. e.* Contagious matter.—*Transl.*