On the anatomical characters of some adventitious structures, being an attempt to point out the relation between the microscopic characters and those which are discovered by the naked eye / by Thomas Hodgkin.

To Professor Allen Thompson
with the author's kind regards

ON

THE ANATOMICAL CHARACTERS

OF SOME

ADVENTITIOUS STRUCTURES,

BEING AN ATTEMPT TO POINT OUT THE RELATION BETWEEN THE MICROSCOPIC CHARACTERS AND THOSE WHICH ARE DISCERNIBLE BY THE NAKED EYE.

By THOMAS HODGKIN, M.D.

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By THOMAS HODGKIN, M.D.

READ JUNE 13TH, 1843.

In the spring of 1829, I had the honour of laying before this Society the result of an inquiry in which I had then been for some years engaged, respecting the anatomical characters of a large and important group of adventitious structures. From that period to the present time, I have not ceased to embrace the opportunities which presented themselves, for continuing the same kind of research.

As I have already published some of the results which I have obtained, in my lectures on the morbid anatomy of the serous and mucous membranes, it is not my intention to trespass on the Society by a repetition of the details which may be found there.

My object, on the present occasion, is rather to endeavour to demonstrate the relation which some of the phenomena connected with these structures, which have been pointed out by able and distinguished observers, bear to those which have been noticed and described by myself, and to show that whilst our observations have been in some respects dissimilar in their kind, they are not, in their general results, to be regarded as clashing, or mutually opposed to each other, but that having been directed to different parts of the subject, they require to be united in order to render it complete.

In the course of this attempt, I shall, however, take the opportunity to reply to some objections which have been urged against my previous statements, and to record some further facts which have fallen under my observation.

My former communication merely claimed to be the announcement of the anatomical character of some of the structures referred to; the main object being to show their assumption of the type of compound serous cysts, the modifications of which I described as a preliminary step. I endeavoured to show, that whilst possessing this type, variously modified by the forms of the cysts, and the relative proportion of the solid to the fluid parts, there likewise existed great and important differences dependent on the material by which this form or type may be assumed, and the character and degree of vascular organisation which it receives. At that period, the very curious and important researches

regarding the function and development of nucleated cells had either not been made, or were generally unknown in this country; and microscopic inquiry, not being necessary to that part of the subject with which I was engaged, had not been undertaken by myself.

Shortly after, that learned and well-practised pathologist, Dr. Carswell, then Professor at the London University College, published, with illustrated plates, his views regarding the production of carcimonia, in which he subscribed his adhesion to that group of pathologists who refer the production of the adventitious structures in question to an error in the blood or lymph, and he adduced some remarkable instances in which a material, resembling that of the adventitious structure, was discovered in the interior of vessels. According to this view, as employed by the Professor to explain the formation of adventitious structures, the necessity for cysts, whether simple or compound, is dispensed with; and he employs an argument against their agency in the production, which makes it evident that my view has not been clearly understood. On this point he is followed by the learned Professor Grose, of the United States.

Perhaps the most laborious and longest sustained inquiry connected with this subject, has been that of my friend Francis Kiernan, whose practised eye and delicate manipulation must attach the greatest value to his researches. Their results have not yet been made public, but it is well known that they are

much admired by those to whom they have been communicated; and it is generally understood that they relate mainly to the mode of organisation, and the condition of the vessels belonging to the structures in question. I may therefore conclude, that they do not necessarily confirm or invalidate those observations to which my inquiry had led, though I conceive that, in many instances, they ought to facilitate its illustration.

In the autumn of 1838, I paid a transient visit to Berlin, where I had the pleasure of receiving from Professor Schwann a demonstration of the nucleated cells, pointed out by himself and Schleiden as performing an important and essential part in the formation of vegetable and animal tissues. I procured, at the same time, the important work of Professor Müller on the structure of cancer and other adventitious structures, which had then very recently appeared. I likewise inspected the preparations in the museum of the university, relating to this subject, which had been made by Müller himself, but, in the absence of the Professor, they contributed little to the explanation of his views, and presented nothing in refutation of my own. In this respect I laboured under a disadvantage, similar to that which Professor Müller himself experienced when visiting the collection at Guy's, when I had not the satisfaction of accompanying him.

The group of structures with which we are engaged, differs so widely from those which belong to the body in its healthy state, as to have obtained the distinction

of heterologue. Microscopic examination affords us the means of becoming acquainted with the most intimate structural peculiarities, and is therefore the counterpart of chemical analysis, which relates to the elements which enter into their composition.

The characters thus brought to light, which Professor Müller was, I believe, the first to point out, have very naturally arrested the attention of inquirers, from their intrinsic importance, and from the high authority of the Professor who noticed them. The most practised eyes, and the best instruments, have been employed in these observations, and the results obtained have been so generally in accordance, that, notwithstanding the doubts which are attached by some to microscopic inquiries, they may be received with confidence, although from the optical characters of the objects themselves, their examination is often difficult.

I may observe, that I have not only been on the alert to obtain specimens, but have been anxious to examine them in their most recent state, in order to avoid the changes which may be induced by decomposition, or by the influence of antiseptics employed to counteract it. I have likewise been desirous of having the concurrent testimony of other eyes beside my own; and my thanks are especially due to my friends, John Dalrymple, George Gulliver, Alexander Nasmyth, William Bowman, and Dr. Barry, who have favoured me in this respect, and whose excellent instruments have been employed as well as my own.

The objects which arrest attention, when a portion of one of these structures is placed in the field of the microscope, and sufficiently extended to admit of examination with a very high power, as for example, with an object-glass of the eighth of an inch focal distance, are,

1st. Nucleated cells of various shapes and sizes.

2ndly. A substance having a filamentous character.

3rdly. Granular matter without definite shape, the particles of which are often smaller than those of the nucleated cells, but by combination forming masses of comparatively large size.

4thly. Very minute spherical particles resembling fat globules, and also much disposed to aggregation.

5thly. Crystals, having for the most part a rhomboidal character, and often forming mackles.

6thly, and lastly. A transparent fluid, in which these objects are contained, and which is made evident by the motion which it permits to take place between them.

These several objects, which will be better understood by reference to the Plate at the end of the volume, are not equally constant in their presence, or in the proportion in which they occur when they do exist.

I shall proceed to notice each of them separately.

1st. *The Nucleated Cells.*—These, from the constancy of their presence, as well as from the great

importance which is now generally attached to them, will, very properly, claim our first attention.

In some specimens they are so numerous and so distinct, as to appear to constitute the greater part of what is placed under the microscope, whilst in others they are so rare and indistinct, that with some difficulty we detect a cell or two amidst abundance of filamentous or amorphous granular matter. In shape, these objects differ no less remarkably. Sometimes they are nearly or quite circular, with a well-defined circular nucleus near the centre. Often they are somewhat oval, and so regular in their shape, as to bear a striking resemblance to the blood-corpuscles of some reptiles.

The oval figure is more often irregularly modified, and the nucleus, instead of occupying a central position, is near the side. It is not rare to find two or more nuclei, but a single nucleus is much more common. The cells appear to be flattened like blood-corpuscles, and, like them, to be transparent and pliant. These cells often assume so elongated a shape, as to present a caudate appearance when the prolongation takes place in one direction, which it seems to do by alteration in the situation of the substance surrounding the nucleus. Frequently prolongation takes place from both ends of the ellipsis, and sometimes at one or both extremities these prolongations are bifid. We meet with these several forms in the cells, in the different varieties of disease included in the group of adventitious structures under consideration, and appa-

rently without any necessary connection with such variety. Thus we may find them most distinctly circular in specimens of cerebriform cancer, and also in those of true schirrus. It has been supposed that the caudate and other elongated forms depend on the transformation of nucleated cells into a true tissue.

In respect to size, the nucleated cells differ very considerably. This difference is not only found between the cells of one specimen and those of another, but the range may be almost equally great in those of the same specimen, some being less than those of a particle of human blood, and others having more than three or four times their diameter. Not having employed actual measurement, I am unable to state the extremes of dimension.

The nuclei also differ in respect both of actual and relative size, being, in extreme cases, almost as large as a human blood-corpuscle, and in other examples scarcely larger than the particles into which these corpuscles appear to be breaking up when they become "*framboisés.*"

There is also considerable difference in the brightness and distinctness of the nucleus. It is sometimes well defined and of a clear white. The margin of the cell sometimes presents a similar character, which may, in degree, depend on the application of light; though I think that the state of the object itself has much to do with it.

There is sometimes the appearance of a nucleolus within the nucleus, and besides one or more distinct

nuclei, the cell itself may also appear to be made up of minute granular matter. Although these cells bear considerable resemblance, especially when well defined, and of a tolerably uniform size, to the large blood-corpuscles of a reptile, they seem to be of a much more permanent character than the particles of blood, since they remain not only a considerable time unchanged in their proper fluid, but bear, with little or no alteration, the addition of water or weak spirit.

2nd. *Filamentous Substance.*—The next material which claims our attention is the filamentous substance.

It is not nearly so constantly present as either of the cells just spoken of, or the granular matter to be hereafter described. It is from its apparent importance and characteristic appearance that I next take it up. It seems to have given the name to one form of the structures in question, which Müller has described as *carcinoma fasciculatum seu desmoideum.*

Whilst in some specimens we discover little or no trace of this substance, especially when the object is taken from the soft contents of a distinct cyst, it appears in other examples to constitute the major part, though taken from a similar situation:—on which I lay some stress for a reason which will afterwards be apparent.

Sometimes the fibrous character is distinct and well defined, nearly resembling that of perfect cellular membrane; but in others it is much more obscure,

more nearly resembling the appearance presented by the fibrine of recently-coagulated blood, in which there is an indistinct transition from granular matter. Whilst large nucleated cells are very constantly present in those specimens which are of an unquestionably malignant character, and are often very numerous in them, the presence of the filamentous matter, though also occurring in malignant structures, is perhaps in itself an approach to the normal, or at least the permanent tissues, seeing that it is not only found in them, but is most abundant in those specimens in which the malignant character is most equivocal.

The filamentous matter present in the portion under observation may sometimes have formed a part of one of the cysts or membranes which enter into the composition of these tumours: but in other instances, where the liability to such mixture has been carefully avoided by selection from a central part as before hinted, filamentous matter will notwithstanding be discoverable.

Such cases are well adapted to throw light on the question, whether fibres or filaments are of necessity produced by transition from nucleated cells, which, having become elongated or caudate, pass through a succession of similar changes until a mere filament is the result.

The appearances which we may observe in some of these growths, as well as those presented by fibrine from recently-drawn blood, make me strongly inclined to the opinion that fibres are not neces-

sarily formed by the progressive elongation of perfect cells, but rather from the amorphous matter which accompanies them.

It is satisfactory to me to know that in this opinion I am supported by my friend George Gulliver, who had, independently, arrived at a similar conclusion.

3rd. *Granular Matter.*—The granular or amorphous matter, which I have enumerated as one of the constituents of these tumours, made known to us by the microscope, is constantly present, but in very different proportions. It may, I believe, be correctly said, that it frequently constitutes the major part. From the fact of its form possessing a negative character, it is one of difficult investigation, and though we may change our power, focus and light with the hope of success, the best instruments which our present skilful opticians produce, in the hands of the most practised observers, have not reduced it to a definite figure.

I believe that this matter is regarded by the firm adherents of Schwann and Schleiden, as composed of nucleoli, cytoblasts, '*débris*' of cells, or under some name or other as referrible to their universal type. Of this I do not presume to form an opinion, confessing myself to entertain doubts regarding some of these points. Be its character what it may, the granular matter is no unimportant constituent of the structures now under our consideration.

4th. *Spherical Particles.*—The material which I have mentioned under the designation of minute

spherical particles is seldom, if ever, absent; but its proportions are very various, and the groups which the aggregation of these spherules produce are not uniform in size or shape. The completely spherical figure, and the great difference of dimension which these little particles exhibit in the same specimen, so completely accord with the character of oil or fat globules, that I cannot hesitate to regard them as such. They may be found, not only in the substance of a tumour, whether of schirrous firmness or of the soft and grumous consistence of cerebriform cancer, but also in the fluid contained in more manifest cysts, in which case, when very numerous, they may impart a slight yellow turbidity. When closely aggregated, either to the number of a dozen, or of hundreds, they generally form an irregular or very imperfectly globular mass, but I have seen them producing a multitude of masses as perfectly spherical as themselves, having some appearance of being contained in a capsule, which, however, did not exist, the semblance being occasioned by the peculiar mode of transmission of light from the margin of the semi-transparent sphere. These aggregations of spherical particles are interesting, not merely on account of their constant presence in the adventitious structures which we are considering, but from their probable connection with the fatty degeneration of normal structures, of which the production of fat liver, as pointed out by Bowman, may serve as an illustration.

5th. *Crystals.*—Crystals, the existence of which

the microscope has made known, are very frequently, but not constantly present. They generally appear as plates made up of the aggregation of a few rhomboidal crystals. They were discovered by Müller in the discharge occasioned by the breaking up or softening of a cancerous tumour, but they may be found in structures much less advanced. They may be very numerous, or they may be so rare as only to be found by careful search, and after placing different portions in the field of view. Their appearance leads to the supposition that they are composed of some of the inorganic crystallizable fatty matters, into which animal organic substances are found to be converted under certain physical conditions.

On learning that Müller had discovered these crystals, I immediately recognised in this fact a fresh analogy between these adventitious structures and the compound serous cysts which are frequently developed in the ovary or its vicinity, and in which I had seen that cholesterine may form crystallised masses resembling the purest biliary calculi of the same substance. I am, therefore, induced to suppose that these crystals may be derived from the oil or fat globules already mentioned, by a process which, although taking place within the living body, is not of a vital character.

The researches of my friend George Gulliver, who has discovered a similar crystallizable fatty matter in the coats of arteries and in several other situations, have thrown an important light on the subject

of this mode of degeneration, which will doubtless be found to play an important part in bringing about the gradual but certain deterioration to which time subjects living animals.

6th. *Transparent Fluid.*—With regard to the fluid in which the several forms of production which have now been enumerated are so placed as to allow mutual change of position, it is difficult or impossible to arrive at any experimental results, seeing that what might be collected as a fluid will, on microscopic inspection, be found to contain particles of one or all of the substances before mentioned. It is most probable that it is not merely derived from, but resembles, the *liquor sanguinis*, and yields, like it, elementary constituents for the development of the different structures connected with it.

It will, I have no doubt, be readily admitted, that neither any of the organic forms which have been mentioned, nor the crystals, nor the containing fluid, are so peculiar to the adventitious tissues in which they exist, as to constitute a character by which they may be distinguished from other tissues. Even the nucleated cells, which are the most interesting of these substances, and which are probably the most intimately connected with the development of the adventitious tissues, can scarcely be said to present a distinctive character, seeing that every animal tissue, whether normal or abnormal, is supposed, if not proved, to have its origin in cells of this description.

But it may be urged by some who concede this

point, that the cells which are concerned in the formation of malignant structures have remarkable and peculiar characters, which distinguish them from those cells which contribute to other formations. Observation in some degree sanctions the truth of such a remark. It is true that these cells are remarkable for their variable and generally large size, but it is also a fact that some of the normal productions also contain cells of a variable and large size; as for example those concerned in the formation of cartilage.

On the other hand, we may find structures of which the malignancy is certain, furnishing cells, little if at all different from those of normal tissues. We also see that cells of a particular character are by no means confined to certain forms of malignant disease. They cannot therefore be referred to for the purpose of distinguishing one form from another.

Chymical analysis cannot at present be regarded as offering a more trustworthy criterion, although we must attach value and importance to those careful researches which have made us acquainted with the principles contained in these productions, and with the proportions in which they exist. We are therefore reduced to the necessity of employing an assemblage of characters to distinguish the malignant from other abnormal growths—a remark which I had occasion to make in my former paper, the truth of which has not been set aside by the valuable contributions which the subject has since received.

The peculiar anatomical structure, dependent on the production of compound cysts on which I have strongly insisted, is so constantly present, and leads to characters so essential to the correct description of individual specimens, that on these grounds I am disposed to attach much importance to it; as well as on account of the manifest relation which it may be shown to bear to the nucleated cellular origin pointed out by Müller.

Although I may safely state that I have never seen a recent specimen of any of the diseases in question, which I have had a fair opportunity of examining, in which I could doubt the existence of the structure alluded to, and though I find it more or less strongly marked in all the specimens preserved in museums in which structural arrangement remains evident, I cannot ask that my views may be admitted without the production of proof, especially as objections have been raised against them.

I believe that the difficulty of admitting the existence of a cystiform structure has arisen from the inquirer expecting to find, in all cases, a much more conspicuous and tangible evidence of a reflected serous membrane than exists in nature, or than has been stated in my description.

To those who are accustomed to trace the steps of even normal development, it must be familiar that the original type may be very much modified in subsequent stages of growth. This, however, is more particularly true of the adventitious and heterologue

structures, the formation of which does not appear to tend to any definite term of form or size. It is, therefore, essential to become familiar, not only with the different forms in which the operation of the principle can be clearly demonstrated, but with the modifications which may be subsequently impressed upon them. We should then be able, although the original character be lost, to detect unequivocal vestiges of its existence.

The most frequent, but at the same time the most satisfactorily explicable cause of obscurity, is the production of more or less intimate adhesion between the different membranous surfaces, by which a group of compound serous membranes, having completely the reflected character, may be converted into a solid mass. It would not be more difficult to exhibit the reflected serous membranes in these cases than to teach the reflection of the peritoneum from the abdomen of a subject who has died with universal chronic peritonitis, by which the viscera have been glued together and intermixed with tubercular deposits. Yet as by a section of such a mass we might exhibit the substance of the liver, cut into the stomach, and recognise the condition of its mucous membrane, and distinguish the small from the large intestines when similarly divided, and perceive, and even name, particular vessels, so, in the tumours in question, when the eye has been accustomed to recognise the form assumed in those cases in which doubt does not exist, it will readily recognise those appearances which result from the

mode of formation, though the separation of particular parts be impracticable.

Evidence of this description may be found upon the surface of a tumour by carefully removing the surrounding cellular and other structures. We perceive a peculiar nodulous character which in the more distinct cases is seen to be produced by the protrusion of subordinate cysts.

When we have recourse to the examination of sections of the interior, appearances may be very much modified by the direction which the incision has taken with reference to the clusters of cysts, but experience will soon familiarise the eye with these differences, which, instead of producing doubt, will then be found truly confirmatory.

In addition to obscurity arising from more or less firm adhesions, we have that which proceeds from the nearly uniform colour and consistence which the new growth thus united may have assumed throughout. Such specimens afford the greatest difficulty to those who, having really recognised the characteristics of these tumours, are seeking for the traces of their existence in obscure cases. I believe that, in most instances, this obscurity would not exist were the section made quickly after death or operation, when we can scarcely fail to discover some satisfactory indication of structure, more especially if sufficient attention have been paid to the exterior in order to direct the course of incision.

Even a very few hours will be sufficient greatly

to obscure traces which when recent would have been readily admitted. Such obscurity may be produced, or greatly increased, by immersion in alcohol, which coagulates the fluid, and gives opacity to some of the semi-transparent parts which, by their contrast, often display internal arrangement.

When we understand the kind of evidence which may be obtained, and are aware of the causes and modes through which obscurity may be introduced, we shall be much more likely to discover and appreciate those traces which yet remain to be perceived.

It may serve, in some degree, to illustrate the difficulty of the subject, to compare it with that which the commencing mineralogist will sometimes find in examining a compound rock, as, for example, granite or gneiss. He is taught that it consists of quartz, mica, and felspar, and he may be acquainted with the characters of good, well-crystallized, cabinet specimens of these substances; and from the great difference between them and the particles crowded together in the almost amorphous fragments of one of these rocks which he may pick up for examination, he may be ready to doubt the existence of one or more of the minerals which enter into its composition.

Whilst I fully admit the difficulty of the investigation, and the causes just assigned, which render it essential that the inquirer should pass from the conspicuous to the obscure, I cannot omit to mention other sources of difficulty which inquirers have

created for themselves, by which they have destroyed that of which they were about to proclaim the non-existence. This is strikingly the case when maceration is had recourse to, prior to dissection. Under the influence of this process, soft and tender structures break down, and become blended with each other, and with the fluid, or grumous materials, of which they had, at one time, formed the distinct receptacles. Although the well-defined vascular cysts may thus be converted into an irregular mass of filaments and blood-vessels, such destruction of original structure is not always the consequence of the inquirer's manipulation: it may have been brought about during the life of the patient, by the natural progress of decay to which these structures are liable, and the objector may make, as he conceives, a triumphant denial of the existence of that, the "*débris*" of which he had alone seen.

Now, these very "*débris*," in the form of tassels of filaments and vessels, will, to one who has watched the changes produced by decay, be sufficient evidence of the pre-existence of the structure in question. An illustration of this remark may be found in cases of soft carcinoma of the uterus, in which, from the perishable character of the new growth, it is often difficult to discover cysts in a state of integrity, though this may, at times, be done in the most conclusive manner.

Another source of the difficulty which has been met with, has been taking for examination a part of a tumour, so removed from the mass as not to

exhibit the whole, or even the part of any principal or subordinate cyst, in which the structure in question could be demonstrated, though, taken in conjunction with the part from which it had been separated, more or less satisfactory evidence might have been obtained.

A similar source of difficulty and failure is encountered by employing a microscope, or even a powerful lens, for the purpose of detecting those appearances which are best seen with a good naked eye, because they require the proper appreciation of neighbouring parts, just as we use the naked eye to learn the constellations, but require a telescope to see the double stars.

No exception to the existence of this type of cysts, in one or other of its forms, having been detected by me, after careful examination, in the whole group of adventitious structures to which I have ascribed it, I could not doubt that it depends on a law of formation common to them all; but I merely offered as speculation that which I regarded as the probable *modus operandi* of such law. When I became acquainted with the theory of nucleated cells, and with the researches of Müller which demonstrated the distinct existence of these bodies in the group of adventitious structures under consideration, it was impossible for me not to inquire how far this fact might go to explain the production of those characters which I had been studying on a larger scale.

It appeared to me, that the adventitious structures having the type of compound serous membranes

admitted of a much more easy and satisfactory reference to the production of cells than any of the normal tissues which had been studied in their transition from cytoblasts and nucleated cells. In fact, the most perfect specimens of compound serous cysts seemed so completely to resemble a collection of nucleated cells with nucleoli, that I should have been ready to adopt this explanation, and abandon my own conjecture as to the operation of coagulation upon the surface of a plastic fluid, had I not witnessed some striking facts, which were strongly opposed to this application of the cell theory, whilst they were perfectly in accordance with that of coagulation. One of these facts I have already laid before the Society, in my former paper, which it may not be amiss for me to quote from that statement, as it was in existence before the announcement of the cell theory.

"The cysts of which I am speaking contained a substance which may perhaps be best described by comparing it to the crystalline lens when it has been in some degree softened by decomposition, though less uniform than it, both in consistence and appearance. That part which was the nearest to the containing cyst, was the least firm and consistent, but the most transparent. It was too transparent and colourless to conceal the firmer interior part, which was rendered distinguishable by a slight degree of opacity, and appeared to consist of a cluster of small pyriform grains, but nothing like a membrane could be distinguished enclosing them individually, and separating

them from the transparent matter in which they were placed.

This observation appears to possess a twofold interest. In the first place, it will enable us to conceive how easily the traces of original structure may be lost when we find them impressed on a material so tender, and which is in contact with another material in composition almost identifical with it.

Secondly, we may draw from it a strong presumption that the cysts of which we have been speaking, in the various forms in which they present themselves, are altogether new formations, and not the result of the extension or development of pre-existing structures, and which, therefore, tends to confirm the opinion which I have already advocated, that they are neither the dilated terminations of the extreme branches of any of the three vascular systems, nor modifications of the cells of the cellular membrane."*

Another of the facts to which I allude, and which is, to my mind, the most conclusive that has occurred to me, was also seen and recorded, before I was aware of the interesting researches of the German microscopists.

In the eleventh month (November), 1836, I inspected the body of a lady—a patient of Dr. Ashwell—who died after long suffering, from the largest tumour which I have ever seen developed in the parietes of the uterus. In the progress of the dis-

* Med. Chir. Trans., vol. xv. part 2, p. 306.

ease, malignant tubercles had been developed in the sub-serous cellular membrane of the abdomen, and it was upon the smooth internal surface of the peritoneum that the appearances to which I allude were seen, not only by myself, but by Dr. Ashwell, Dr. Ridge, and some other medical men, to whom I pointed them out.

I transcribe the account of them from my report of the inspection, published as a part of the case by Dr. Ashwell, in the Guy's Hospital Reports, No. IV.

"On separating the recently-adhering parietes, it was evident that the material interposed between the two surfaces of peritoneum was not ordinary coagulable lymph, but a soft white cerebriform matter, somewhat like stationers' paste, intermixed with spots of extravasated blood of various sizes. On carefully separating further portions of the attached peritoneal surfaces, it became evident that the soft cerebriform matter was not irregularly effused upon the inflamed surface of the peritoneum, but that it was collected into circumscribed depositions of very various sizes, but having almost universally a rounded but very compressed form, the flatness evidently depending upon compression between the two opposed surfaces of serous membrane. The circumscribed rounded figure seemed to depend on the cerebriform matter not blending with the general secretion of the peritoneum, but rather remaining as a drop of oil would do upon a wetted surface. It likewise appeared that on the surface there was an

extremely tender pellicle, which rendered it possible to move the soft deposits without breaking them, although their form might be changed.

"A very slight force, however, produced rupture; when the contained material escaped as a grumous amorphous mass. They might, in fact, be compared to little yolks of egg separated from the white, except that their form was more flattened, and the enclosing pellicle comparatively more tender. These little collections of cerebriform matter possessed different degrees of translucence. Some presented an uniform milkiness: others were spotted with points of extravasated blood; and in some the spot of extravasated blood formed a defined rounded body, which appeared just as distinct from the white cerebriform matter as they did from the surrounding texture or secretion.

"These appearances were most beautifully seen on the omentum, which was thin and delicate, and, with the exception of these appearances and the old adhesions before mentioned, retained a perfectly healthy character. On the omentum, some of these little circumscribed deposits of cerebriform matter might be seen scarcely so large as pins' heads, whilst others were nearly as large as a shilling."

As it is unphilosophical and consequently unsatisfactory, to admit two causes for the production of a phenomenon, when one will suffice, I was rather staggered by the apparent necessity to admit the two principles which I have here referred to; the cell theory being strengthened by the accession

of the best physiologists and observers adducing phenomena, some of which I had myself witnessed, and that which I may term the coagulation principle, having the support of, at least, equally strong evidence. Practically there seemed to be a link wanting to connect the large nucleated cells exhibited by the microscope with the most minute yet perfect compound cysts, which the unassisted eye may perceive; as, for example, in the neighbourhood of some breast tumours. In theory, we could easily conceive one of these large cells surpassing its fellows, and becoming persistent as a serous cyst, producing others in its parietes by the development of its nucleoli; but multiplied and careful examination has not, that I am aware of, ever detected one of these large cells surpassing the rank of a microscopic object possessing, at the utmost, about four or five times the diameter of a blood corpuscle. I had repeatedly seen the cells of cancerous tumours, and other productions of the same family, and been satisfied of their existence under the different forms which I have mentioned, but without being enabled to overcome the difficulty which I have stated, when careful attention to the phenomena presented by cells pointed out by my friend Dr. Barry, in his account of the early development of the mammiferous ovum, appeared to furnish the desired solution, and not merely to combine the two modes of formation to which I have alluded, but to throw light on other parts of

the subject, of considerable interest and importance in a practical point of view.

In the development of the ovum, the production of nucleated cells appears to perform the double purpose of preparing organisable matter, hyaline, by a process of assimilation, and of giving origin to important parts by superior development, which, in this state, exert an important influence on the surrounding materials derived from other cells, inducing the coalescence of the hyaline which they have furnished. That which struck me as the best illustration of this process will be found in Dr. Barry's Third Series on Embryology, in the Philosophical Transactions.

It will be seen from this, that only a small number of the nucleated cells carry out their own development, but that the majority are the preparers and contributors of the pabulum of the new growth. Now the coalescence of the particles of hyaline, whether somewhat retaining the form of cells, or more completely broken up, appears to take place precisely in such a manner as to produce the external coagulation, on which, from observation, independently of any theory, I have been induced to insist.

Hence it becomes extremely probable, that some of the more considerably enlarged cells, which are observed in the microscopic examination of the matters of these adventitious growths, become the means of determining the coalescence around them,

of the hyaline furnished by other cells, and thus account for the great tendency to the production of cysts having the compound character, as well as that of reflected membranes.

This disposal of the materials thus supplied by the hyaline of other cells, which, in breaking up, prepare the way for other nuclei to go through the same stages, not only accounts for the material of which these adventitious growths are composed, differing in infinite degrees from the plastic material employed in healthy structures, but also for the extraordinary rapidity with which the growth of some of these structures is effected. Thus, in a case which recently fell under my observation, but a few weeks elapsed from the period at which careful examination could detect nothing abnormal in a very spare and emaciated subject, to that at which a large nodulous mass could be seen as well as felt projecting in the epigastric region. The death of the patient, which soon after followed, showed that this tumour was occasioned by the growth of fungoid or cerebriform tubercles in the liver, more than one of which was as large as a good sized orange. There were numerous other tubercles intermediate between these and the smallest observed, which might be as large as a grain of hemp. Though a marked difference of consistence was observable in the material composing the different tubercles, and even in different parts of the same mass where the tumour was large, there was a striking resemblance

in the microscopic characters of the cells taken from the different parts which were examined. Nucleated cells of considerable size, and remarkably distinct, existed in extraordinary abundance, which seemed satisfactorily to account for the rapid growth which had taken place in this instance.

With this view of the subject, it is not surprising, that under the field of the microscope, a small portion of soft matter taken from a malignant structure should often suggest a striking resemblance to the blood of some of the inferior animals, seeing that this compound of nucleated cells, granular matter, and fluid, has to perform the part, in the adventitious structures, which the blood itself does in the growth of the ordinary structures.

This view, which I believe to be in strict accordance with the best observed facts, stands decidedly opposed to the theory, that the peculiar matter of cancer and other allied diseases exists as such, ready formed in the blood, from which it is eliminated at those parts at which the tumours are formed. Were the blood so contaminated, the continued healthy nutrition of the body at large could not proceed as it often does, and healthy cicatrices, after wounds and operations, would not be formed, as is frequently the case. At the same time, I would by no means deny the possibility, or even probability, that some of the nucleated cells may find their way into the blood, and be arrested at particular parts, giving rise to productions similar to the original tumour, more

especially when the latter has advanced to the softening stage, and the lymphatic glands have become affected.

The frequency with which the first carcinomatous or other adventitious production, with which the patient is affected, may be satisfactorily traced to some local injury, would seem to show that these cells may be developed *de novo*, and consequently that their transport, though probable, is not absolutely necessary. The superior tendency which particular textures, and even particular parts of textures, exhibit to the production of these structures, when the system has become effected, is more worthy of remark, than easy of explanation. I could adduce some striking illustrations, but I will not extend this paper by details of cases, which the Society will probably be willing to receive on a future occasion.

With regard to that interesting part of the subject which relates to the vascular organization of these adventitious structures, I feel that anything which I could offer would be imperfect, and of doubtful authority, so long as the researches of Francis Kiernan in relation to it remain undisclosed.

I think, however, that it may be safely concluded from such observations as the naked eye will occasionally enable us to make, that there must be some analogy between the production of vessels in these structures, and their formation in cellular pleuritic adhesions, and other comparatively normal adventitious structures, and I confess that my present

opinion accords with that of Lippi, in regarding the new vessels in new parts as the prolongations of the vessels of contiguous older parts, and that there is not a production of independent vessels which subsequently inosculate with those in their vicinity.

To me, it appears most satisfactory to refer the formation of vessels to coagulation taking place at the surface of the blood, which thus no sooner forms a stream than it acquires the conduit, or vessel, in which it is to be contained: a theory which will, I believe, satisfactorily account for the production of the three systems of vessels, the venous, the arterial, and the lymphatic, as I some years ago suggested in the medical section of the British Association, at its meeting in Bristol. If this view be correct, the vessels in a fungoid, or other adventitious structure of the class we are considering, being essentially derived from the more healthy coagulable matter of the blood of the body generally, and if in any degree only partially and at the exterior, receiving the material of their growth from the morbid hyaline of the new structure, we may easily understand why these vessels should to a certain extent possess their normal characters, although such vessels are often remarkably weak from the imperfect character of the part through which they ramify. It cannot be doubted, that the blood supplied by these vessels to the adventitious structure, furnishes the materials for its continued growth; and, in accordance with this, we may often find the vessels of a very large size, where the growth of the tumour has been great

and rapid. That a large part of such growth consists in the successive production of the abnormal nucleated cells, described in the preceding part of this paper, seems to be extremely probable. Yet I am led to believe, that it is not the whole of the materials which the blood may supply to the tumour, which is so disposed of, but that comparatively healthy blood being sent to the new growth, it may retain sufficient of its normal characters to produce more or less analogous tissues, which in different proportions may be almost invariably found pervading the mass,—as, for example, where well-formed cysts are produced, and adhesions of loose or condensed cellular membrane are established.

It seems to be perfectly in accordance with this, that the nearest approach to a normal tissue is found in the membranous cysts, and their immediate vicinity, which membranes not unfrequently form the bed in which the vessels ramify.

Although I have, in accordance with the phraseology which usage has sanctioned, employed the term nucleated cells in speaking of those corpuscles which present one or more brightish spots within their circumference, and have a circular, or more or less elongated figure, I confess I have some hesitation in completely admitting the cellular character, as neither when these are entire, nor in their breaking up, do they seem to exhibit any defined capsule or membrane. The appearance which seems the most strongly to sanction the idea of a cell, is that of one nucleated corpuscle containing one or more

within it; but even this, which is comparatively rare, is by no means conclusive. It would seem, that as these bodies are formed from the blood, and exhibit themselves in the first step towards consistence or coagulation, something less determinate than a sac of skin or membrane would be produced. The kind of consistence which suggests itself to my mind when viewing these corpuscles, as well as those of the blood, is that of a substance soft throughout, rather than that of a fluid contained in a vesicle. Where a distinct nucleus exists, such corpuscles might be compared to the ova of frogs in their mucoid envelope, or to certain seeds, as, for example, those of garden cress, which after maceration in water become surrounded with a more or less consistent viscid substance.

This view seems quite accordant with their function of producing plastic matter, or hyaline, by the assimilation of principles dissolved in the *liquor sanguinis*, or other fluid, in which they are placed.

Such corpuscles would contribute to the building up of structures by yielding the material of which they are composed, so as to form a homogeneous mass, which is more consistent with the cohesion as well as microscopic characters of the tissues, than that of the employment of cells in their individual character, like bricks in the construction of a wall. At the same time it must be fully admitted that there are some structures in which the nucleated particles to a great degree retain their character. The epithelium seems to be the most striking exam-

ple of this kind, but such exceptions seem rather to confirm the rule than to set it aside, since in the disintegration of epithelium, we obtain the scattered fragments in the form of nucleated particles, which seems to indicate that a perfectly new structure had not been formed. In such instances the nucleated particle appears individually to have acquired a more complete development, and at the same time to have been rendered unfit to be worked up in the composition of a new living tissue. The individual particle has advanced a step further in those cases in which it becomes furnished with cilia. The same principle is seen in hair, nails, feathers, &c., of which there is no absorption.

I am aware that it may be objected to the opinion which I have offered, that by the addition of certain re-agents something like the existence of an enclosing pellicle may be demonstrated, but such a pellicle may easily be formed by the process employed, or even spontaneously in some cases in which the existence of the corpuscle is protracted by a mere act of superficial coagulation, and in this way a true nucleated cell containing other corpuscles may be produced. Some of the nucleated corpuscles discoverable in adventitious structures, the blood corpuscles of the proteus, and some transformations of cells in the advancing ovum, may come under this description, without invalidating the opinion which I entertain, or confirming that which I feel a difficulty in adopting.

There can be no doubt that great and important

light is to be thrown on the characters and formation of this class of adventitious structures, as well as upon the normal tissues, by the aid of animal chemistry, and I would be one of the last to depreciate any accessions to our knowledge from this quarter; but up to the present time, whilst distinct characters may be satisfactorily made out with respect to form, as seen with the naked eye, or discoverable only with the microscope, chemical analysis does not furnish us with any sufficiently strongly-marked distinctive characters to constitute the boundaries of a class, though they may indicate varieties of great practical importance, of which some of the varieties established by Müller may be adduced as illustrations. A great obstacle to our deriving a satisfactory test from chemical analysis arises from the progressive changes which both solids and fluids undergo in the course of their production, and also when produced. We may be satisfied of this *à priori*, when we consider that the embryo commences in what appears to be a single cell, which produces others, in their turn, to become producers, in almost infinite series, and that springing from this single point a great variety of structures, differing chemically as well as mechanically, are produced. Again, if we examine the subject *à posteriori*, and take a part which has acquired something like the form which it is to retain through life, and subject it to chemical analysis at different ages, we shall find important differences between the fœtal and the adult composition. Similar

changes take place in the adventitious structures, both as regards the successive development of parts and the changes effected in such a structure, or even in parts of it when produced.

I have elsewhere had occasion to notice that from a tumour having all the closeness and firmness of schirrus, a new growth may proceed, having the softness and rapid increase of fungoid disease. The most distinct specimens of compound adventitious serous cysts which form the type of this group of structures, which in their appearance so closely resemble the normal tissues that they cannot be regarded as malignant, and which from their want of influence on surrounding parts, and on the system generally, justify their benign character, will sometimes give origin to a fresh growth on some part of the tumour which they constitute, presenting all the characters of a truly malignant adventitious structure. We often find melanosis combined with another variety of the same class, and when, as is sometimes the case, a succession of operations are performed at the same part for the extirpation of the tumour, there is a progressive alteration in the physical as well as chemical characters of the adventitious structure, which is constant only in exhibiting the type of compound serous cysts upon which I have so long insisted.

It will, I hope, be generally understood that these remarks are not designed to underrate or discourage any extent of chemical investigation which may be devoted to the subject, but merely to point

out the objections to which it is liable when in its present state it is appealed to as a distinctive test, except as between varieties.

Dr. Carswell has urged an objection against development through the production of compound serous cysts, as pointed out by myself, which is adopted by his successor, as well as by Professor Grose, of Cincinnati, who regards it as triumphant. An objection sanctioned by such authorities is too important to be allowed to pass without consideration, either to be received as a correction, or to be refuted if invalid. The Professor observes that there is an ambiguity as to whether the cysts produce their contents or are produced by them, and that in the latter case their importance is overrated, and that the adoption of the reflected serous membrane as a type, attributes to the adventitious structure a position which in fact is exterior to the investing membrane, precisely as the heart is not literally inclosed in the pericardium.

I shall notice the latter objection first, as being of the more tangible character, and preparing the way to the better understanding of the former.

For the comprehension of this, as well as of almost every question connected with the subject in which anatomical character is concerned, I would appeal to the ovarian cysts, which are not only examples on a large scale, but much less liable to obscurity through alterations produced by successive change.

Let us commence with a large containing sac.

This has, like other parts within the abdomen, an extensive covering of peritoneum: in fact, it has its close and reflected portions, and this very membrane may serve as an illustration of the Doctor's objection, seeing that this membrane is wanting as a covering at the more or less extensive base of attachment of the tumour.

The peritoneum is the accessary, and not the essential part of the tumour. This we may find, as to bulk, chiefly to consist of the peculiar fluids which may be withdrawn by the trochar, and which we find everywhere enclosed by the lining membrane, which forms a perfectly continuous closed sac. The fluid in the sac is therefore partly enclosed by the peritoneum, as the blood in the heart is by the pericardium, but it is perfectly enclosed by the sac, as the blood is by the lining membrane of the heart prolonged into the large arteries and veins and their ramifications.

Let us now consider the second order of cysts that arise in the parietes of the principal one. Each of these commences as a perfectly closed spheroidal sac beneath the lining membrane of the principal one. In the progress of its development it pushes forward the lining membrane of the original sac, beneath which it is formed, and consequently has from this source a close and reflected covering, though these may be widely separated from each other by the copious contents of the first sac, but the broad base or attachment may be so extensive that the very character

of a reflected membrane may, with difficulty, be recognised, or it may be so slender, and the secondary growth so filamentous, that the existence of the second sac may be rather inferred than demonstrated. Sometimes, as I have also shown, in the second sac, in the progress of its development, an opening may be produced through its own membrane and that which invests it, producing a communication between the first and the second, which latter pours its secretion into the larger cavity, and thus becomes a true follicle, probably illustrative of the cellular origin of other follicles. It is needless that I should describe the succession of sacs which not in theory only, but in fact continue to be developed in this mode. Enough I think has been stated to show that on the principle of the formation of reflected membranes, the peculiar matter of the tumour, whether fluid or solid, is not left partially uncovered by membrane. In considering the reflected character, we must not lose sight of the lining membrane, and in considering the tendency to more or less rapid development, we must not lose sight of the subordinate cysts, the development of which produces the reflected form in the membrane, in the parietes of which it has been produced, which reflected character forms an important part in producing the anatomical characters of the mass.

With respect to the other part of the objection, viz., that it is not shown whether the sacs or their contents are first produced, and that it is con-

sequently uncertain which is cause and which effect, I may, perhaps, be allowed to observe that I may be content to leave this point in the same situation with others to which it is most intimately allied, I mean all those productions to which a cellular origin is conceded.

Of this description are the pulps of the teeth, which in many respects bear a close analogy to the compound serous cysts observed in the production of the adventitious structures. Whilst yet of microscopic size, we find both cysts and their contents; and in their advance to their ultimate condition, both pursue their changes in mutual dependence on each other.

The membrane, however, in both cases seems to be the more important, seeing that it is, in both, the medium of nutrition, and also in some degree the determiner of form.

I have elsewhere stated that in the neighbourhood of a malignant or cancerous growth, the tendency to contamination of the surrounding structures appeared to be determined by the occurrence of inflammation in these textures—an idea that has been opposed as an hypothesis devoid of proof. The remark originated in the observation of facts, and for its explanation I have merely conjecture to offer. The fact however is of such uniform occurrence, that I have no hesitation in appealing to my most experienced professional brethren for its confirmation, and I think they will unite with me in regard-

ing it as of great importance with regard to the result of operation.

When the adventitious structure is of considerable size, and has been of long standing, we shall find the surrounding structures perfectly healthy, or a little condensed, provided no inflammation has been excited. On the other hand, where inflammation has been known to exist, either repeatedly or obstinately, the neighbouring textures are frequently, though not invariably, affected with the disease in what has been termed the infiltrated form.

It is also probably to be ascribed to the occurrence of neighbouring inflammation, that a material having, in some respects, the character of a malignant growth has occasionally been found in the vessels leading to or proceeding from a malignant tumour.

Instances of this kind have been adduced in favour of the theory that malignant disease commences by the production of an abnormal principle in the blood, an idea which appears to me equally untenable in theory and in fact.

We see wounds heal with perfect facility and in the healthiest manner in persons labouring under malignant disease, provided the part in which they are situated be exempt from the disease; a fact which seems to be irreconcileable with the supposition that cancerous matter is circulating in the blood in quantities sufficient to occasion the obstruction of vessels of considerable size. When we find in connection with parts suffering from inflammation of different

kinds, the arteries, veins and absorbents, somewhat similarly affected, in which examples we cannot doubt the influence of local disease, there does not appear to be any necessity to reject a similar influence in cases of malignant disease, in order to resort to another more improbable and more difficult of proof.

It may not be amiss for me now briefly to state the conclusions which I wish to be drawn from the observations contained in this paper.

1st.—That continued observation has confirmed the constant presence of the type of compound serous cysts in a class of adventitious structures, which comprehends the whole family of cancerous diseases. I may add, that I have found it, not only in man, but also in the inferior animals, as, for example, the horse, the ox, the cat, and different species of birds.

Several practised observers have fully confirmed my conclusions, and I may here be allowed to record that the late Professor Delpech, and the present Professor Rokitanski, have personally informed me that they had independently been led to take similar views.

2ndly.—That the microscopic examination of these tissues, though extremely interesting, does not furnish perfectly conclusive tests of any particular form of adventitious structure to which a specimen may belong, but that it demonstrates the application of the nucleated cell theory, whilst it is fatal to that of cancerous matter being formed in the blood, and

eliminated at the spots at which the tumours become manifest. It therefore furnishes an important argument in favour of operation, though other practical considerations require to be attended to, before operation is decided on.

3rdly.—That to have a complete view of the mode of production of these structures, we must combine the cell theory of Schwann and Müller, the coagulation principle which I had previously suggested, and the process of organization investigated by Kiernan—three stages of development which appear to occur in the order in which they have been enumerated, and that none of the phenomena, taken singly, is an adequate test of malignancy, which, as stated in my first paper, must be regarded as the sum of several characters.

4thly.—That chemical analysis, though extremely important and interesting, affords an imperfect and inadequate criterion; as the principles concerned may vary, or be changed, in the progress of development.

5thly.—That in operating for the removal of a tumour of this class, it is extremely important to leave behind none of those minute cysts which often form granules in the surrounding cellular membrane, though it may appear to be in other respects perfectly healthy: this appears to be a mode of extension of the disease, independent of inflammation.

6thly.—That experience teaches us that the infiltrated form of these diseases occurs in the structures in the neighbourhood of the purely adventitious

DESCRIPTION OF PLATE.

Fig. 1.—Nucleated cells, some containing nuclei, others nucleated cells and nucleoli.

Fig. 2.—Nucleated cells assuming an elongated figure.

a cells simply caudate.

b cell with the pliant caudal extremity bent on itself by movement of the containing fluid or other cause.

c cells prolonged at both extremities, some bifid.

Fig. 3.—Different forms of filamentous matter.

Fig. 4.—Amorphous or granular matter from the breaking up of cells or other sources.

Fig. 5.—Fat globules.

a individual globules of different sizes.

b aggregations of globules of different forms and sizes.

c a globular aggregation of fat globules having the semblance of an envelope.

Fig. 6.—Crystals of a substance supposed to resemble cholesterine.—N.B. For other representations of this substance, as well as of the fat globules, see the plate illustrative of the valuable paper of G. Gulliver, published in this volume.

Fig. 7.—Drawing of cancerous matter from tubercles in the liver, magnified 410 diameters, by G. Gulliver. It exhibits several forms of the large nucleated cells occurring in malignant structures, which according to careful measurement by G. Gulliver, vary from $\frac{1}{5000}$ to $\frac{1}{800}$ of an inch. Fat globules and granular matter are also represented in this drawing.

Fig. 8.—Development of the ovum after Dr. Barry.

cho. chorion. *f* zona pellucida.

b s germ including *b b* rudimental embryo.

N OF PLATE.

some containing nuclei,
ells and nucleoli.
assuming an elongated

ate.

t caudal extremity bent on
nt of the containing fluid

both extremities, some bifid.
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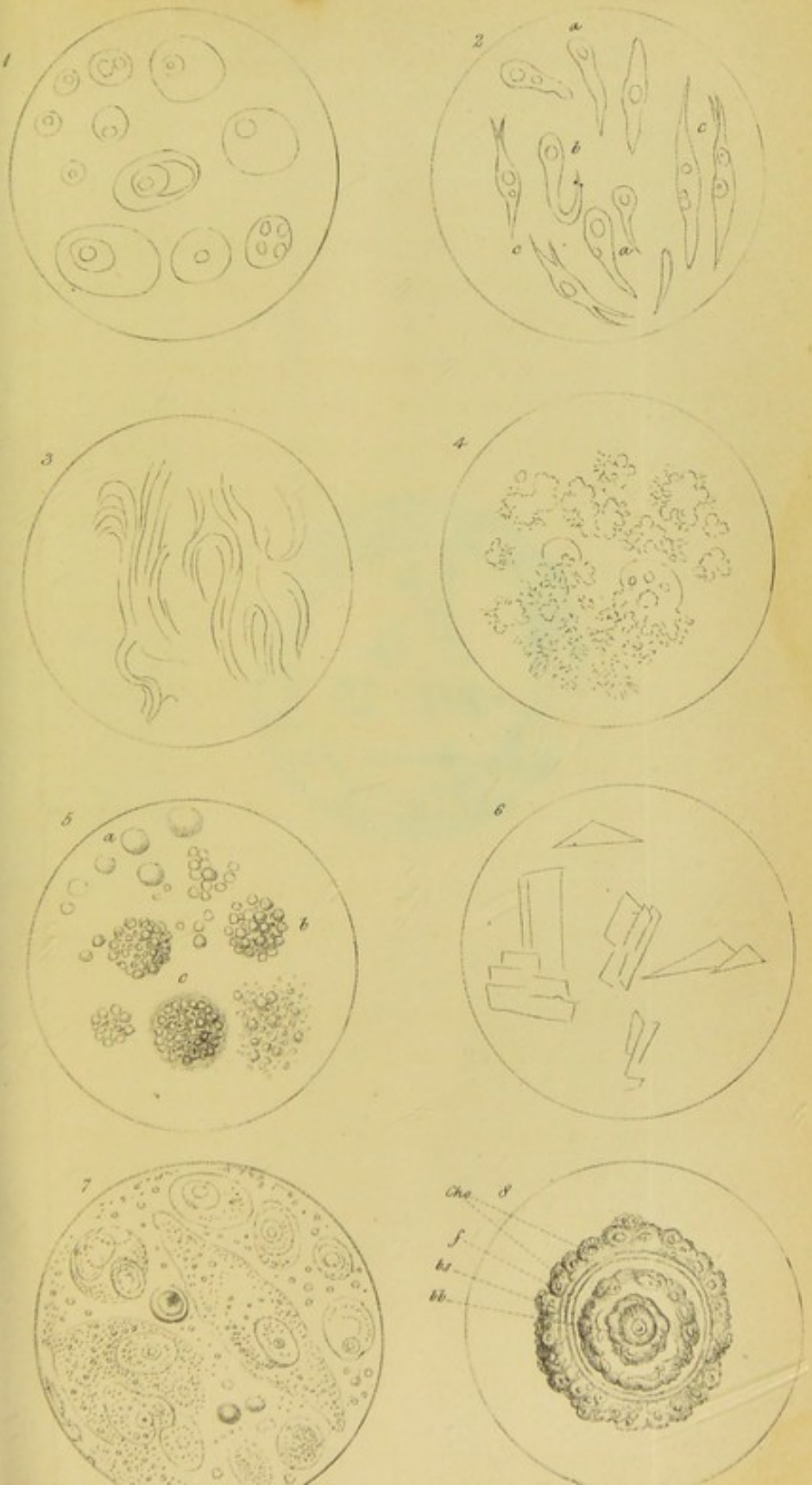

10.

ON THE

BLOOD-CORPUSCLES OF THE HUMAN EMBRYO.

By James Paget.

The examination of an embryo between three and four lines long, and about four weeks old, given to me by my friend Dr. Brownless, afforded an opportunity of examining the human blood at an earlier period of life than

corpuscles I found these measurements; 1-1500 by 1-2300 of an inch; 1-1600 by 1-3000; 1-1700 by 1-1800; and the nuclei of these (whose various apparent forms may be ascribed to their being seen in different positions) measured from 1-3700 to 1-4500 of an inch.

In the crowd of cells that formed the tissues and rudimental organs of the embryo, and of which many were loosely scattered over the field of view, it was not easy to discover any colourless blood-corpuscles; but I saw some

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The blood was observed as it flowed from the omphalo-mesenteric vessels, and afterwards while its corpuscles lay singly or in clusters. The great majority of the red corpuscles presented a circular outline, and, as they rolled over, appeared spheroidal and vesicular, or like cells filled, but not tensely, with a clear

they may be seen even more plainly than in the

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In the crowd of cells that formed the tissues and rudimental organs of the embryo, and of which many were loosely scattered over the field of view, it was not easy to discover any colourless blood-corpuscles; but I saw some resembling the nucleated red-corpuscles in every thing but colour: so that there can be little doubt that the development of the human blood corresponds with that of the other mammalia in this, as in other respects—namely, that a colourless state precedes the coloured state of the nucleated red-corpuscles.

The foregoing description of the

1845.

10.

Paget

Blood Corpuscles

of the Human Embryo.