Contents

Introduction.

I was induced to direct my attention to the question which I have chosen as the subject of the following pages by the considerations which suggested themselves in enquiring into the arguments which are brought forward by Prof. Kölliker in his well-known Article on the Spleen in Dr. Todds Cyclopedia, in support of his doctrine of the function of that organ. In reference to this investigation, the subject has at least some importance, and I think possesses in itself more than sufficient interest to make it worthy of all the labour which I have been able to bestow upon it.

While my attempt has fallen far short of the success which my self-confidence had led me to anticipate, and while I am fully aware that it is unworthy, not of the author, but of the occasion, yet I venture to hope that the novelty of the subject as well as the consideration that the whole of its literature is to be found in a language with which I deeply regret that I am not more familiar, will be accepted as in some measure a palliative, if not an apology.

J. Scott Anderson

Chapter I

Preliminary.

[1] General Sources of Colour in the living Organism

Without taking into consideration those forms of pigmentary matter which are included among the normal constituents of certain tissues such as the pigmentum nigrum of the eye, the cuticle &c, which are unconnected with our present subject, colour may be said to owe its origin in the living organism to one of three causes. Either it may be due to the presence of fatty granules, which though they appear colourless when viewed individually, by transmitted light, communicate a yellow tinge to any tissue through which they are infiltrated in any quantity, as in the case of the corpus luteum the reticulum of cancer. one form of yellow softening of the brain &c; or, on the other hand they may owe their origin to more or less altered bile, or lastly, which is by far the most frequent source of abnormal colour, to blood either in its original condition or variously changed.

With respect to the first two of these, as they are unconnected with our subject, their consideration will be overlooked, except

Except in so far as to enquire whether or not they may primarily depend to a certain extent on the first of the sources of colour mentioned above. It is believed by many indeed that the colouring matter of the bile is derived from that of the blood. The grounds however upon which this theory is founded, which will be enquired into below, are not very satisfactory

[2] Normal Metamorphosis of the Blood-Corpuscles and their Contents

On this subject numerous theories have been held at different periods. In former times it was supposed that the corpuscles being the nutritive constituents of the blood, applied themselves to the walls of the capillaries and so disappeared in the surrounding Parenchyma. This was founded on observations which have been long proved to be fallacious. Schultz advocated the view that the corpuscles were thrown off by the liver and thus conduced directly to the formation of Bile. More recently Prof Kölliker has maintained that the Spleen performs the same office. The considerations of the phenomena on which he grounds this theory will fall under a later Section.

If we examine a specimen of healthy blood taken directly from the circulation of a living adult animal, we are as much at a loss to point out, from any peculiar characters which they present, those corpuscles which have fulfilled their functions and are on the point of dissolution, as those which have only recently originated and have not perhaps arrived at their full developement. When we add water however or any dilute acetic acid, we at once recognize differences which were before unappreciable arising from the various degrees

† The question occurs on acting upon agents & other kinds of calls. Does the author mean to infer from this that the calls are of different ages. & the same that the agents attend every call? Ans.

of susceptibility possessed by individual corpuscles to the action of these reagents, some being acted on and disappearing at once, others not at all, or not till after a considerable period has elapsed. As to the signification of these differences, it is rather difficult to form a precise opinion. It must in the first place be remembered that the apparent disappearance of a corpuscle when subjected to the action of water must not be considered as equivalent to its solution - is there is no reason to suppose that the very transparent enveloping membrane is necessarily altered.

The action of water on the corpuscles is of two kinds. In the first place it produces a swelling up or enlargement to a greater or less extent (with respect to which I am not aware that any difference in the susceptibility of different individual corpuscles is observable), and secondly, it dissolves the colouring matter, and it is to differences in the solubility of this constituent at different periods of the development of the corpuscle, that the peculiarities above referred to in the action of water are attributable. This explanation is confirmed by what we observe in extravasated blood, in which the first change appreciable consists in a gradual diminution in the solubility of the hæmatin, which diminution may, with some probability be supposed to arise in both cases from a coagulation of the contents of the corpuscle consequent on the loss of its vitality.

With respect to the actual mode of disappearance of the blood corpuscle, although no satisfactory observation can be made

R. Remak. Bemerkungen über das Zellen-Leben und die Entwickelung des Froscheies. Müllers Archiv. 1848. S. 63.

* It is difficult to understand how the oval nucleus of the lymph corp. blood corpuscle, should ap[illegible] the round appearance of the lymph corp. in the same animal — J. H. B.

in the highest animals, yet I think in Reptiles and especially in the Foetus ~~some~~ results sufficient to throw some light on the subject may be obtained. Thus Remak states that in what he calls the "retrograde development" of the corpuscle of the Frog - the following facts are observable. The corpuscle first loses its colour while the nucleus becomes more apparent and assumes a granulated aspect. The cell-membrane becomes wrinkled and ~~irregular~~ at its margin, disappears or nearly, becomes clearer and clearer so as finally only to appear as a pale shadow. Finally the nucleus only remains and is undistinguishable from a lymph-corpuscle." *

In fig 5 Pl. VIII I have represented the appearances assumed by the foetal blood-corpuscles at the 12th day of incubation - when undergoing a process of melting away perhaps analogous to that above described. In these corpuscles, when no reagent was added I could almost observe the colour gradually fading under the eye and I think it very probable that the phenomenon was not merely accidental, as it was Repeatedly ~~observed~~ noticed, but really normal. It is unnecessary to say, however, that all such observations are extremely vague and uncertain, and that no great importance is to be attached to them. If they be correct the mode of disappearance of the blood-cell may be considered as analogous to most other cells in which the membrane becomes altered and dissolved, before any changes take place in the contents.

In whatever mode the blood corpuscles become dissolved & disappear

* In a paper "On the colouring matter of the Blood & Bile
Ann. di chimica applicata à la Medicina - 1846 p. 283

it is probable that the colouring matter becomes diffused in the surrounding serum in a nearly unaltered condition. probably communicating to it that straw-colour, which is characteristic of it. Does this colouring matter become subject to chemical change and, as such, disappear, or does it, as some suppose, retaining the character of pigment, become metamorphosed into the colouring matters of the biliary or renal secretions? For the determination of this question we must consider, first, the mode in which these colouring matters can be ascertained by observation to originate and, secondly, the points of correspondence, — if any exist, — between them and the colouring matter of the blood.

On the subject of the convertibility of the pigment of the blood into that of bile, various opinions have been held and observations detailed. Thus, it is maintained by Polli* that the distinctive property of the colouring matter common to the blood bile and Urine is that it is rendered yellow by reduction, red by oxidation, and that as the red blood-colour becoming deoxidized in the Liver & kidney it is converted in to the yellow - wh. characterizes the secretions of those organs. This theory he founds principally on a number of Experiments in which he endeavoured to shew that reducing agents turned the coloured corpuscles yellow, while oxidizing agents turned the bile red. This theory seems to be based on too slender foundations to be worthy of much confidence. Various chemists who have investigated the question of the existence

× No support is given to this assertion. It is especially opposed to what may be observed in the livers of many of the lower animals ——— J. Hb.

Note. The colouring matter in question presents another point of analogy in being combined with a fatty compd as is also the case with the colouring matter of the bile in those animals.

of the constituents of bile in healthy blood — have concluded that the biliary colouring matter found in that fluid was identical with that of blood itself. Thus Denis detected such a colouring matter as a constant constituent of healthy liquor sanguinis. On the other hand it is maintained by Simon that a marked distinction exists between the two — which is especially indicated by the different action of Nitric acid on each.

As to the mode of origin of the colouring matter of the Bile we know nothing. We certainly have no proof that it is formed in the cells of the Liver — for the appearance often observed of yellow granules occupying these cells — upon which much stress has been laid by some authors, is an abnormal one† — and is in fact an indication of the first step in the establishment of the condition of jaundice consequent on obstruction, namely — an icteric state of the secreting organ itself, the colouring matter being thrown back upon the cells and absorbed in accordance with a general fact of which we shall have other illustrations in the sequel.

There is just one other observation which seems worth mentioning, as tending to confirm the doctrine of the convertibility of the blood-pigment into that of the bile. In the three higher classes of vertebrate animals, the bile assumes in Mammalia a bright yellow colour — while in birds and reptiles it presents some shade of green. In connection with this it is not a little remarkable that the colouring matter of the blood in apoplectic cysts — in process of time assumes, in each of these tribes of animals alike, exactly corresponding with that of the bile.

General Phenomena observed during the changes which take place in Stagnant or Extravasated Blood.

[3] Preliminary Changes directly consequent on Extravasation or Stagnation.

After fluid blood has undergone extravasation into the tissue of any organ, or into any of the cavities of the body, or has become stagnant in a vessel obstructed artificially or otherwise, the first change which it undergoes is that of the coagulation of the fibrine. This process, as it occurs within the living organisms, though essentially identical with the corresponding one observed to take place in blood which has been removed by venesection or otherwise, is considerably modified by the existing circumstances by which it is surrounded.

On examining a recent apoplectic clot in the Brain or other organ, the whole of it is found to consist of a soft and, in many cases almost diffluent homogeneous mass. — No part assuming the firm gelatinous consistence of the clot of healthy blood when formed external to the body. We know from observation that the firmness of the clot in blood obtained by venesection or otherwise is almost always dependent varies with on the proportion of its fibrinous constituents in relation to the other corpuscles. Thus in diseased conditions in which this proportion is diminished, the blood-clot is observed to be fragile and easily broken down; so also in healthy blood, that part of the clot in which the corpuscles are accumulated in greatest numbers, namely in its lower portion, the same condition exists. Another

circumstances which in a recent extravasation - clot, causes it to assume a very soft consistence, ~~consists~~ is the large quantity of serous fluid which it involves in its meshes at the period of its formation, which, however, rapidly undergoes absorption. In most cases both these causes are probably present and operate at different periods, the first being dependent on the infiltration which takes place of the fibrine along with the serum into the surrounding tissues, while the corpuscles are detained as by a filter.

During the period immediately consequent on extravasation, and before the commencement of the changes preparatory to the organization of the clot, it undergoes no further alteration except that dependent on its gradual contraction, and the disappearance of the serum. It will be perfectly necessary, before entering on our immediate subject, namely the metamorphoses of the blood corpuscles — which of course take place after the period referred to — to consider the process of organization of which the above constituents become the subjects, and in which the corpuscles themselves are involved. In describing the facts connected with these changes, they naturally divide themselves into those connected with the development first, of fibres & fibroid structures — secondly of cellaform structures.

[4] General Facts connected with the development of fibrous tissue in organizing coagula

This process has been described by Reichy in his two memoirs "on the Corpus Luteum" and "on the Metamorphosis of the tissues

Note.— I have been unable to obtain possession of either of these works — as they do not exist in any of the libraries in Edinburgh — and am only acquainted with their contents by the abstracts which have appeared in the German Journals and especially in the "Rationelle Pathologie" of Prof. Henlé

See this work Bd. II S. 22

of arteries". Important observations have also been made on the same subject by Zeisin (Zeitschrift für rationelle Medizin - Bd II S.129) and by Bruch (Ibid. - Bd VIII S.104), to which we shall have opportunity of referring subsequently

Preparatory to the commencement of organization - the substance of the coagulum, when microscopically examined, is observed to have lost that appearance of fibrils running in various directions, which it invariably presents immediately after its formation. Its appearance is homogeneous and transparent and its consistence has become - according to Henle - more fragile & brittle than before. In the Thrombus in Arteries, according to Twicky, towards the end of the second week after the application of the ligature, the developement of permanent new structures in the form of nuclei commences. These when they first present themselves are generally small, of a round form, and seldom provided with a nucleolus. Regularly they present no definite arrangement with reference to each other, but subsequently they arrange themselves in rows, and become elongated in the direction which is afterwards to be assumed by the fibres to which they give rise

At this period a new element presents itself in the form of broad fibres, which can now be more or less distinctly defined, and to which the nuclei above described bear a peculiar relation. The appearances of these are various according to their stage of developement. Besides unaltered nuclear cells (Remzeleim) which are perfectly round in form and others similar in other respects, which had elongated in both directions,

broad and flat fibres are seen, which become more and more distinct towards the end of the fourth week (in the Thrombus, to which all these observations refer) - and, being here and there provided with nuclei, present an appearance similar to the unstriped muscular fibre - About the 5th or 6th week, these fibres have split into fibrillæ and have become wavy - they themselves being connected into bundles of white fibrous tissue.

The foregoing series of facts may be considered as those characteristic of the process when complete in all its parts. All these changes are however only completed under certain circumstances. They may as above stated be well seen in the conical clot of ligatured arteries. In hæmorrhagic cysts in the areolar tissue generally, and in the coagulum consequent on fracture they may also be admirably studied. In cysts in the Brain and many other situations the process cannot be observed to go beyond the preparatory stage of the developement of nuclei and nuclear fibres or even not so far.

It is to be remarked that the metamorphosis which the coagulum of stagnant blood undergoes is the same in every respect with that of which coagulated exudation is the subject under similar circumstances, not only as regards the developement of fibres, but as will be seen hereafter, in reference to other changes.

[5] General Facts connected with the developement of cellaform Structures in organizing coagula

In almost every extravasation if it be of sufficient size, it will

be found that while in the peripheral portion of the resulting coagulum, the changes described in the last section are to be observed in process of time, in the more central parts other structures arise which present very different characters. The changes which were above described as preliminary to organization goes in the same manner and at the same time! Every where but owing to causes which we cannot very easily define — the superficial portion gives rise to fibres — & fibrils — that more removed from the influence of the surrounding tissues gives rises to cells — by a process simultaneous with its assuming a fluid form.

Here again in this fluid we have to observe the same changes as those with which we are acquainted in that of an exudation, each giving rise to forms essentially identical. Hence in describing the evolution of these forms, we are only describing facts and phenomena with which we are familiar under other circumstances. It is true that the cell-like bodies ufound to are much altered in their appearance by the presence of blood corpuscles either unchanged or in a more or less metamorphosed condition, but this circumstance is perfectly unimportant as regards their essential nature or the conclusions to be formed as to the conditions of their origin.

With regard to the physical characters of these bodies (we cannot call them cells in the strict sense, although surrounded by an apparent membrane) as they present themselves in extravasated blood a short time after extravasation has taken place,

Rel. Path. - Bk II L 699.

they are at all times the same, namely those presented by what has been called by some writers, the "Exudation corpuscle" by others the "compound granular cell" &c &c. and which differ in several important particulars from those of every other cell-form body with which we are acquainted as existing in the organism, whether healthy or morbid. They are distinguished by consisting of a spherical or spheroidal aggregation of oleo-albuminous granules or other bodies, which appear to be surrounded in many cases by a distinct membrane - differing however from all other proper cell membranes in being almost unaltered when acted on by water or dilute acetic acid. Many of them contain a vesicular, transparent, nucleus - which may be either central or peripheral in its position. In their mode of development, as will be shewn in the sequel, they are also peculiar - the contents becoming collected together into a spheroidal mass before the formation of the cell-membrane, or rather of the structure which appears to be such. The proof of this lies in the fact that unaltered blood-corpuscles are found among the contents of these bodies, which of course cannot be supposed to have originated subsequently, or to have been developed in the position in which they are found.

These "Conglomerates" / to use a term which has, I think been applied to them with more propriety than any other by Prof. Goulee / occur under various circumstances. They were first described by Gluge in inflammatory exudations under the as occurring

X Are the bodies here referred to the same as those which include blood corpuscles. I am inclined to think not, although it having been shown that a membrane may form round blood globules, accordingly analogy is in favour of a membrane also being capable of forming round aggregations of fatty granules. If however it is maintained that this is the only, or even the common mode of formation of the compound granular bodies, I am satisfied the opinion is incorrect.

J.P.

along with pus globules under the title of Inflammation-globules (Entzundungskugeln). In healthy Pus however they are usually entirely absent, or occur only sparingly. They may be seen in Pneumonic Expectoration or in the fluid which may be squeezed from pneumonic lung. What are the exclusive conditions of their production - or the precise nature of the membrane-like structure which appears to surround them wall, though unconnected with our immediate subject, almost unavoidably fall under our consideration in a future section. ×

[6] General Facts connected with the metamorphosis of the Blood-Corpuscles & their constituents in extravasated or stagnant Blood.

A short period after blood becomes stagnant, whether it be enclosed within the walls of a blood-vessel or not, the blood-corpuscles undergo one of two changes. Either they become colourless and almost invisible and finally disappear altogether, as a consequence of the dissolution of the boundaries in the surrounding medium, or returning to a greater or less extent their colour, they become gradually incapable of being acted upon by water and acetic acid and subsequently shrink and lose their peculiar form with their smooth contour and transparency, their contents undergoing various changes in the course of its transformation into granular pigment. The first of these forms of alteration, - that in which the blood corpuscles become decolorized, affects in

Virchow – Die pathologische Pigmente. Archiv für path. Anat. und Phys.
Bd I 1853.

every case, the greater proportion of them, and in consequence the surrounding fluid becomes deeply tinged of a reddish or brownish colour, as for example is observed in certain apoplectic conditions of the lung, in which this condition is often present to a marked extent. In consequence of this process, the blood corpuscles become almost entirely invisible owing to the great transparency and slightly refractive property of their membrane, as compared with that of serum or water. It is quite unnecessary to suppose that in disappearing they undergo immediate solution or indeed that they are at all altered. Eventually, however, like all other organized structures they no doubt break down and undergo absorption.

In the other case - that, namely, in which the colouring matter undergoes its transformation into granular pigment, while it still remains included in the walls of the corpuscles, various modifications are observed. First, a form of by no means unfrequent occurrence is described by Virchow as occurring in various situations in soft and imperfect coagula, which have become more or less completely broken down into a dark red - diffluent mass, as occurs in the centres of large apoplectic clots in the brain and other organs as well as in the fluid of sanguineolent serous effusions, as in Hæmatocele. This is distinguished by the following characters. The margins of the altered corpuscles are more distinct and refractive than in the ordinary condition, while their diameter is much diminished, and they are observed to contain at their

Kölliker. Art. Spleen. Cyclop. of Anat. & Physiol. Part XXXVI

These crystals are represented after Kölliker in Pl. V. fig. 4.

edges or more rarely in their centres - Several minute granules which are characterized by presenting dark margins with transparent centres. These bodies when acted on by dilute acetic acid are rendered clearer - but are dissolved by the same reagent undiluted They are unaltered by water but soluble in strong solutions of caustic alkalies - The further changes which they undergo consist in their gradual diminution in size and the dissolution, first of the granules and, subsequently, of the membrane which surrounds them - Beale has described similarly altered corpuscles in large apoplectic cysts in the Brain and Eden (Canstatts Jahres bericht - 1847/Bd. I S 246) in extravasated blood in the Thymus Gland.

Secondly, - By far the most frequent kind of transformation which the corpuscles undergo under similar circumstances, presents somewhat different characters. They gradually, as above mentioned, become insensible to the action of Water and acetic acid, as well as of saline solutions. Their contents assume a shining yellow or brownish red or even black colour. After this, the disk-form and the smooth margin is gradually lost; the whole corpuscles becoming wrinkled and gradually diminishing in size, until at last they form only dark points

3edly Another very remarkable form, but one which is not very often seen to exist in which the colouring matter assumes a crystalline form in the centre of the corpuscle. Several instances of this phenomenon have been recorded by Kölliker; the only one in which he observed it in the Mammalia, he relates as follows. "In a dog

whose Spleen abounded in dissolving blood globules, the blood of the splenic vein distinguished itself by a very great quantity of colourless blood-corpuscles, almost all of which contained numerous nuclei, and often had a deceptive resemblance to pus-globules. In the blood of the liver were found a great number of altogether different blood-globules. These were swollen & almost colourless, but contained from one to five thinner or thicker small rods of a dark yellow colour. Part of these possessed the same length as the blood-globules, part were shorter. Kölliker found in two instances similar bodies in the Splenic blood of fishes.

In very many of the cases in which the corpuscles undergo the second form of transformation described above, the appearances which they present during the change are remarkably modified by the additional circumstance of their aggregation into spherical masses, and their becoming surrounded by a membrane as has been already mentioned in the preceding Section. This may take place either shortly after exhaustation, in which case the appearance of cells containing blood-corpuscles (the supposed blood-corpuscle-developing cells as seen in the Spleen of Gerlach & Schaffner) is observed, or the formation of these structures may not take place until a later period, when the blood-corpuscles have become more or less altered. This seems to occur in the metamorphosis of the Thrombus according to Stocky, and probably in many other situations.

At whatever period however, the formation of these cell-like bodies takes place, the ultimate result is the same, namely that they present

the appearance of pigment cells, which communicate to the tissue throughout which they are diffused or to the mass of altered blood which they contribute to form, various shades of colour according to the amount of change which they have undergone. They differ from proper cells in not always disappearing after an indefinite period - and their contents seem in general little liable to absorption. Thus I have found them in the so-called atrophy of the convolutions of the brain the result of an acute lesion which must have occurred many months if not years before, and Turnbull has observed them in a Thrombus of 12 years duration, apparently altogether unaltered. In most cases however they break up after a certain time has elapsed, nothing being left but granular pigment and the oleo-albuminous granules, wh. are usually associated with it

[7] General Facts relating to the formation and mode of origin of Col.r Crystals

It was stated above that, whenever stagnation of blood occurred, the greater part of the corpuscles became entirely decolorized. The principal proportion of the removed colouring matter becomes chemically changed and absorbed by the veins & lymphatics. Another part is involved to a greater or less extent in the formation of very peculiar crystalline bodies of a siemna-red or dark blood-colour, which wherever they occur seem distinctly traceable to altered blood. As far as my observations go they only are seen in altered blood clots of some size, being absent in diffused Extravasations, a circumstance wh. is no doubt owing to the substance which forms their basis existing in a more concentrated form in the former than in the latter situation.

Bruch - Ueber Pulzündungskugeln - Henles Zeitschrift Bd. III S. 47.
Henle - Op. cit. Bd II S. 733

These crystals have been investigated by several authors both results somewhat contradictory — especially with reference to their chemical composition. On this account there is considerable difficulty in arriving at a definite conclusion as to the conditions on which their formation depends. We shall return to this subject in a future section.

Chapter II

On the Metamorphosis of the Blood-corpuscles and their contents as observed in obstructed vessels and extravasations, according to the special organs & tissues in which they occur — with illustrative Cases & Observations

[8] Observations of Zwicky on the metamorphosis of the corpuscles in the Thrombus of Arteries

For the following facts I am indebted to an abstract of Zwicky's results in a paper by Carl Bruch, on Inflammation-globules as well as to the notice previously referred to in Prof. Henle's Pathology

Zwickys observations on the Thrombus extended both to the lower animals and the human subject — and the changes were recorded day by day as they occurred. The general results agreed in most respects with those which are to be obtained relative to hæmorrhagic clots in the brain & other organs to be subsequently detailed.

In accordance with the general observations contained in a previous section (Sect. 6) Zwicky found that the corpuscles & their

contents became changed in two distinct modes. A proportion of them — by far the most numerous disappears without leaving any visible trace, a circumstance which is attended by a gradual diminution in the size of the clot itself, along with an alteration of its colour. which between the second and fourth week was observed to pass gradually from scarlet through rose-colour to a yellowish white. By this time most of the corpuscles had dissolved, and about the 5th week, but few were to be found. Whether could not determine whether, during this process, the membrane burst, allowing the escape and subsequent dissolution of the contents, or whether the corpuscles, without bursting gradually became clear as after the action of water.

The other and less considerable proportion of the corpuscles undergo a chemical alteration of the membrane and contents They become insensible to the action of water & acetic acid. and losing their characteristic form. and are finally converted into reddish brown granules, just as is described in section 6, as the second mode of transformation mentioned.

In their arrangements with respect to each other, these altering corpuscles presented some peculiarities. They formed in certain parts of the clot, which had in consequence assumed a brown colour, little clumps or masses of pigmentary granules. which were however not surrounded by a membrane, and were most of them very transitory. having entirely disappeared by the sixth or 8th week, a few being however traceable in a Chorion of 2 years duration.

These bodies may in all probability be considered analogous to the more developed cell like bodies which we shall find occur in organizing clots under other circumstances.

[9] Metamorphosis of the Blood-corpuscles and their contents in Cystiform Structures.

Under this head will be included the facts connected with the metamorphosis and formation of hæmorrhagic cysts or apoplectic cysts in whatever tissue they occur, as well as the consideration of certain cystiform structures which arise from circumscribed exudations, in which blood-corpuscles are accidentally present. We know from accumulated observation that a cyst consisting of a well-defined wall, lined by a structure which approaches more or less to an epithelium, may arise in any tissue which presents the requisite mechanical conditions, entirely as a new formation morphologically independent of any previously existing. This doctrine is well illustrated by the history of those serous cysts which are known to originate from large extravasations into the substance of the brain, and it will be seen from the following details, that whenever such an extravasation takes place into a loosely connected, and consequently, non-resistant tissue, it unfailingly undergoes those changes, which will finally result if not interfered with by accidental circumstances, in the formation of such a cyst.

In accordance with the above observations

three or four modes may be enumerated which a cystiform structure may be developed, so as to constitute an abnormal growth. First, It may take place by an exudation into a previously existing normal structure of the same kind as into a Graafian vesicle, into a mucous or sebaceous follicle or into the dilated capsular termination of a kidney-tube. Secondly, An infiltrated mass of exudation, (as the gelatinous Exudation into the cells of the Thymus gland in Bronchocele) may often centrally and eventually give rise to a well-developed cyst. 3rdly. A circumscribed exudation may take place in any case tissue (as in the formation of Colloid cysts in the loose cellular tissue of the chorord) with the same result. Lastly, a cyst will arise from an Extravasation into a tissue which presents the same mechanical condition, as in the apoplectic cysts of the brain above referred to.

Of the contents of those cysts even which do not arise in the first instance from Extravasation, blood is frequently found to be a constituent. In these the corpuscles & other elements undergo the same changes as in those of apoplectic origin in accordance with the observation which was made above, that the metamorphosis of an exudation & extravasation is, under similar circumstances, precisely the same

(a) Apoplectic Cysts of the Brain

An extrav-asation which will result in the formation of an apoplectic Cyst may take place in the Brain in various ways.

Rokitansky Path. Anat. Vol III P393

In some cases a number of capillaries or rather minute arteries over a limited space give way, producing in the first instance the appearance of what is called "capillary apoplexy". One or two or a greater number of these minute extravasations enlarging and breaking down the tissue immediately surrounding them may coalesce so as to form a large more or less spheroidal clot, with ill-defined margins. In other instances the result is produced somewhat differently. A single blood vessel gives way and the blood continues to escape from it - breaking down the neighbouring tissue as it gradually enlarges. The clot which is produced presents much the same appearance in either case, except that in the first it is not so well defined and spherical as in the second, and contains mixed up with the blood which constitutes it, a larger proportion of broken down tissue.

The first change which the extravasated blood undergoes is the process of coagulation. In the greater number of cases, the coagulum forms a dark red homogeneous mass which fills out the cavity and assumes its form. Occasionally however, according to Rokitansky, part of the fibrine separates into a colourless central or peripheral portion, an occurrence which he describes as having an important influence in retarding the process of absorption.

In the more common cases, the soft mass, which consists of the Blood-corpuscles & Serum imbibed in the meshes of the coagulated fibrine - undergoes rapid absorption, - in the first instance

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owing to the disappearance of the serous fluid and latterly even of the greater part of the corpuscles & fibrine. While these changes are progressing an exudation of liquor sanguinis from the surrounding tissues takes place. This concurs with the fibrine of the peripheral part of the clot itself to form a fibrous cyst, which completely surrounds it, and is lined by an inner layer of material undergoing organization of another kind, consisting of the development of cell-like bodies or conglomerates, which include blood-corpuscles in various stages of their metamorphosis into granular pigment. In large extravasations, the mass of blood corpuscles and fibrin at the centre are not concerned in any well marked process of organization. The latter undergoes that process of softening, which is preparatory to further change - but no nucleae or other structures are developed init, while the former becomes decolorized and disappears - or without losing their colour simply shrink up into little irregularly shaped bodies.

In a large apoplectic cyst, which was removed from the anterior lobe of ___ hemisphere of the brain of an ___ and the duration of which was about ___, on microscopic examination, I found the following structures to be presented.

The cyst, which had unfortunately been for some time immersed in alcohol, measured about 3 inches across. It was well defined externally and of firm consistence. The contents consisted of a soft pulp of broken blood globules, which had undergone the changes above referred to, and were most of them in a state of dissolution preparatory to absorption — along with cholesterine crystals and flakes of broken down fibrine. The cyst

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L. Pl I Fig 3 Explanation

itself consisted of an external firmer portion about 1/50 line in diameter, which was perfectly colourless, and an internal soft and more friable layer of a pale yellowish pink colour. The external layer was found to consist of smooth bands of fibrillated substance running more or less parallel with each other, in which were embedded numerous minute granules but no pigment. These did not present the appearance of fully formed white fibrous tissue, nor did they shew any nuclei or so called nuclear fibres. They seem rather to be the direct result of the "splitting up" process described by Henle & others in organizing fibrine, which may and does take place without the intervention of nuclei. × The internal layer presented under the microscope, a homogeneous glutinous looking substratum without appreciable structure, and in which also numerous fine granules were embedded. Besides these a considerable number of conglomerates of various sizes (from 1-1500th to 1-1000th of an inch) were observed, which consisted of yellow granular pigment. None of these displayed a surrounding membrane, so that they could only be considered attempts at the more distinct forms found under similar conditions in other situations.

With reference to the changes undergone by the blood corpuscles forming the soft central mass, Prof Henle has related that in an apoplectic cyst which he examined of 4 months duration, he found "the blood corpuscles smaller and more distinct than in the fresh condition, rounded and bordered with small dark points. They resembled blood-corpuscles, which had been treated with a concentrated saline solution and subsequently caused to swell out by the

Amelé - Op. cit. P. 135

action of water, the result of which is that the colouring matter instead of being equally distributed over the corpuscle appears in little masses at the periphery."

After the fluid contents of a cerebral apoplectic cyst have been reduced to the condition above described, their absorption takes place without their being subject to further change, and finally if the healing process progresses favourably, they will altogether disappear giving rise to a linear cicatrix, consisting of an external fibrous portion, which may be observed in general, enclosing a more or less granular, highly coloured centre - the remains of the internal or fragmentary layer of the cyst. In some cases the cavity never closes but the fluid becoming gradually clearer & clearer, the whole at last arrives at the condition of a true serous cyst, in which it may remain for an indefinite period.

(b) Apoplectic Cysts in the Areolar Tissue.

In accordance with the general facts referred to at the beginning of the section, circumscribed haemorrhages in loose areolar tissue give rise to lesions similar in every respect to similar haemorrhages in the substance of the brain, and result in cysts even more fully organized than those that occur in the brain. The special facts connected with their history will be best illustrated by the following observations.

Obs. I In removing the scalp for the purpose of examining the brain of a pigeon, I observed, embedded in the intervening loose cellular tissue, and connected with it a tumour about the size

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The general relations of this tumour to the surrounding cellular tissue are shewn in Pl. V F 2 - it being magnified about 8 diameters

of a millet seed, and of tolerably firm consistence. On removing and examining this tumour I found it to present the following structure. It consisted of two parts. The external portion or cyst was of a dull yellowish colour and resistant texture. Under the microscope it presented the structure of fully developed wavy white fibrous tissue with a very few of the cell-like bodies to be next described. The internal portion or nucleus was of softer consistence and of a dark sap green colour. It presented the following elements. 1st. Cell-like bodies. These were of a round, oval, or occasionally irregular form. They presented the appearance of a distinct membrane and well-defined margins and measured from 1-2200th to 1-750th of an inch in diam.^{r}. In almost all a vesicular clear nucleus was visible beneath which they contained a. highly refractive oleo-albuminous granules, perfectly spherical and apparently colourless of very various sizes. b. Amorphous granules of various sizes and of a yellow green colour. These granules seemed to form the sole contents of the smaller cells. c. Coloured Crystals. These crystals not only occurred within the cells, but in great numbers in a free state. They were of a deep sienna-red colour. of a rhombohedroidal form. the respective angles formed by them sides, as far as I was enabled to measure them being 60° & 120° respectively. They were remarkably regular in their form and it was remarked that while the thinner examples presented more of the yellow tinge, in the thicker, the red was more observable. Lastly All the above described bodies ~~form~~ were also found in large quantity in the free state.

Sie ~~Pl. II Fig. 4, 5.~~ Expl.ne Pl. III Fig. 3 & 4

Transition stages between the cell-form and the fibre were observed at that part of the tumour where the external & internal portions of the tumour blended together. These occurred in the form of fibre cells which, while they contained the green granules above described in their central portion, had split into fibres at their ends. This circumstance would seem to point not only to a similarity in mode of origin in the two forms of structure, but probably a similarity in chemical composition between the fibre and the material forming the apparent wall of the cell.

Obs. II. In a frog which had been kept for three months without food, I found in opening the abdomen a tumour of about the same size as the one last described occupying the loose subserous cellular tissue of the mesogastrium. It was of an oval form and consisted of a fibrous cyst enclosing semi-solid contents. The latter, when microscopically examined, presented a finely granular material of a distinctly grass-green colour - among which were dispersed numerous spherical fatty granules which possessed the same colour and were of very various diameters. None of these appeared to be enclosed in cells. They were unaffected by Acetic Acid Sulphuric Acid & Sol. of Caust. Potash, though they were entirely decolorized by Strong Nitric acid.

The external portion of the cyst consisted of well-developed white fibrous tissue - but it was lined by an inner layer, which presented the following remarkable elements, namely, Cell-like Bodies Each of which contained an irregularly spheroidal or mulberry shaped

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See Pl III Fig. 4 & 5 Explanation

Carl Bruch, Zur Entwickelungsgeschichte der pathologischen Cystenbildungen. Zeitschrift für rat Med VIII Bd 1861

Central mass of pigment. This mass presented a granular appearance and was of a dark brown colour at centre - of a lighter yellowish brown externally. It was surrounded by a distinct membraniforme structure which, under the microscope, displayed faint concentric lines as if it were composed of several laminæ. On adding acetic acid (diluted) the membrane was unaltered - but it was dissolved by that reagent when undiluted. Caustic Potash in solution and Nitric Acid produced no effect on the membrane, but the latter converted the brown colour of the pigment-any matter into bright yellow.

Although in the two examples which we have been considering there is no distinct proof that the appearances described originated from extravasation of blood either into previously existing cysts, or, as is more probable, into the areolar tissue in which they were found, there can be little doubt that such was the case. In the first place they agree in all essential points of structure with formations which we know to originate in that manner, and secondly we should come to the same opinion by excluding, inasmuch it is impossible to conceive of any other mode of origin assignable to them.

Obs. III The following case of Hæmatocele, in a patient in whom there was also encephaloid disease of the testicle, I have extracted from the Papers of C. Brooks on "Pathological Cyst-formations"

Three months before the patients death he had received a severe blow on his left testicle, which was attended with much pain and swelling. On post mortem examination the testicle and epididymis

on that side were found to be healthy. The tunica albuginea was
unaltered, but between it and the tunica vaginalis, there was
found, in contact with the former and pressing somewhat upon
it, a clot of the size of a nut of a brownish red colour, with
a yellowish firm peripheral portion, and a pulpy broken down cen-
tre. The former displayed a concentric arrangement of lamina,
and was about a line in thickness, blending externally with
the surrounding loose cellular tissue. Besides this larger one
a smaller was found, which resembled it altogether, except in con-
taining yellowish serum. Microscopic examination shewed
that the central portion, which was of very friable consistence
was formed of a loose network of fibrinous material along with
numerous blood corpuscle-nuclei, - rounded heaps of granules, "masses
of yellow pigment & clump-like bodies as large as pus corpuscles,
wh. were rendered clearer but not dissolved by acetic acid" Many
of the blood corpuscles had become insensible to the action of acetic
acid and all stages of transformation between them and pigment-
granules were seen. The fibrine displayed less and less organiza-
tion, as you passed in examining it from the peripheral to the
more central and fluid parts, which consisted of altered blood-
corpuscles only. The external portion on the contrary consisted only
of concentric layers of fibrine, the blood-corpuscles having disappeared,
of which the most internal displayed no nuclei, but simply
a network of flattened fibres, while those most external and
consequently most developed possessed long small nuclei, and

distinct isolated fibres, the characters of which blended insensibly into those of the normal tissue of the part.

The cyst above described is an example of a structure altogether analogous to those just alluded to the origin of which from an extravasation however is more certain and distinct; and the appearance of the smaller cyst which occurred along with it affords an illustration of the ultimate condition wh. such a structure with in most case assume - that, namely of serous bag.

The following observation (also extracted from the same author) affords an example of a similar formation containing blood, but originating in a manner somewhat different.

Obs. IV In a young man in whom there were tubercular cavern at the apices of both lungs, and in whom the Thyroid gland was enormously enlarged, that organ presented, on examination after death, the following appearances. The right lobe seemed to consist of several lobules each of wh. were as large as eggs. The left was similarly divided and contained at one part an earthy concretion as large as a bean, while at another a colloid cyst, not less than a goose egg projected. In some parts the gland appeared quite normal in texture, shewing the semi-transparency and orange tinge of the parenchyma, which, at the parts where it was diseased blended into yellowish white. From the lobes which presented a normal appearance could be squeezed abundance of the fat-globules and nuclear structures which are usually found in the organ. The characteristic vesicles of the gland

could also be detected easily - embedded in the parenchyma.

On making a section of the portion where the cyst was observed there were found, besides the larger cyst several smaller ones, which were filled with "an opaque yellow gummy fluid, in which floated crumbling flakes of a red colour". These consisted, as shewn by the microscope, of clumps of Blood-corpuscles connected together, which were partly deprived of colour and had swollen out or lost their shape, & were partly confluent forming rows or small groups of a deep red colour, along with which were numerous free blood-corpuscles, granules, nuclei and cell-forms such as are observed in the normal parenchyma, - and isolated gelatinous looking small masses. In other cysts in the neighbourhood, a denser honey-like material, like softened parenchyma existed which contained, besides the above mentioned elements, "heaps of granules of a yellow colour, which included large, dark yellow shining angular corpuscles, and very probably consisted entirely of agglomerated shrunk Blood-corpuscles". Many of these bodies possessed a clear margin which disappeared when treated with acetic acid."

As to the mode of formation of these cysts, it would appear, from their being surrounded by tissue, in which a gelatinous exudation had taken place into the gland vesicles, and from the fact that the smaller cysts now possessed a distinct membrane, but were only surrounded by the parenchyma altered by this exudation, that they were originally mere vomicæ

Kussmaul. Zeitschrift für Rat. Med. 1852. Bd III

produced by softening, & the which had become subsequently provided with a distinct membrane, and into which accidental hæmorrhages had taken place. In the large cyst which occured in the left lobe of the gland, a clear yellowish serous fluid was found, and it was provided with a smooth lining membrane.

The following Case of Hæmorrhage into the Peritoneum - followed by the formation of cystiform tumours, & which is attestation of the same facts is recorded by Adolf Kussmaul in Henle's Zeitschrift for 1847.

Elizabeth Dietrich æt. 36. Cheese-maker, was first seen on the 4th of Jan.y 1846, when she suffered from want of appetite sleeplessness - ringing in her ears, irregular menstruation &c. Abdomen much swollen with distinct fluctuation. Pulse & temperature of skin natural. A hard tumour as large as a hens egg was felt in left groin. Slight pain on pressure at umbilicus. No ædema. Urine very scanty & pale. Leeches were applied to the abdomen which was followed by mercurial inunction, which was continued till salivation was produced. A mixture with digitalis and tart. of potash was ordered.

Jan.y 21st No increase in quantity of urine but profuse sweating has come on. Pain much aggravated. Various other diuretics were tried with no better effect upto Feb.y 24th when paracentesis was performed. The Trochar was introduced halfway between the ant.r sup.r spine of the ilium and the umbilicus. No fluid passed from the Canula. The trochar was again introduced an inch higher up with the result of a full stream of blood.

The blood was of natural appearance, except that it presented a slight buffy coat. For a time she was much relieved, but towards the middle of March the abdominal swelling was again considerable. On the 15th the pain became very severe and the patient appeared much emaciated, and was feverish. By her own desire the paracentesis was repeated with the same results as before. After this she sunk fast, the countenance became hippocratic, pulse rapid & feeble, death following on the 8th April.

Sectio Cadaveris - The cavity of the abdomen was filled with blood, which, though it appeared unaltered did not coagulate within the usual period. Various parts of the Peritoneal Surface were beset with innumerable tumours. Along the smaller curvature of the stomach and on both aspects of the great omentum they existed in great numbers, but for the most part of inconsiderable size. The largest were found in the serous covering of the intestines and in the mesentery. In size the tumours varied from that of a pins-head, to that of a gooses egg. In form they were generally round. In all the attachment was narrower than the width of the tumour, and some were pedunculated, the pedundles being occasionally more threads, and not less than an inch in length. In many of the larger ones numerous smaller ones were attached, so that the whole resembled a bunch of grapes. The colour, especially of the smaller ones, was light reddish, while the larger ones were generally darker, more like masses of blood clots.

The tumours were examined by Prof^r Henle with the following results,

The small tumours on the surface of the intestine were found to be covered by the peritoneal investment, and those which existed in the omentum were between its layers. They appeared to consist simply of extravasations. The large tumours all possessed a membranous investment, which was continuous with the peritoneum, which it appeared to have carried before it in its growth. The structure of this covering was however different from that of the peritoneum. It consisted of newly formed fibrille, and contained no fully developed fibrous tissue. On removing this membrane the contents were seen to consist of a soft or even partly diffluent pulp, through which a network or stroma of fine fibres was seen to ramify. These fibres when examined were formed like delicate blood vessels, about 1/3''' in diameter which were characterized by the oval nuclei scattered throughout their walls. It was easy to demonstrate their numerous branchings and anastomoses by washing a little of the pulp with water.

This last consisted in the large tumours for the most part of blood-corpuscles, which had aggregated into large round or oval globules resembling inflammation-globules. The largest of these measured 1/2'' in diam. Among them were numerous emulation corpuscles.

Some of the tumours were filled with freshly coagulated blood and had burst. These probably had given rise to the hamorrhage into the peritoneal cavity. Some of the smaller tumours had become firm and yellow at certain points, or

throughout their whole substance. Others had become converted into round thick-walled vesicles as large as peas, of elastic consistence. The yellow spots consisted always of a yellow fat in large and small globules - which at some parts, where the colour was browner, was mixed in granules with cholesteamine. In these parts the globules containing blood-corpuscles displayed a remarkable attention, having assumed a bright yellow colour, and broken down into fine granules distinguished by their equal size and regular sharp contour.

A Tumour as large as ones fist was found, under the peritoneum occupying the space behind the root of the mesentery, which had a very different structure. It was lobulated and while part of it presented a fibrous structure, another part was of cheesy consistence like tubercle. The fibrous portion consisted of the well-known stiff flattened fibres peculiar to cancerous growths, along with masses of exudation corpuscles & caudate cells. The cheesy portion consisted entirely of caudate cells easily separated from each other.

In the above very interesting case, which although I have given at some length, is much condensed from the original, we have an excellent illustration of the facts observed in the various stages of the transformation of blood-corpuscles generally.

In the first place in the smaller tumours, we have simply unaltered corpuscles of extravasated blood. Secondly, in the larger examples, we have the fibrine of that coagulum become organized at the periphery so as to form a well-marked

vascular cyst, and in the central portion being transformed into a stroma, also containing blood-vessels, while the corpuscles forming the great mass of the central pulp, have aggregated into conglomerates of various sizes as a preparatory step to their metamorphosis into granular pigment. Thirdly in some of the other tumours described we have a deposition of fatty granules and cholesteamine crystals forming a fatty degeneration of the newly formed tissues, a process most strikingly illustrative of what takes place normally in the transformation which the corpuscles of blood extravasated into the graafian vesicle undergoes and which results in the formation of the corpus luteum in the human subject.

With reference to the special conditions in which the singular pathological results above described as having apparently originated in the subserous tissue of the peritoneum, are to be considered dependent, it is more difficult to form an opinion. It presents some points of resemblance to that peculiar morbid growth, which is well known as colloid cancer, except that here the cysts were filled with extravasated blood instead of gelatinous matter.

From the fact that the smallest of the tumours, in the case before us, were in general evidently the most recent; it would appear that the process of extravasation must have been a gradual one, or rather that in each tumour, it must have been repeated at longer or shorter intervals. This supposition

fupine
favoured by the fact that the tumour which was found to have burst and which was the source of the haemorrhage into the peritoneal cavity was not a recent one, but had itself undergone considerable organization.

As regards the indirect cause of the whole disease, when it is considered that the patient had not menstruated for a considerable period, although no observations were made during life, as to the periods at which the various haemorrhages took place, to justify such a supposition or the contrary, the case might probably be considered to be one of vicarious menstruation assuming this remarkable form.

The Corpus luteum

The changes which the blood which is poured out into the ruptured Graafian Vesicle undergoes have, I believe, been very fully investigated by Lwicky in his work "De Corporum luteorum origine &c" I have been unable however either to obtain the work itself or to meet with any abstract of it in the Journals. I am therefore compelled to depend on the results of the few observations which I have had the opportunity of making myself on the subject, as I am not aware that any one except the above mentioned observer has enquired into it.

The corpus luteum as seen in the lower animals especially in the cow & sheep, differs very considerably in general appearance and to a certain extent in structure, from what we observe

in the human subject. In appearance the most obvious difference consists in the distinctness of the latter with a central cavity or colourless space with irregular waved outline can be traced on making a section through the corpus luteum of the human female. It is also considerably smaller and the coloured portion is more granular in its appearance. In structure the human corpus luteum possesses much less consistency and firmness than that of the cow or sheep, which is owing to the much less complete development of fibrous tissue in the former, and its smaller proportion to the colouring matter.

In the fully formed corpus luteum of the sheep, I found that the pale yellow glandular looking substance of which it was composed owed its colour to large cell like bodies of various forms, which contained spherical highly refractive granules (fatty granules) of a bright yellow colour, ... which differed very considerably in size from each other. These bodies were embedded in a fibrous stroma consisting of fusiform fibres-cells which were provided with staff-shaped nuclei. The history and mode of development of these fibre cells as observed by Twichy has been already alluded to in Section [5].

Towards the centre of the corpus luteum in the sheep, instead of the general yellow colour, it assumes a more or less reddish tinge. This was found to be partly owing to diffused blood, and partly to the fact that at that part the cell-like bodies

See Pl. III Fig 1 Expl.n

*Pl. II. Fig 1.

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contained, besides the above-described fatty granules, granular pigmentary matter of an orange or brick red colour. Besides these elements and blood vessels, there were interspersed between them altered blood-corpuscles more or less completely converted into pigment-granules. ~~Whether~~ Whether the above mentioned cell-like bodies had originally contained unaltered blood-corpuscles, or not is uncertain, as well as whether they were of subsequent or antecedent origin to the fatty granules. However that be, we know that they are not at all necessary for the production of these last, as they exist in the human corpus luteum where the cell-like bodies are absent.

The Corpus luteum in the human subject. On examining the ovary of a young female who had poisoned herself 5 weeks after her last Menstruation two corpora lutea were found in the course of formation. The one described below consisted on section of a central and peripheral portion, which possessed the relation of form and size represented in the drawing.* The central part was of a red colour, and glandular consistence, and was easily separable from the rest. On microscopic examination it presented a substratum of fibrillated material, in which no trace of nuclei or fibre-cells could be detected. Embedded in this material the following elements were observed Viz. 1st. Decolorized Blood-corpuscles, 2ndly, Spherical or ovoidal bodies with well defined margins & very refractive, about 1-4000 inch in diam, which were evidently blood-corpuscles partially transformed

3. wrong reference —

into pigment granules, 3rdly Rhombohedroidal Crystals of very regular forme and of the same colour (Sienna red) The largest of these only measured 1-2200 inch in its longest diameter. 4thly Some crystalline bodies the same transition forms between these two last. 5thly, Irregular masses of coloured material one of wh. is figured (Pl. 3 Fig 6). These display the remarkable phenomena when viewed by transmitted daylight of showing at some parts not the red colour which they possess generally but a bluish-green colour, which, however, does not seem to be exactly complementary to the original red.

On adding acetic acid no change was produced. On adding strong nitric acid, the fibrinous stroma was first converted into a reddish brown. On then adding caustic Potash in Sol^{n}, Effervescence was produced in the affected tissue and it was converted into a very bright orange yellow. No change whatever was produced in the crystals and altered blood corpuscles.

The peripheral or yellow portion of the corpus luteum presented a somewhat different structure. It was separated from the internal portion by a distinct border and presented on examination, 1st, A fibrinous substratum which toward the exterior was becoming organized and shewed nuclei which were beginning to arrange themselves in rows 2ndly, Fatty granules of various sizes to which the colour was probably due, but which under the microscope, appeared to be colourless like the granules of the yolk which they very much resembled.

x That is, no fibrous structures are developed in it.

In comparing ~~the foregoing~~ the foregoing histological facts[41] with what we know of the history of the changes which the corpus luteum undergoes in the appearances which it presents to the unassisted sight, and the mode in which it originates as described in the researches of Dr. Robt. Paterson and others, it would appear that, as regards its more intimate structural relations, the nature of the process which results in the formation of that body may be supposed in the human subject to be of the following nature.

1st. Immediately after the rupture of the Graafian vesicle, a coagulum, the result of the extravasation of blood at the period of the escape of the ovum completely fills the cavity of the Graafian vesicle, presenting the appearance of an homogeneous mass of firm consistence and of a red colour. (See Fig 2 of Dr. Patersons Obs.[ns])

Secondly. At the same period an exudation takes place external to the coagulum, and to the so called "internal membrane" of the Graafian vesicle.

Thirdly, The coagulum gradually contracts in bulk while retaining its original consistence, until about the 6th week, (when it presents the appearance wh. I have figured Pl. V Fig. 1), after which it softens and becomes absorbed, its place being occupied by the central cavity, which was found by Dr. Paterson to exist as early as the second month, and to contain a small quantity of clear fluid. During this period ~~the coagulum~~ the coagulum does not undergo organization properly so called[x], while the blood globules and their contents either become directly

absorbed, or converted into crystals or amorphous pigmentary material, as described above. That these last ever undergo absorption is very improbable. It is more likely that, while the fibrous substratum in which they are embedded softens & becomes dissolved, they remain unaltered and would be found in the fluid which subsequently fills the central cavity.

Thirdly, The coagulated exudation external to the central coagulum, presents, on making a section of the Corpus luteum shortly after the escape of the ovum, a narrow rim of material, which at a very early period assumes a bright yellow colour. In the course of the first few weeks it gradually thickens, and at the same time, from the contraction of the surrounding tissue, as well as of the central clot, it becomes plicated so as to present the jagged margins so characteristic of the fully developed corpus luteum. The intimate structural changes which it undergoes, are two fold. First, in the fibrillated substratum of which it originally consists, a deposition of fatty granules takes place by a process perfectly similar to that in which fatty granules become deposited (constituting Atheroma), in a fibrous layer previously formed on the inner surface of the walls of arteries, in which this morbid condition is present. Thirdly. It undergoes a process of organization consisting in the development of nuclei & fibre-cells and finally of true fibrous tissue.

Although the corpus luteum in the human subject, differs considerably in some points of structure from those of the Sheep & Cow,

Is there any difference between the structure of corpora lutea
unconnected with impregnation, & those which are? —

See Bouchet - & Renaud —

AB.

yet we cannot fail to observe the exact similarity in the forms assumed by the colouring matter, namely, that of fatty granules. Whether or not these granules owe their colour originally to the colouring matter of the blood, is uncertain. It is at least perfectly conceivable that as they increase simultaneously with the gradual decrease of the central coagulum, that the fatty material of which they are principally composed may be tinged by its colouring matter. The difference in colour is no argument against such a supposition, as there is every reason to believe that hæmatin, when united with oil in the form of globules may give rise to a different colour in the mass of such globules, from that which it communicates, when in the form of corpuscles, amorphous granules or crystals.

In examining the contents of the more fully developed superficial graafian vesicles in an unimpregnated ovary, it is extremely common to find that evidences exist of partial extravasations, not followed by any further changes, having taken place into them. These consist either of blood corpuscles in the course of transformation into granular pigment, or of cells infiltrated with blood-pigment by absorption. Those minor extravasations have no doubt occurred at various previous menstrual congestions.

Cysts of the Kidney

In the cysts which occur so frequently under various conditions in the cortical substance of the kidney, it is very common to

Virchow. Arch. für Path. Anat. und Phys. Bd. I S 387

? Thrush

find Evidences of Extravasation either in the form of altered blood-corpuscles in a free state or of more or less cell-like structures containing such altered blood corpuscles or granular pigment. Thus Virchow relates that in a collard cyst, wh. he submitted to examination, he found, besides cholesterine crystals & large colourless or pale-yellow masses, which were somewhat swollen out by acids, but rendered more transparent by ammonia, — peculiar dull-red or yellow globules from .012''' to .002''' in diam. These bodies were considered by Virchow rather to be compact masses of a colourless substratum, in which colouring matter either in a granular or diffused form was imbedded — than true cells. No membranous membrane could be shewn to exist, and reagents produced no effect. When a mass of them was heated to redness on Platinum foil, a red ash was left, wh. was found to contain Iron.

In Pl. I Fig. 4 I have represented similar cell-like structures also derived from a large cyst occupying situated in the cortical substance of the kidney. These were also insoluble in the action of acetic acid & acetic acid, and presented the other characters of those described by Virchow. They appear to be as much entitled to be considered as cells as any of the other cell-like bodies wh. have fallen under our notice as developed in Extravasations generally. They probably were originally formed round aggregations of blood globules, wh. had subsequently become altered so as produce the appearance presented. The figures

× (if there is time, before death)

Zeitschrift für exp. Med. IV Bd 1 H

[10] Metamorphosis of the Blood Corpuscles and their contents in diffused or infiltrated Extravasations.

Diffused Extravasations in the substance of the Brain, in accordance with the circumstances under which it takes place, under two modifications. Either it may occur in consequence of softening, from whatever cause or of whatever nature, or independently of it entirely, in which case it may produce it. Under both of these modifications it must be remembered in taking into consideration the nature of the changes, to which the Extravasated blood undergoes, that besides this blood, Emdation is also present and may modify the results.

In every case of cerebral Extravasation a large proportion of blood becomes diffused and infiltrated into the surrounding tissue communicating to it a yellowish tinge and a consistence softer than natural, which are sufficiently appreciable even if when the Examination is made shortly after the occurrence of the lesion. In illustration of the remarkable alterations which the blood corpuscles and their contents undergo under these circumstances I shall relate ~~the following~~ some Observations, which were suggested by reading the details of the following Experiment by Prof. Kölliker in his paper "On the state of the Blood-vessels in inflamed parts" He states that in wounding the hemispheres of the brain of a pigeon, and thus producing extravasation and sanguineous infiltration in the substance of the brain, that many of the so called "inflammation globules" which were developed in the neighbourhood of the wound

contained, besides their usual constituents, unaltered blood-globules. With a view of verifying this result, and ascertaining the further history of these "cells containing blood-corpuscles" I made the following experiments. In a number of pigeons at different times I passed a common surgical suture-needle through the upper part of both hemispheres of the brain with a view of producing extravasation. Of these a considerable proportion died from the effects of the injury. In others little or no extravasation was produced, and in these on examining 3 or 4 days after, I only found the usual compact granular cells indicating the presence of Exudation in the track of the wound. From those which lived a sufficient time, and in which other circumstances were favourable, I obtained the results detailed below, namely

First, Three to four days after the infliction of the injury it was found that the substance of the brain in the immediate neighbourhood of the track of the wound had assumed a yellowish green colour and somewhat soft consistence, the track of the wound itself being occupied by a clot. In the softened part, on microscopic examination, the following Elements presented themselves. 1st, Cell like bodies provided with a distinct membrane — containing finely granular matter and one or two oleo-albuminous granules. 2ndly, Similar bodies completely filled with oleo-albuminous granules (so called "Compound granular Corpuscles"). Both of these last Elements measured from 1-2000th to 1-1300th of an inch in diam. 3rdly, Angular Bodies Cells containing both oleo albuminous granules and perfect

2

Pl II F1 The outline of the surrounding membrane of the cells is represented much too strongly marked. It was extremely delicate though perfectly distinct

2

Pl II Fig 4. a

blood corpuscles. These last were very numerous, and some of them were observed as large as 1-800th of an inch. The blood corpuscles contained in them resembled entirely those which were floating free around them, and where water was added, it was observed that they were similarly acted upon, their nuclei being displayed. The drawing which I have given was taken from the brain of the first person successfully operated upon. It was compared with the appearances observed in subsequent experiments and corresponded exactly. I may add that Prof. Bennett was kind enough to verify these results.

Secondly, from seven to eight days after the infliction of the same injury, the following appearances were observed. In the case to which the description refers, no signs of a clot were observed as before in the track of the wound, which was only indicated by a yellow softening. In the softened part were observed similar bodies to those last described, but which appeared to have diminished some what from their original size, when compared with those from the more recent lesion, their average diameter being 1-1500th of an inch. They possessed well defined margins and contained albuminuous granules and bright yellow finely granular matter, besides occasionally altered and contracted blood corpuscles. When submitted to the prolonged action of acetic acid, they remained unaltered, and were quite unaffected by water. On adding solution of caustic potash, the colour of the granular matter was converted into a rich reddish brown.

Pl II Fig 4 b

Thirdly, In a pigeon whose brain was examined 48 days after the infection of the same injury, it was observed that the greater part of the blood was generally diffused in the neighborhood of the track of the wound, as indicated by the yellow coloration, while in one spot a minute coagulum, not larger than a mustard seed could be distinguished. On microscopic examination the following elements presented themselves. Generally diffused in the track of the wound, there occurred bodies altogether similar to those last described, containing oleo-albuminous granules and a bright yellow amorphous material. In some of these, the one constituent preponderated, and in some the other. Their diameter was about 1-900th of an inch, and they almost all presented either at their centre or circumference, a spherical clear space indicating a vesicular nucleus. Lastly, In the coagulum above referred to, ~~cells of~~ similar bodies of smaller diameter, as if contracted, which contained almost nothing but the yellow amorphous matter, were observed. These differed from those above described in not presenting the appearance of a smooth transparent membrane surrounding them, so that they rather resembled masses of conglomerated amorphous matter than cells. Their colour was not so bright as that formerly mentioned, rather being of a ochre- than a gamboge-yellow.

The results of the above observations seem to be important in two points of view. First, they go to prove that the hitherto received doctrine that the so called "compound granular corpuscle" or

Bennett, "On Inflammation of the Nervous Centres." Vol. I
Edin^r Med. & Surg. Journ. Vol XIX P. 326

* It is very difficult to see how this is proved in any way -
J.H.B.

husband -

"Exudation corpuscle" as observed in the brain "is formed like all other primary cells, a nucleus being produced, from which a cell-wall arises," is a false one. Secondly, They illustrate and explain the mode in which the appearance of cells containing blood-corpuscles (Blut-körperchen-haltenden Zellen) on which so much stress has been laid by Gerlach & Schaffner, may be produced and afford the Experimentum crucis in proof of the doctrines of Prof. Kölliker, that, under certain circumstances, the corpuscles in extravasated blood become enclosed in an apparent membrane before undergoing further change.

The same facts are illustrated by the post-mortem appearances which were observed in the following case.

Mrs Mc Pherson ætat 32 was admitted into the Clinical Wards of the Royal Infirmary on the 22nd of Decr 1850. On admission, she suffered from intense dyspnœa with cough and copious expectoration, along with other very urgent pectoral symptoms, which were liable to occasional paroxysmal exacerbations. Under them, she continued to labour during the whole period of her stay in the house, that no suspicion was excited in the minds of those under whose care she was placed as to the probable existence of any affection of the nervous system. Unfortunately, no investigation was made into her history, and she died on the second of January. Subsequently, however, the following facts were elicited from her friends. Five years ago she had a paralytic attack affecting

x (for correct history of this case see Lectures on Clinical Medicine - No. 4) — TRR —

her left side, from which she recovered perfectly in two or three months. Four months ago she had a similar attack with loss of consciousness, and more complete paralysis of the same side. The insensibility gradually disappeared during the ensuing fortnight, but it is stated that she never entirely recovered the use of her limbs and that there was a permanent impairment of memory. ×

Sectio Cadaveris Thorax. There was dilatation of the left ventricle of the heart with diminution of the thickness of its walls and mitral incompetency. Besides the usual appearances of Bronchitis on both sides, the left lung was non-crepitant throughout and a bloody serous fluid oozed out on section & pressure. At the base posteriorly, there was an extensive hæmorrhage. The Rt. Lung was also generally non-crepitant, except at its anterior margin where it was emphysematous.

Head. On removing the calvarium, the membranes presented the normal appearances. The Ventricles were moderately filled with fluid, which on the left side was tolerably clear, but on the right was very turbid, — of a greyish colour and displayed under the microscope numerous comp.d granular corpuscles. On making further examination, it was found that the post.r three fourths of the right corpus-striatum at its outer border was softened & ~~at one part~~ almost diffluent. On one part wh. was most diffluent, a few masses of inconsiderable size, which possessed a firm consistence and a bright yellow colour were observed,

See Pl. III fig 3

N. B. I regret extremely, that, owing to the unfortunate absence of the pathologist to put up the part in Spirit, I was unable to examine this most interesting lesion so satisfactory as I could have wished.
Kölliker – in op. cit. P. 784.

The softening extended to the medullary substance in the neighbourhood.

In the centre of the Pons Varolii, a limited portion of red hæmorrhagic softening, not exceeding a garden-pea in size was observed. It was situated a little to the right of the middle line and was of recent appearance.

Microscopic Examination. In the softening last mentioned, besides blood corpuscles, and the somewhat broken down elements of the normal structure of the part, consisting of fine granules & nerve-tubes, there existed large cell-like bodies of various diameters (from 1-220th inch to 1-100th inch). Of these some contained apparently nothing but unaltered blood-corpuscles and a transparent fluid, the proportion of the one to the other varying considerably in different instances. In others the corpuscles had become more or less completely converted into granules, and to had assumed during this change an intense golden yellow colour.

These bodies were totally unacted on by water. Their membrane was perfectly homogeneous and apparently structureless. In some cases they assumed the appearance of flask-shaped dilatations of minute vessels, inside of which they probably had originated. This reminded me of a similar appearance, which Prof. Kölliker has described & figured as occurring in certain fishes. He found "cells containing blood-corpuscles and their metamorphoses included in round delicate-walled vesicles - which resembled pouchings or dilatations of the sheaths of minute arteries.

See Pl. II. Fig 2

A it was found to

?

On examining the creamy fluid obtained from the most different part of the softened corpus striatum, I found the following elements, namely, 1st, Compound granular corpuscles, varying from 1-1500th inch to 1-1000th inch in diameter, and containing oleo albuminous granules of very various sizes. 2ndly, Similar corpuscles containing in addition, finely granular pigment of a bright-yellow colour, diffused among the granules. 3rdly, Similar corpuscles, containing besides both the above constituents, pigment-grains - spherical or spheroidal in form and of a bright brick-red colour. These last appeared to be altered blood-corpuscles. 4thly, Free oleo albuminous granules & pigment. It was observed that the red pigment always assumed the form of the spheroidal grains like contracted blood-disks, while the yellow was always in the amorphous or finely granular condition. Both forms were unaltered by Acetic Acid, Caustic Potash or Water.

On examining the yellow material of firm consistence above alluded to, consist of a sub stratum of transparent pretty firm material, somewhat like coagulated fibrine, in which were embedded oleo albuminous granules & pigmentary matter. It might probably be considered as an indication of the former presence of an apoplectic cyst in the situation in which it occurred.

Since making the above observations, I have seen a Memoir by a German observer on the similar facts are recorded.

Ecker "Zur Genesis der Entzündungskugeln"
Henle's Zeitschrift Bd VII. S 87.

Prof. Eckes in a paper "On the genesis of Inflammation globules" records the following case.

A little girl, 4 1/2 years old, who was attacked in the course of an epidemic of hooping cough, which prevailed at Basle in the winter of 1846, after two months duration of the disease, died with the symptoms of general Tuberculosis. On making a post-mortem examination, a softened portion, about the size of a dollar of a yellowish colour was detected, which was scattered over with numerous bloody points. The microscopic elements met with in this portion were, besides the usually observed fragments of nerve-tubes &c, 1st." Unaltered Blood corpuscles (Coloured). 2ndly, Colourless blood-corpuscles. 3rdly An extremely finely granular material, soluble in Caustic Potash (Coagulated Fibrine). 4thly, Cells which contained, besides a greater or less number of dark or yellowish granules, — blood-corpuscles. The cell-membrane was remarkably distinct and the blood-corpuscles altogether unaltered" The number of blood-corpuscles contained in one cell was various. A few contained only one, and had a diameter of .010 mm. Others which measured from .015 to .025 mm contained from 6 to 8 blood corpuscles or even more. In saline solutions the surrounding membrane, which adhered closely to the contents was less distinct. Water made it swell out and it was easy to satisfy oneself by rolling the globules, that the blood corpuscles lay within a membrane. In most of the globules, the membrane was unaltered by the prolonged action

of water, while in others, it at length became indistinct.

Thirdly, Heaps of similar granules to those occupying the cells above described along with the blood-corpuscles, some of which were surrounded with a membrane - others not.

There does not appear to be any evidence from the facts related, to infer that the changes which the blood-corpuscles undergo when diffused through the substance of the brain are at all dependent on their being enclosed in cells or cell-like bodies. In the first place the preliminary attenuation in their susceptibility to the action of water and acetic acid, takes place in the corpuscles which are free just as in those enclosed - and the same is being probably true of the later stages of their conversion into pigment. It is however impossible to decide whether the granular or amorphous yellow pigment in old lesions resulting from Extravasation may not always have arisen from broken down cell-like bodies. This is illustrated by an observation I made in an example of what is known to pathologists as Atrophy of the Convolutions (see Cruveilhier, Livr. 20 Pl 3 - Livr. 33 Pl 2), a lesion in which the place of the grey matter seems to be occupied by a fibrinous material infiltrated with yellow colouring matter, and which seems to be the result of a former acute Exudation accompanied with Extravasation. In the case in question which, according to what we know of the history of the lesion, must have been of considerable standing, it was found that the yellow coloration was still principally due to cell like bodies which I have represented in Pl III Fig 5 and which contained finely

granular pigment of a dark yellow colour. These bodies had most probably originally contained blood corpuscles, wh. had undergone within them, their metamorphosis into pigment.

Diffused Extravasations in the Lungs. Of the changes which the blood corpuscles undergo in pulmonary extravasations, I can say little as I have had no opportunity of making direct observations. They probably however will be found to resemble those wh. we have already seen in the brain pretty exactly. It is stated by Virchow that they corpuscles become converted in the lung into black granular pigment. This may sometimes be the cases but seems very doubtful, and I donot find that Virchow made any observations to prove it. In one case in the chronic pneumonic indurations which surrounded certain obsolete lesions of a questionable character in the lung of a man who died in the R.I. Infirmary of Dysentery, I observed infiltration of a considerable quantity of a pigmentary material, which, on microscopic examination, was found to consist of amorphous masses of bright yellow granular pigment, some granules being observed to be enclosed in the so-called exudation corpuscles, which existed in considerable numbers.

In many many cases of extravasation into the substance of the lung, the coloured contents of the corpuscles, becoming dissolved in the infiltrated serum or other fluid, afterwards reassumes the solid form, that of the so called hæmatin crystals, which have been described by various authors. Then it is not uncommon to find

Guizot Archives Generales de Brd. T. VII 1815 P. 166.

1995

not only in the substance of the lung, but also in the sputa, in cases of Phthisis & chronic Pneumonia.

[Gluge has recorded a case in which black crystals large enough to be seen by the naked eye were found in great numbers in the tissue of a tubercular lung, and Rokitan has recorded the following case, which may be considered as an exemplification of one mode in which the coloured contents of the blood corpuscles in pulmonary extravasations may become metamorphosed

Carl Engel Saxonian æt. 33 - admitted into the Charité Hospital Berlin 18th of October. For 22 weeks, during which he had worked in a damp situation, he had suffered from pains in his extremities, cough & dyspnœa, There was œdema of the lower extremities and ascites Urine was scanty: Pulse 96. These symptoms continued to the 22nd when he became worse. There was profuse diarrhœa with sharp pain in the left hypochondrium. There was also much fever - pulse 120 weak & small - and great difficulty in expectoration & dyspnœa. He got gradually worse till he sunk on the 8th of November.

On Post-mortem examination, it was found that the right pleural sack was half filled transparent serum - the right lung being compressed & very melanotic with some isolated masses of obsolete tubercle and a hepatized portion at the base. On section, an ink like fluid could be squeezed out - The bronchial mucous membrane was much reddened & somewhat thickened. Many of the branches of the bronchial artery were blocked up with old clots of coagulated blood. The right lung was very emphysematous, but otherwise presented

the same characters as the left. The inky fluid above referred to contained black pigment in quantity both in the form of granules & crystals. The crystals consisted of flat-tened rhomboidal tables with very sharp angles so long in proportion to their thickness, as to make them almost spear shaped. The length of the largest was from ·008‴ to ·016‴ the breadth being ·002‴ Among these, others of less considerable dimensions occurred in far greater numbers, which did not exceed from ·0012 to ·0032 in length.

As was above remarked, there is no proof that in this case the black pigment whether in the granular or crystalline form was derived from the colouring matter of blood, as there seems to be no circumstance in the history of the case e.g. the existence of cardiac disease &c, from which it might be assumed that Extravasation to any extent had taken place.]

[11] Metamorphosis of the Blood corpuscles and their contents in the Liver. Although in Man & the Mammalia we have little or no evidence that the transformation of the blood corpuscles into granular pigment takes place to any great extent or under any condition whether normal or morbid, in this organ we have abundant proof that such is the case in some of the lower animals, especially in the batrachian reptiles. In these last indeed the process is carried on so regularly, and, as it appears to me, assumes so much the characters of a physiological process, that it is surprising that Prof. Kölliker and others who have fixed on the

breaking down of the blood-corpuscles as one of the functions of the spleen, have not allowed a share in this office to the liver, in the case of which, as far as the batrachians are concerned, the evidences appear so much more conclusive, as I think will appear from the following facts.

If you examine the liver of a Frog or Newt during the Summer months, when the animal is obtaining abundance of food, you will find that the liver cells are more or less filled with fatty granules. Towards the end of autumn, when the period of what is not very correctly termed hybernation is approaching, these fatty granules disappear to a greater or less extent & the organ undergoes other changes of an interesting nature. With respect to these I have made the following observations.

1st On examining the liver of a frog about a week after it had been taken (on the 6th of November), among other elements of the normal structure of the organ, I found vesicular bodies existing in pretty considerable numbers which contained in their interior other smaller bodies, which presented the form & colour of blood corpuscles, and on which nuclei could often be observed. These I have represented in Pl II Fig 3. That they really were what they appeared to be, and were in fact produced by an analogous process to that by which we have seen similar structures originate in the brain, I think there can be little doubt. In the drawing will be observed other smaller spherical

bodies, containing granular pigment of a dark brown colour
These occur sparingly at all seasons in the liver of the frog,
and are probably the remains of vessels wh. have formerly
contained blood-corpuscles the previous season.
Lastly, in making similar examinations at later periods during
the winter, somewhat different appearances present themselves.
Thus, in a frog which was kept without food, and examined
on the 22nd of Jan^{y}, the liver presented on microscopic ex-
amination, no perfect liver-cells. Nuclei presenting the
usual appearance were however to be observed, along with
very numerous minute fatty granules. Besides these,
the bodies which are represented in Pl. III Fig. 2 existed in very
great numbers, so as to give a decidedly dark colour to the
whole organ. These presented the following forms, viz, 1st, Bodies
with well-defined and sharp margins, not so transparent
as blood corpuscles, of an olive-green colour, and frequent-
ly containing a smaller nucleus-like body in their centre.
2ndly, Others similar to these but of a reddish-yellow or yellow-
colour. 3rdly, Others containing brick-red or reddish brown
pigment, arranged either in masses or granules and situa-
ted either peripherally or centrally, or occupying the whole
as represented in fig a. These most probably were altered
blood-corpuscles and had originally been enclosed in a cell-
membrane, although ~~there was~~ no such membrane ~~could~~
could be detected surrounding any of them.

* What relation do the cells containing blood corpuscles in the liver to those of the liver?

E. H. Weber, — Ueber die Bedeutung der Leber für die Bildung der Blut-körperchen der Embryonen

Zeitschrift für rat. Med. Bd IV. S. 160.

From the foregoing facts, I am inclined to think it probable that in the frog & Newt that the blood corpuscles undergo a process of progressive breaking down in the liver during the winter months, in some cases becoming surrounded by an apparent membrane, previously to their undergoing any change, while in others this accessory phenomenon may be absent. ×

In spring when the animal again begins to feed the process seems to be suspended, for, at that period, as has been shewn by Weber in a paper on the relation of the liver to the development of the blood-corpuscles, the organ undergoes a very remarkable change in appearance. From possessing a reddish brown colour, it is converted to a greenish yellow. This alteration is owing to the accumulation of yellow fatty granules in large quantity, which Weber supposes to be partly owing to a deposition from the circulating blood, which has assumed at that period a quantity of the fatty matter accumulated in the lymphatic system during the winter. In connection with this source, it is probable that a considerable quantity derived from the food which is ingested after the long winters of abstinence. During the summer, Weber's observations tend to shew that these granules gradually disappear, two other processes being at the same time set up, viz. on the one hand, the development of young blood-corpuscles, and the active formation of bile on the other. If this is the case it will afford an example of an organ in which, at different periods, the function

*Does not this point to a chemical change in the fatty particles by means of which they were converted into pigment — TRB.

analogous processes of destruction and evolution of the blood-corpuscles go on at different times.

The occurrence of the destructive process in the liver of the frog during winter is probably rather owing to the state of the blood produced by the deprivation of food, than to any periodical influence of the season. Thus, in a newt which was taken last July and was kept without food until the 28th of September, when it was examined, the liver was of a dark colour, - almost black, and, instead of presenting on examination the normal cells containing oil globules it was found that these were completely broken down and that the colour was owing to very abundant dark brown pigment granules, which displayed an active molecular motion. These appearances were sufficient to indicate that a process analogous to that described above had taken place in the organ. *

(3) Metamorphosis of the Blood-corpuscles & their contents in the Spleen

There is no organ in which the phenomena which form the subject of the present enquiry have attracted so much attention as in the Spleen, or in which they have given rise to so much speculation. Although the various observations, which have been made on the subject are most of them worthy of credit as being correct, yet unfortunately, such undue importance has been attached to certain particular facts

to the neglect of others, according to the theory which the observer has happened to have in view, that it has become extremely difficult to assign to all their proper positions, and thus to arrive at correct conclusions. It is hoped however that by approaching the subject in the proper direction viewing it in connection with analogous phenomena, the questions connected with it will be reduced to a more simple form, and that we shall have no difficulty in shewing that the structure which the organ presents, when in the normal condition, furnishes no pretext whatever for considering it to be directly physiologically concerned in the destruction or breaking down, any more than in the formation of the corpuscles.

It will be necessary to notice shortly the researches of the various observers, whose enquiries have been directed to the subject. — In reference to the supposed physiological relation of the Spleen to the coloured corpuscles, it is scarcely necessary to state that two opposite doctrines have been held by different observers. According to the one of these it is the function of the organ to form, according to the other to destroy these corpuscles. The decision of the whole controversy depends on the signification to be assigned to certain structures which observers holding both of these opinions concur in considering as normal constituents. These we shall find to be analogous to the cellular bodies containing unaltered blood corpuscles

Eckers Zeitschrift für rat. Med VI Bd. S 261

Kölliker Cycl. of Anat. & Phys. Part XXXVI Pp 782, 783

which we have already seen to occur in such various situations. In the spleen they have attracted a much larger share of attention from their having been made the subject of the researches of Ecker Kölliker Gerlach, Schaffner & others.

The first mentioned observer describes them as occurring in the spleen of the Calf under the following forms.
1st Cells about 1-7000 ths of a Mill. in diam. containing a single blood corpuscle, the rest of the cell being either quite clear or finely granular. By adding water to these the cell burst and the corpuscle having escaped became clearer and soon disappeared. Others somewhat larger contained two blood-corpuscles. Many of them also contained a granular nucleus, and thus resembled the surrounding Spleen-cells.
2ndly. Large cells more than 3-100 ths of a Mill. in diam. filled with shrunk blood-globules, of an intense yellow-colour and no longer altered by the action of water. "Also among the free corpuscles many transitions occurred between the unaltered and the shrunk condition."

Kölliker represents the so called "cells containing blood-corpuscles as originating not from a nucleus, but by the formation of membrane round a heap of agglomerated blood corpuscles, in the same way "as the inflammation globules of Gluge convert themselves into cells" or as the "smaller globules of fission of the yolk form themselves into vesicles. He however believes that nuclei, which either

originate previously to the process of aggregation, or as a consequence of it are directly concerned in affording the conditions necessary for the developement of a cell-membrane. In all animals Kölliker found that the blood globules contained in these bodies, disappeared and were disintegrated in a similar manner, and that ultimately the cells themselves became colourless, the method in which this takes place, differing according to the animal observed. He has succeeded in discovering cells containing unchanged blood-corpuscles in Man, the rabbit, the sheep, calf & dog, in all which he found the number of included blood-globules from one to twelve, and by the steamushing together and falling to pieces of these, just as described by Ecker, he believed that "granule cells" filled with golden yellow or rusty-brownish-yellow contents were formed, which by the further breaking down of the granules and their final disappearance, became at last entirely colourless. In some animals he also observed that the metamorphosis of the blood-globules took place, without any definite indication of the formation of a cell-membrane around them.

Prof. Kölliker admits that in man and the Mammalia, it is difficult to demonstrate the cells containing completely unaltered blood-corpuscles, though he states that with care it is perfectly possible to satisfy oneself of their existence. Especially in the rabbit, calf, sheep

Lee Pl. V. fig. 5. Explanation

and dog. This I have in vain endeavoured to do, but have seen the later stages repeatedly. In reptiles, and especially the naked amphibia Kölliker states that the cells containing blood-corpuscles are most distinct, and their changes most easily traced. Although this is equally true, I have been unable to verify the constant occurrence of these bodies in the spleen of the frog or newt, when in a perfectly healthy condition - at least I may say that in numerous examinations of the spleens of recently captured newts, I have found either no traces or very few of the appearances alluded to. In newts in a state of starvation however I have found them in considerable abundance, though not so abundant as in the liver.

In these last they presented the following forms, which I have endeavoured to shew in Pl III Fig. 1 & 2 a, b, c. 1st, Corpuscles similar in size to the surrounding spleen's corpuscles, but resembling blood-corpuscles in colour, without their transparency (partially altered blood-corpuscles). 2nd, Cell-like bodies containing one or more similarly altering blood-corpuscles. These last had often assumed an orange tinge. 3rd, Larger cells which contained in their interior, besides altering blood-corpuscles, smaller secondary cells similar to the last. In almost all of these cells a vesicular nucleus (colourless) existed similar to that described by Kölliker, and in many the clear fluid which they contained appeared to be deeply tinged

throughout of the pale yellow colour of the corpuscles.

A series of experiments instituted by Saudis at the advice of Prof. Kolliker, on no less than thirty rabbits, took to the conclusion that the cells containing blood-corpuscles are normally formed in animals in great numbers, at a short period after feeding. In 15 of these observed two five & eight hours after eating, cells with unchanged blood-globules were found in eleven, while in the other fifteen, which were examined 12, 24 & 48 hours after, these were in as many cases absent, the golden yellow granule cells having taken their place. How it happened that Saudis obtained such remarkable results, I cannot conjecture, as I am quite certain that observations which I have made with the greatest care on animals similarly circumstanced as regards their periods of feeding, have not yielded similar ones. Even admitting the importance of these experiments, Prof Kolliker at the same time admits that it is impossible to prove that the phenomena to which they refer are really normal. Until this is done, there can be no reason for assuming that such a doctrine is true especially when, although it may seem to explain some facts, it is contradicted by so many others.

If on the other hand, we enter on the consideration of the same phenomena in a more proper direction, viewing them from the first as ~~physiological~~ pathological, we in the first place

observe that, in as far as our limited acquaintance with the pathological anatomy of the spleen will allow us to judge, the most common lesions to which it is liable are those dependant on hæmorrhage. Two distinct forms of hæmorrhagic lesion may, I think be noticed as existing in the spleen. The one of these constitutes the ordinary so called "hæmorrhagic infarction" of the organ, which is so commonly observed in some epidemics of Typhus fever. Of the second or slighter form, I am unable to find any description, though I cannot conceive that it is unknown to pathologists. It consists essentially of hæmorrhage into or around the Malpighian Saccule. On making a smooth section of a spleen in which it exists, dark-red or reddish-black spots or similarly coloured rings of about 1/3 line in diameter are to be observed, which are spread over the whole surface of the organ at slight intervals. The centres of the rings are occupied by dull-whitish looking material, and on further examination they are found to correspond to minute hæmorrhages which take place at the circumference of the Malpighian saccule, the central portion corresponding to the saccular contents. As to the anatomical relation of the hæmorrhage to the saccular membrane I have not been able to satisfy myself; I am inclined however to believe that it takes place into the cavity of the saccules that is, between the membrane and contents.

The appearances above described may probably originate

in a healthy person from any unusual cause producing a certain amount of congestion of the organ. The form of the lesion is very satisfactorily accounted for from anatomical considerations. The retiform plexus into which each of the minute arteries which supply blood, - one to each Sacculus, consists of capillaries which are, I believe, more minute than those which constitute any other part of the capillary system of the organ. In the examples which I have seen of this lesion in the pathological theatre here, I have some have presented it in its more recent condition, others after the extravasated blood had undergone more or less of change. In all the rest of the organ appeared normal.

It is not uncommon to observe spleens which present on section blackish or dark circumscribed spots at irregular intervals. On examination these are found to consist of concretions of black pigment-granules which are generally aggregated in amorphous or irregular masses but are sometimes included in cell-like bodies. These may probably be obsolete Malpighian corpuscles which have undergone the change described above.

With respect to the other more extensive lesion which was mentioned, as the "hemorrhagic infarction" of the organ which occurs in typhus fever, in the more severe forms of intermittent, and in connection with certain other acute dyscrasic diseases, and in which the fibrous

tissues of the organ are often eventually destroyed, and the whole reduced to a pultaceous mass, in most cases from our only seeing them in their recent and acute stage the changes which the blood-corpuscles undergo are not observed. In other cases, however, probably owing to the circumstance that frequently repeated congestions attended with hemorrhage have taken place, these may be seen without any difficulty. Thus in every case of the chronic tumour of the spleen so well known as a consequence of ague, such indications may be expected, inasmuch as every such tumour in its acute stage has presented a hemorrhagic character.

I have given in Pl. F the microscopic appearances which such a spleen presents, viz numerous spherical or spheroidal aggregate bodies which consisted of pigment granules of a yellow colour held together apparently by a transparent matter. Some of these were surrounded by a distinct membrane, and their forms were irregular. The pigmentary granules were evidently altered ~~and~~ broken down blood-corpuscles, with which some of them nearly corresponded in size

The spleen from which these were taken was found to be enlarged to about 6 inches in length, and present all the obvious characters of the fever-spleen.

See Pl. II Fig 6 Explanation

Eckert in op. cit. p. 90

[13] Metamorphosis &c in the Lymphatic Glands

The lymphatic glands are liable to congestive hæmorrhage like the spleen, and when so affected present the same obvious characters. By microscopic examination we also find that the blood corpuscles undergo precisely similar changes, becoming aggregated into masses, in some cases surrounded by a membrane, while still remaining in their unaltered condition, and afterwards being subject to those further transformations which have been already so frequently alluded to.

[14] Metamorphosis &c in the Thymus Gland

The changes wh. extravasated blood undergoes in this organ have been studied by Prof. Ecker. He describes the following case as illustrative of the results of very numerous observations

"In an altered apoplectic Extravasation in one lobe of the Thymus Gland, which constituted a reddish brown fluid, there occurred yellow globules of from ·012 to ·050 mm in diam. which were composed of yellow granules. Many of these globules showed on the addition of Water a distinct membrane, and, when the granules were not too numerous, a nucleus could also be detected. Between and among these ~~globules~~ globules, numerous small yellow granules from ·002 to ·050 mm. in diam. were detected, - which in every respect resembled those contained in the globules. As these bodies floated about, it could be observed that they were permanently connected, several one to the other, inasmuch as they did not alter their mutual relative position.

O. Müller – Ueber die Blutkörperchen im zurückgehaltenen Menstrualblut. Zeitschrift für ext. Med. V Bd S. 140

They were often so arranged with reference to each other as to form a semicircle, and it could be frequently recognized. Especially if they had been treated some time with water that a number of them were connected by an extremely fine intermediate substance so as to form a corpuscle (the former blood-corpuscle). The granules themselves however were altogether unaltered by water. This corpuscle is evidently the remains of a blood-corpuscle. The coloring matter probably splits into individual granules, which while the rest of the substance of the blood corpuscle is dissolved, gradually fall asunder. Among the above, shrunk blood-corpuscles occurred which were unaffected by Water, and evidently formed a transition stage from the former"

It is unnecessary to remark that the changes which are so carefully described by Eckes as above, are identical with those to which we have already referred as occurring in the blood. (See Section [6].)

[15] The following observations of Heinrich Müller on the metamorphoses which the blood corpuscles had undergone in the menstrual-blood in a case of retention of the Catamenia from imperforate Hymen, may serve as an illustration of what is generally to be observed in large coagulated accumulations in the various mucous & serous cavities &c.

"In a young woman who from congenital imperforate hymen

had never menstruated, several pounds of a brown fluid like tea was evacuated by operation. Microscopic Examination shewed - 1st, a few normal coloured blood-corpuscles. 2ndly, Flattened & wrinkled blood-corpuscles, as they appear after treatment with Salts. 3rdly, All transition-stages of shrinking from these down to the size of a pigment grain to which many of the corpuscles had the greatest resemblance, could be demonstrated, shewing an active Molecular Motion. Concurrent with the shrinking there was an alteration in their behaviour when treated with water and acetic acid, those least altered immediately swelling out and disappearing, others only after prolonged action, very many on the other hand not appearing at all affected. 4thly, Dark Bodies of various sizes, much resembling the so-called inflammation-globules, occurred in quantity, which were evidently conglomerates of the bodies above described. Their external surface was sometimes uneven, sometimes more or less smooth & rounded. Unaltered blood-corpuscles could not be detected in them.

In another case of the same nature, the evacuated blood presented, as regards the isolated corpuscles, similar characters. The conglomerates were, however, smaller in diameter, and displayed yellow masses somewhat more symmetrical. In some I believe I also observed a Nucleus in the interior, but cannot speak decidedly either of this or of the existence of a surrounding

Membrane"

In the case of aman Bernard Linden who died under the care of Mr Lyme in the Royal Infirmary on the 19th of December 1835 affected with encephaloid disease in various organs & tissues, numerous cancerous masses of various size were distributed through the substance of both lungs. One of these much larger than the rest (as large as two fists occupied the right lateral region of the chest involving both the right lung and pleura. The external portion of the tumour which appeared here and there to be limited by a delicate fibrous cyst, was of brain-like consistence and distinctly fibrillated, the direction of the fibrillation being perpendicular to the surface. Towards the centre of the mass wh. was occupied by a recent soft coagulum, the texture was more friable, and surrounding the coagulum it had assumed a dark reddish-yellow tinge, owing to the presence of diffused blood.

On Microscopic Examination - in the central coagulum, nothing was found but exultima blood-corpuscles. In the soft yellow encephaloid substance which surrounded it, besides the ordinary cancer cells containing nuclei and nucleoli, many of which were loaded with oleo-albuminous granules, other cells were found which contained granular matter of another kind, namely pigment of a bright golden yellow colour. These were spherical or spheroidal in form

See Pl II Fig. 5

† This is not observable in the Fig.

and varied in diameter from 1-2500th to 1-250th of an inch. They always possessed a surrounding membrane and sometimes presented the appearance of a distinct colourless peripheral space. They contained besides pigmentary matter floating in a yellowish fluid, a greater or less number of oleo-albuminous granules. The pigment assumed different forms in different examples. In some it consisted of grains of various sizes which seemed to be either contracted blood-corpuscles either isolated or in little masses. While in others it had assumed the finely granular form and was equally diffused throughout the cell-cavity. In some of the cells blood-corpuscles in a nearly unaltered condition were observed.

In reviewing the foregoing facts, the circumstance which appears least explicable is that the cell-structures which contained altered blood-corpuscles and the results of their transformation were identical with the large forms of cancer-cells (mother-cancer-cells) among which they occurred, being of the same size and containing the same oleo-albuminous granules with which many of them were loaded.* This seems to indicate that in some instances at least (if not in all) we may be wrong in calling these "mother-cells" and in supposing them to exist previously to the cells or granules which they include. Unless we make some such admission

Bruch, Ueber Entzündungskugeln
Henles Zeitschrift III Bd S 51

I do not see how we can consistently explain such cases as the above

I find that Busch in his paper on Inflammation-globules forms the same conclusion fr. similar facts. Speaking of exudation corpuscles in cancerous growths, he says, "In one case instead of the usual granular heaps which have a pretty constant diameter, I observed very large ones, three or four times as broad as the others which contained, instead of one, sometimes as many as sixteen nuclei. These large heaps occurred both without membranes surrounding them and with, forming in the latter case colossal cells filled with granules & nuclei. Among these forms, I found what are often called "Cancer-mother-cells" that is, more or less transparent large vesicles, which contained a number of nuclei & daughter-cells and between these and the granular cells above described there were all transitions from endogenous nuclei to endogenous cells in such a manner that the included granules became smaller and smaller, the more developed was the generation of endogenous cells (Die Endogene Bent)."

From the above facts, which, it must be admitted, are not very clearly related, and from others similar Busch concludes that the granular conglomerates without membranes are but early stages in the development of what, if this view be correct, are improperly termed Mother-Cancer-cells.

Chapter III

On the chemical nature of the changes which the contents of the blood-corpuscles undergo, in their transformation into the various forms of granular, crystalline & amorphous pigment.

[17] Chemical properties of the contents of the coloured blood-corpuscle in relation to their transformation

Of the two constituents which in solution participate in forming the contents of the coloured blood-corpuscle, viz. Globuline & Hæmatine, it has been taken for granted by almost all those who have investigated the subject that the latter is alone concerned in those transformations which we have been considering, the former being supposed in all cases to dissolve and disappear. I shall endeavour to shew not only that we have no sufficient ground for making such an assumption, but that there is presumptive evidence in the opposite direction.

The substance which is known to chemists as Hæmatin is a material of a dark brown colour with a slight metallic lustre. It is without smell or taste and insoluble in Water Alcohol Ether fixed or volatile oils, in almost all of which properties it differs from that histologists are familiar with as communicating the beautiful pale-yellow tinge to the coloured blood-corpuscle.

Lw. Lehmann, Lehrbuch der physiologischen Chemie
S. 316.

The mode in which Hæmatin is obtained may be shortly stated as follows. To a given quantity of Blood about 8 times the quantity of sulphate of soda is added. The result is filtered and washed as completely as possible, and now consists entirely of blood-corpuscles. These are next dissolved in water and coagulated by the application of heat. The coagulum having been washed then dried and finely pulverized, is repeatedly treated with spirit of wine containing Sulphuric Acid as long as the latter is coloured. By the addition of excess of ammonia, sulphate of ammonia is thrown down and some globulin. The filtered fluid is then evaporated to dryness, and the result, after being treated with alcohol, ether & water is again dissolved in an alcoholic ammoniacal solution, to get rid of the last traces of globulin.

There is evidently no proof that the final result of the above process is totally identical with the soluble colouring matter of the unaltered blood-corpuscle; it may no doubt be considered that the one stands in the same relation to the other as coagulated to soluble albumen - yet we are equally entitled to consider the hæmatin as a completely altered product, inasmuch as, although there is reason to believe that a distinct colouring matter does exist in the blood-globules in their natural condition, yet we are totally unacquainted with it. Except as in conjunction with globuline and inseparable from it, owing to totally al-

tering its properties

The principal characters of hæmatine, in addition to those already advanced to, are the following.

It is very soluble in alcohol which is slightly acidulated with Sulphuric or Muriatic Acid. The solution possesses a brown colour is coloured red by alkalies and is precipitated by the addition of water.

It is also very soluble in watery and alcoholic solutions of caustic and carbonated alcalies. The solutions resulting being coloured green by heat and blood-red by the addition of sulphuric acid.

It derives these characters from the presence of iron, of which however it may be deprived without losing its essential properties. Its ultimate chem[ical] composition differs considerably from Globulin, being represented, according to Mulder by the formula $C_{44}\ H_{22}\ N_3\ O_6\ Fe$.

Globulin belongs to the class of so called Protein compounds, scarcely differing, if at all in composition from albumen from which it is principally distinguished by its requiring a somewhat higher temperature to coagulate it. In the soluble condition, as it occurs in the blood corpuscles, it is, like hæmatine, unknown in a separate state

Note. According to Rokitansky when hydatid cysts in the liver occur at a very considerable age, they may give rise to the bursting a blood vessel and a consequent extravasation of blood into their cavity. Virchow further states that he has repeatedly seen evidences of such extravasation in obsolete hydatid-cysts.

In the case from which the crystals referred to were obtained he states, that, "at one point in the circumference of the cyst where the gradual disappearance (Verschwinden) of the substance of the liver atrophied by pressure could be traced with ease, an intensely vermilion-coloured mass which presented a rather remarkable surface, which on more careful examination, was found to consist of very peculiar distinctly broad lines, which formed sometimes reticulate anastomoses, sometimes circular and concentric figures. These lines consisted entirely of very large yellowish red crystals of Pigment

[18] Experiments and Results of Virchow with respect to the Chemical constitution of the red (so called Hæmatoidine) crystals, which occur under various circumstances in Extravasations.

The name Hæmatoidin was assigned by Virchow to the substance of which the crystals in question consist, on the ground that, although not altogether identical with Hæmatin, it was analogous to and in fact derived from it.

The following are the results which he obtained from the chemical examination of crystals which were taken from an extravasation clot, existing in an hydatid cyst of the liver.

(1) Part of the crystals saturated with some mucous fluid containing bile was laid on a glass plate, then agitated with ether — no alteration was produced.

The whole glass plate was then boiled with ether and left immersed in a closed vessel for a week. No result.

(2) Another portion was treated with alcohol of 86 p.c. without being affected.

(3) Another portion was repeatedly heated, and then subjected to the prolonged action of Alcohol containing a small prop.n of Sulphuric Acid. No change resulted.

(4) The same experiment was performed, with the substitution of Oil of Turpentine. No result.

(5) Another portion submitted to the action of Chlorine Gas for 48 hours, was unaffected. When however it was submitted

Unfortunately the identity of these lines could not be proved either with obliterated blood-vessels, or with obstructed gall-ducts, although on examination of the preparation, one could not help assigning them to one of these elements"

In them also no trace of iron could be detected

to the action of caustic ammonia and caustic potash, the crystals were reduced to a crumbling mass, but otherwise unaltered. On the addition of Nitric Acid they became brownish red, and successively in the course of time assumed various shades of colour such as intense green blue and rose-tint - and finally dirty blueish red.

(6) Another portion similarly prepared, was treated with Sulphuretted Hydrogen under water for half an hour. No effect was produced.

(7) Another portion was dried on a glass plate which was then strongly heated on a sand bath. The crystals were found to be blackened, but to retain their general form, though they had lost the sharpness of their angles. The plate was then broken over a naked flame, when a strong smell of horn was given out. The crystals were now found to be reduced to a white ash Soluble in water.

(8) A similar portion was heated with concentrated Sol^{n} of carbonate of potash. First the intermixed biliary matter became green, and the fluid assumed a slightly yellow tinge. Under the Microscope was then apparent a gradual dissolution of the crystals from their Edges, a yellowish margin however still remaining, in the centre of which the yellow red colour was perceptible. After several days, the colouring matter was entirely dispersed, and yellowish or yellow greenish plates could only be detected

which possessed somewhat irregular contours

The supernatant fluid was then boiled and filtered, the remainder was then washed with distilled water, which for the most part dissolved it, forming a saffron yellow-coloured fluid which did not effervesce with acids.

(4) When solution of Caustic Potash was added to another portion, if the action were not too violent, the crystals split into numerous small plates cleaving in a direction parallel to their shorter sides, while the colour changed to brownish red. When, after the action of Potash was continued for some days, Sulphuric Acid was added, the crystals first became darker, then gradually assumed a violet tinge which changed to deep-blue, until the whole disappeared without undergoing further change the final result being a mere granular trace. Nitric acid produced a similar effect, the colours observed being first reddish violet, then rose colour, then blue & lastly green

(5) By the direct addition of concentrated Sulphuric acid, along with the destruction of the colouring matter, the formation of a yellowish red margin round each crystal was observed. Most of the crystals were entirely destroyed, some however remaining little or not at all altered

(6) Direct addition of nitric & Muriatic acids only produced slight alterations of form & darkened the colour.

Note- Lehmann (Phys. Chemie I Bd S 311) states that he has occasionally found the red crystals to be dessolved on the addition of Alkohol containing Sulphuric acid or Ammonia.

Note, These Crystals are represented after Reichert's Phys Pl V Fig 3

From the above condensed view of the results of Virchow it will be apparent that they alone are insufficient to warrant any very definite conclusions. The assumption being set out with that the crystals are constituted of Hæmatin in some form, most of the experiments are contrived with a view to a comparison with this substance. The result is that Essential differences are found to exist especially as regards the solubility of the so called Hæmatoidin in alkaline solutions and in alcohol acidulated with Sulphuric Acid

[19] Researches of Reichert

The following results, which are contained in a paper (Ueber eine eiweiss-artige Substanz in Krystall-form) by K. E. Reichert in Müllers Archiv for 1849, appear to me to be of great importance in relation to the present enquiry.

The crystals on which Reichert's observations were made were obtained from the surface of the Placenta & membranes of an almost mature fœtus of the Cavia cobaya, as well as on the adjoining mucous membrane of the uterus. The uterus contained 4 fœtuses and connected with all the same appearances presented themselves, - in all the above mentioned surfaces being coated with a material of a red colour resembling dried blood. This material when examined microscopically was found to consist of tetrahedral crystals, more or less intermixed with mucus & epithelial

The crystals presented very regular forms (tetrahedra), the inclination of their sides to each other being 70° 31" 43" and of the sides opposite the angles 54° 44' 8p". Their size was various the length of the axis being from 1-600th to 1-15th of a line. Their colour was a dark blood red, varying however considerably in different crystals in intensity. In general the larger they were the more intense was the colour. The smallest only possessing a yellow tinge. In these cases however the colour varied without any reference to size, and that to a considerable extent, a circumstance which seemed to indicate that they derived their colour from some material foreign to the substance of the crystal itself.

In consistence they were elastic being capable of returning to their original form and size, after being submitted to the action of the compressorium.

On examining them chemically it was found that when subjected to the prolonged action of concentrated Nitric acid or when boiled in a saturated sol.n of Potash, they were dissolved. They were also soluble in Water at a high temperature. The immediate effect of the action of concentrated nitric acid was to convert the crystals, Carbonic acid being disengaged, into a substance, (Xanthoproteic acid, Mulder) which by treatment with Potash or Ammonia assumed an intense orange colour. This circumstance was

alone sufficient to set at rest the question of the chemical nature of the crystals - as the reaction implied by it could only take place when an protein-compound was concerned.

When treated with acetic acid the crystals were enlarged, without losing their form or being altered as to their general appearance. The Mineral acids produced a similar effect accompanied with a change of colour, varying according to the acid employed. Solution of caustic Potash also caused the crystals to enlarge and to assume a yellowish brown colour.

If the facts related by Reichert are correct, and of this, when we consider their unmistakeable nature, there can be little reason to doubt. (if in other words it can be shown that an albuminous compound exists which is capable of assuming the crystalline form) it is evident that they must have an important bearing on the present enquiry. Although the crystals above described differ so completely in form - from all we have hitherto considered as existing in Extravasations, yet we cannot doubt the identity of their mode of origin, nor the probability of a corresponding similarity in chemical composition. To which of the hitherto-known protein compounds, the crystallizable material of Reichert most closely approximates, we have of course no means of determining. May it not be conjectured with considerable probability, inasmuch as it is evidently so intimately united with haematine, to be some modi-

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fecation of the albuminous constituent of the content of the blood-globules by the Globulin.

[20] Researches of Zwicky

The results of Zwicky, as quoted from his work on the corpus luteum by Virchow, were obtained from the chemical examination of crystals which were found in the corpora lutea of pigs cows & dogs. They are however remarkably at variance with the results of other authors and are entirely wanting in that clearness, wh. according to Virchow characterizes the rest of the work. He distinguishes two kinds of crystals.

1st Small yellow or chestnut-brown (spadices) crystals - pursuing in form

Oddly "Red & for the most part square plates (pag 20); reddish larger or smaller crystalline plates (pag. 16); very red plates mostly of square or angular forms (p 20); small crystals with acute angles which more frequently constitutes heaps"

On examining these chemically it was found that they were all rendered colourless by Chlorine Water. The brown crystals were found tote soluble in ether. "In another place it is shown that the crystals are unaltered in Alcohol Ether Potash Acetic Acid Muriatic & Nitric Acids, while on the other hand concentrated Sulphuric acid, in a short time colours them blue and finally converts them into irregular black globules" This is compared with the reaction of Sulphuric acid on fluid fat - which is coloured byt "just green then blue &

* See P. 42

and finally appears to be dissolved

I have introduced these results of Twichys principally with a view of shewing that all crystals which present a red colour and are found in connection with Extravasations, are not necessarily identical with the so called hæmatoidin crystals of Virchow, and with the similar crystals which I have described as occurring in the Corpus luteum. There seems good reason to believe that some at least of the crystals described by Twichy were in reality fatty in their nature, and it is evident that they were found not in the central clot but in the yellow portion external to it. If so they were probably composed of cholesterine (or of some kindred substance, and formed in the same manner), which almost always exists so abundantly in parts which are undergoing a process similar to that by which the yellow material of the corpus luteum is formed * for example in the atheromatous deposit in arteries There is no reason for believing that fatty crystals may not be coloured by hæmatine in the same manner as it has been already shewn that albuminous crystals may and the probability of such a supposition becomes the more evident, when we consider a fact which is related by Virchow. In the case of a man who died after amputation of the fore arm, he observed that the adipose tissue on the inner surface of the flap had assumed

Virchow, in op. supra cit. p. 395

Scheer, Chem. und microsk. Untersuch. 1843, p. 194.

a peculiar reddish yellow colour. On microscopic examination, it was found that the falcicles displayed on their surfaces the well known appearance of striæ diverging from a point - supposed to be owing to a commencing crystallization of the contents - They presented however a very remarkable peculiarity in that a hæmatine crystal was very uniformly placed at the point of divergence of the striæ, in the direction of which a light red, gradually fading tinge of colour ~~gradually~~ extended towards the circumference.

Scherer also relates that in a case of contusion of the thigh a sanguineous fluid was obtained in which occurred fat-globules (Fett-tropfchen, - Fat cells?), the most of which contained in their centre, "a ramified structure with small reddish-yellow rhomboidal crystals", which were considered to be crystals of cholesterine. That both these crystals and those described by Virchow were really fatty in their nature can, I think, hardly be doubted; and that they owed their colour to hæmatine is, from the position in which they occurred, more than probable

[21] General conclusions as to the chemical relations of the various modifications of pigment which have been described in the foregoing pages.

These modifications may be arbitrarily divided into the following classes

I Red Crystals (albuminous?)

Free Crystals { Tetrahedral — (Reichert)
Rhomboidal —

Crystals contained in cell-like structures? See P. 25

Crystals contained in altered blood-corpuscles — (Kölliker)

II Coagulated Contents of Blood-corpuscles (red).

Amorphous aggregate masses — (Pl 3 F 6).

Spherical or spheroidal bodies somewhat smaller than blood-corpuscles (altered blood-corpuscles) — (Pl 3 F 6 & Pl 1 F 9)

III Fine Granular Pigment

Yellow chestnut or brown occurring in the brain, lung, liver, spleen, kidneys, ovaries &c. &c.

Black Spleen? Lung?

III Fatty Pigments

Red or yellow crystals of various forms

Corpus luteum (Zwicky). Cellular Tissue, — (Scheer)

Adipose Tissue (Virchow).

Fatty granules —

Lip Cream — In extravasation-cysts in Birds & Reptiles

Yellow — Corpus luteum — Extravasation cysts in Mammals.

Note It may be proved Experimentally that various kinds of crystals, if formed out of a liquid wh. contains much hæmatine in solution will assume a deep red colour. Hence it may be considered perfectly possible that some of the red crystals described by Authors are impure salts of lime coloured in this manner.

See Pl V Fig. 4

It has already been shewn that an albuminous compound exists which under certain circumstances which may occur in the living organism, is capable of assuming a crystalline form, and that the resulting crystals may have a deep red colour communicated to them from the presence of hæmatin.

The simplest condition in which we can observe the crystallization of the contents of a blood-globule, is that under which it has been described by Kölliker, namely, when a red crystal is formed within the membrane of an altered corpuscle. This crystal can scarcely be doubted, when its size is taken into consideration, to be constituted of the whole original solid contents of the blood-globule, or in other words to be an albuminous crystal coloured by hæmatin.

In the corpus luteum I have observed, as detailed in a previous section, all gradations of form between the red spherical body which is the simple result of coagulation of the contents of the blood-corpuscle, and these similarly coloured crystals - as if the material which in one case remained in the amorphous condition had in others made variously successful attempts to assume the crystalline form. If this observation be correct - we may suppose that these crystals like those of Kölliker, were in like manner formed for the albuminous contents of the blood corpuscles.

The difficulties experienced in every attempt-

to determine with precision the chemical constitution of the crystals we have been considering are very great. The most decisive of all tests for the Protein-compounds, that, namely, recommended by Millon, of the Employment of the solution of the nitrate of Mercury, is obviously inapplicable from the fact that the reaction obtained consists in the production of an intense red-colour, which of course could not be distinguished from the original colour of the crystals themselves. The same is true with regard to the otherwise sufficiently characteristic purple colour, produced by Muriatic acid. The best test of all as being most readily applied in such a manner that the results may be observed under the microscope is that recommended by Reichert, namely the Employment of Nitric Acid followed by solution of Caust. Potash. The bright orange colour produced is quite unmistakeable.

Of the chemical composition of the true granular pigment alluded to above I know nothing, nor am I aware that any special researches have been made into its nature. It is produced by the complete breaking down of the blood corpuscles, and is always characterized by a colour between yellow and brown, each of the granules possessing an opacity and hardness of outline which distinguishes them very obviously from the material from which they are derived. It probably differs in chemical composition from any constituent of the

++ This statement is singularly at variance with a large
No of undoubted facts — Eds —

+ This sentence is very contradictory —

unaltered blood-corpuscles and perhaps approaches in its characters to the physiological pigments. This must always however be very difficult to decide, as it always exists only in small quantities together and is most intimately intermixed with other tissues.

There seems to be no evidence to prove that a black pigment identical with the true melanotic is ever directly derived from altered blood, still less that all black pigments whether normal or abnormal owe their origin in some way or other to transformed hæmatin, as is supposed by many.** The only circumstance of importance favouring such a conclusion is probably the remarkable point of similarity which all such pigments present to hæmatin in the large proportion of iron which they contain as exemplified in the pigmentum nigrum &c. &c. It is certainly unusual to find black pigment in any form as the result of the transformations we have been considering; both in the human spleen however and still more abundantly in that of fishes, it occurs very frequently in old extravasations.* See Pl V, F 6. & Pl I Fig 5

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†

Vogel – Pathological Anatomy – Transl.n P.

Bruch. Untersuchungen ueber das körnige Pigment.
1844 P. 50

Conclusion

I shall arrange the results to be obtained from the facts detailed in the preceding pages in the form of some general propositions, the truth of which appears to be more or less clearly established.

[a] The transformation of the contents of Blood-corpuscles into the various forms of pigment may take place and be completed without the intervention of any cellular structure

As the relation which pigment which is the result of the transformation of blood holds to the cell-structures with which, it is so frequently associated, the following are the views held by authors, viz,

1st Virchow believes that pre-existing ordinary cells take up by their metabolic power pigment-granules as contents.

2ndly, Busch on the other hand maintains that the pigment-granules originate before the cells, the membrane being formed "um den gegeben Inhalt." Inflammation-globules are first formed by the union of Elementary granules into

Gluge – Atlas der path Anat. Lief. III Art. Melanosis.

Rokitansky – Allg. path Anat. pag. 301

See Virchow in op. cit. p. 382

* The conclusion here is very indefinite –

round heaps, which become infiltrated with hæmatin, escapes from blood-corpuscles, a nucleus being finally formed and a surrounding membrane.

Gully, Lange maintain that granules agglomerate themselves from a blackish brown Blastema which subsequently become surrounded by a membrane.

4thly Rokitansky believes that nucleated cells absorb blood-pigment, which subsequently as their contents assumes the granular form.

5thly. The theory of Kölliker and Eckes which as now know to approach nearest to truth has already been sufficiently detailed.

All the stages in the production of the granular form of pigment are observed in situations where no cell-like elements exist. Thus we have its constant occurrence lining apoplectic cysts in the brain, where although we can without difficulty make out attempts at the development of the structures in question, in the form of conglomerates, yet a great proportion of the pigmentary material is in a perfect by free condition. Here it presents the same colour and other characteristic peculiarities which it possesses in other situations.

[b] The cell-like structures containing blood-corpuscles and the results of this transformation described by Kölliker

× The term inflammation globe has only been used by Gluge, & is now unknown in science — As formerly seen, it has not been found that term bodies ever always found in the manner here described — The Author has taken no notice of the observations opposed to this view — JHB.

× This term is also abandoned —

× On the contrary they are altogether different bodies —

Eckes, Busch, Engel & others are identical in their mode of origin & functions with the so called inflammation globules. ×

That the cell-like bodies containing blood-corpuscles which have been described in a former Chapter as occurring in Extravasations in the brain, are essentially identical with the Exudation corpuscles × observed in the same organ is evident from the fact that they are produced simultaneously by the same causes, and that they merge insensibly into each other. The unusual forms represented in Plate Fig 3. may perhaps be thought not to admit of the same explanation. But they, however, must be admitted to correspond to the others in every really important character. × The same analogy is also to be observed in other situations, but no where, probably is it so well marked as in the brain.

[C] The above mentioned structures always originate in the previous aggregation of their contents into a spherical or spheroidal mass, which subsequently becomes surrounded by an apparent membrane. ?

The evidences in support of this conclusion are to be derived from several sources. 1st, The fact that unaltered blood-globules are found to be included within the apparent membrane and that these cannot be by any possibility supposed in many of the situations in

+ By no means as to the word 'always' in the proposition —
See also Bruch, Ueber Entzündungs-Kugeln
Zeitschrift für rat. Med. IV Bd S. 61

Kölliker - Müllers Archiv, 1843 S. 68.

+ This is a different process altogether - Also all masses in point of fact being the melting together of previously existing molecules —

which they occur, to be developed in that position, is in itself quite sufficient to set the question at rest. ×

Lastly, very distinct evidence may also be derived from such cases as that recorded by Lewis & Busch (see Spp. I) in which a series of apoplectic extravasations had taken place into the substance of the brain, the resulting lesions, as seen after death displaying all the various stages of the formation of the bodies in question.

To these considerations may be added that of the fact that conglomerates occur as the result of the physiological process of the clearing of the milk in animals, and that their mode of formation during it, corresponds to the above definition. In certain parasitic worms according to Kölliker, the formation of each new cell as observed during this process is preceded by the aggregation of the granular material in relation to a central vesicular nucleus, the surrounding membrane being subsequently formed. ×

[d] They possess certain definable characters by some of which they may be recognized as distinct from true cells and are not destined to undergo any further development.

1st Their membrane remains altogether unattacked when treated with water and acetic acid (dilute), although by concentrated acetic acid and the prolonged action of

water is dissolved. 2ndly, In their primary condition as conglomerates, the elements composing them are held together by a gelatinous-looking transparent & structureless intermediary substance. At a later period this substance seems to project so as to form a distinctly visible transparent margin, especially when water is added, which causes it to swell out. Finally, this margin assumes the character of a distinct membrane, from the internal surface of which the contents become disengaged & free, as is shewn when the globules are caused to roll by moving the cover-glass upon the other. This must be owing to a softening of the central or first-formed intermediary substance, as might be expected to occur when we consider that the whole structure eventually disappears by a softening or breaking down of the same kind. The final change which the pigment derived from blood undergoes is to become decolorized and absorbed. This may either while it is yet included in a cell-membrane, as occurs according to Kölliker in the Spleen, or, as happens by far more frequently after that membrane has disappeared.

From the mode of its formation, the membrane sometimes presents a laminated appearance, a number of concentric rings, indicative of the successively formed layers of material of which it is constituted being visible.

(See Pl. III fig. 5-

Lee Remak, Untersuch. ueber die Entwickelung der Wirbelthiere - L. 23.

[C] They have no influence on the changes which their contents undergo. This proposition is illustrated by the fact already alluded to, viz. that the conversion of the contents of the blood-corpuscles into granular pigment progresses precisely similarly, whether they be surrounded by a membrane or not. Again, in cerebral exudations - the oleo-albuminous granules which are such constant constituents of the conglomerates and "exudation corpuscles" which occur, seem to be formed and to disappear without reference to them and according to a law applying to fibrinous exudations in general in various situations - whereby they undergo a process similar to the fatty degeneration of muscular fibre or of the tunica adventitia of arteries.

[D] They are not necessarily the result of exudation.

Among other proofs of this fact may be mentioned their occurrence in stagnant blood in obstructed veins and it is also strikingly illustrated by in the occurrence of the so called "Blut-inseln" in the foetus; which are nothing more nor less than conglomerate-cells, such as we are considering, containing blood-corpuscles. They consist of agglomerations of blood-corpuscles surrounded by a clear and smooth membrane, and have been thought by some who have described them to be "mother blood-cells." They occur about the 3rd day of incubation in the vascu-

lar area of the chick and are owing to particular stagnations occurring of the causes of which we know nothing.

It may be generally stated that the liquor sanguinis undergoes the same changes as exudation fluid, when placed under similar circumstances. Thus we have circumscribed extravasations & exudations giving rise to organizations not only of the same general form, but altogether analogous in every respect, and similarly we have diffused extravasations and exudations also producing appearances perfectly identical, except as regards the presence or absence of blood-corpuscles.

As to the conditions which are necessary for the development of that form of organization which we have been considering and which we may call, the conglomerate cell, we can form no definite conclusion. We observe in the process of the formation of apoplectic cysts that, while the peripheral portion of the mass of coagulated fibrin becomes highly organized and often even vascularized, as is so beautifully shewn in extravasations into the arachnoid, the central portion shews no sign of ~~vascularization~~ organization at all, being out of the reach of the influence of the surrounding tissues. Between these, however there is an intermediate layer in which conglomerates are developed, the whole arrangement seeming to indicate that these form the connecting link in the ascending chain of pathological cell-form structures, an inference which seems to be born out by their history as observed in other situations.

Appendix I

As supplementary to the illustrations which I have given in Chapter II of the effects of diffused extravasation into the substance of the brain, I append here the accounts of two cases, the one of which is quoted from Prof. Henle, while the other refers to a patient who fell under my own observation.

The first of these which is recorded by Prof. Henle as follows was also separately observed by Brucke, and is described by him in his work on granular pigment.

From the history of the case it would appear that the patient had three successive apoplectic attacks of which "the first occurred a year, the second 6 months, the third only one hour before the fatal event. The most recent and directly fatal apoplexy in the left hemisphere of the Cerebellum, contained coagulated blood with unaltered blood-corpuscles & fibrinous fibrilla, but inflammation globules existed neither in the coagulum nor in the surrounding softened brain-substance. In the second older coagulum, in the middle lobe of the left cerebral hemisphere, which was firmer & less dark-red, very few unaltered blood-corpuscles were visible. The great mass con-

listed of blood-corpuscles which were somewhat smaller & clearer than normal - of a round form and beset with small dark points. These remodeled blood corpuscles which have been first caused to shrink up by treatment with strong saline solutions, and then caused to swell out by adding water, in which case the colouring matter does not in general become again equally diffused, but accumulates in isolated clumps at the periphery among these corpuscles and also in the yellowish-red and softened brain-substance which surrounded the apoplectic clot, I found various forms of inflammation-globules, which were partly colourless - white by reflected light -, partly coloured. The colourless examples were of the ordinary form. The coloured, which possessed all gradations of tints from deep blood-red to yellow - were the more finely granular the nearer the approached to the latter colour. Among these there occurred isolated yellowish & red corpuscles, the latter being from ·003" to ·001" in diam. The largest of these were remarkably shining, like particles of granate - being for the most part - round - sometimes angular or discoid; in some a central depression could be detected. I can scarcely doubt" says Henle" that the red globules are formed by agglomeration of the isolated, and that the last are direct metamorphoses of the blood-globules. It seems to me further probable that the red heaps & globules become changed into yellow, and finally into colourless by a peculiar chemical process. At the same time here last may

be otherwise produced. As they also occur in exudation which contain no blood-corpuscles worth speaking of that the peculiar tinge of colour of the softened brain substance is owing to these globules may be assumed as certain. Lastly, the third and oldest softened portion which was situate in the roof of the lateral ventricle of the left side contained no blood but was yellow and here and there even brownish black. There occurred also coloured inflammation-globules, which principally followed the course of the vessels with true nucleated pigment cells, and blackish brown pigment-corpuscles."

In this case Heule considers that the "exudation corpuscles" were the results of the transformation of the blood-plasma alone, and that there was no trace of the presence of exudation. Although the latter part of this conclusion may not be proved perfectly satisfactorily yet I think the former is tolerably evident. In the next case however, in many respects very analogous, the accuracy of a similar view is even more apparent.

George Crichton aet 28 Brewer admitted to the Royal Infirmary Jan 4 31st 1851. It appears that 3 weeks before admission he was attacked with pain in the head, which from that time gradually increased in intensity until the Monday preceding his admission when he was seized, while attending to his business, with vertigo and dizziness. He did

not however loose his consciousness, but walked home without assistance. On Tuesday he ~~felt~~ discovered that the use of his left arm was impaired, and on Friday - the day of his admission, his left leg also began to be affected, the loss of power in the arm having now become complete. From this period, he gradually sunk into coma, along with occasional convulsive twitchings which increased until he died on the 10th of Febr -

(Sectio Cadaveris - Febr 14th - On removing the Dura mater it was observed that the convolutions were much flattened, and on opening the lateral ventricles they were found to be occupied by about 130z of limpid serum. The lining membrane was perfectly healthy. On lifting out the brain, a semi-opaque or opaline flocculent exudation of a grayish colour, was observed which corresponded in position to the anterior subarachnoid space, but extended forwards to the Sylvian fissures involving the branches of the carotid artery and the second & third nerves It also extended considerably backwards on each side of the corpora cerebri. Immediately behind the commissura of the optic nerves, the exudation was 1/8 of an inch in thickness, and possessed of semi cartilaginous consistence and passed back presenting similar characters, until it became continuous with a thick harder

mass of about 1-3rd of an inch in thickness, which corresponded to the posterior perforated space, and entirely filled up the cavity in front of the anterior margin of the Pons Varolii, besides encroaching on the substance of the brain.

In making a section in the middle line and then slicing the optic thalamus, it was found that a clot of about the size of a pea existed in the substance of that body about its middle or posterior third, which was surrounded by a softened portion of the brain substance forming the wall of the third ventricle, and a capillary apoplexy which extended principally posteriorly.

On microscopic examination the coagulum was found to present the following elements, viz. 1st Blood corpuscles of the normal appearance or slightly decolorized, 2nd Portions of nerve tube, 3rdly, Irregular shaped bodies with double outline, consisting of the white substance & axis-cylinder forced out of the nerve tubes. 4thly Finely-granular matter, 5thly Spherical or spheroidal bodies about 1-1200th of an inch in diameter, which contained finely granular matter, the irregular shaped bodies above described and occasionally blood-corpuscles, but never any of the oleo-albuminous granules which so commonly occur in the ordinary inundation corpuscles in the brain. They were sometimes surrounded by a delicate membrane, sometimes not.

In the softened tissue in the neighborhood, nothing was

found but fragments of tubes, the same irregular shaped bodies, and fine molecular matter. In some places where a brownish tinge was perceptible, cell-like bodies like the preceding, but containing yellowish brown granular fragment. Cysted. These however were never surrounded by a membrane. They seemed to indicate the traces of former extravasations.

The circumstance in the appearances presented in the above case, which seems to me to indicate most distinctly, that the exudation-corpuscles which were found were in reality dependent for their origin on extravasation and not upon exudation, consists in their having occurred not in the softened brain-tissue surrounding the coagulum, but in the coagulum itself, whereas on an opposite supposition the reverse of what we might have expected. On comparing the foregoing facts with the history of the case, it seems probable that previous to the Monday before admission, when the patient was first seized with giddiness the condition of capillary apoplexy had alone existed, but that, subsequently to that period the large clot had become gradually to form giving rise to all the succeeding train of symptoms. That the clot did in reality form gradually, that is by the coalescence of several previously existing small ones which had gradually enlarged, seems indicated by the large proportion of broken down nervous tissue which it presented throughout its substance

Appendix II

The subject of cells containing blood-corpuscles may be approached in another and a different point of view. It has been already shewn that their occurrence in a tissue or organ cannot be considered as any indication, - much less proof of the physiological connection of such organ, with the normal breaking down of the coloured blood-corpuscles, - and that in fact, if the account which has been given of - their mode of origin and history be accepted, they cannot be considered as normal structures.

Another set of observers have, however, assigned to them a totally different signification and have founded upon them most opposite results. They have considered them as indications rather of an Eliminative than of a disintegrative metamorphosis, of an act of new formation, - not of decay. Among them may be mentioned two german observers Dr. Gerlach & Schaffner, and Mr. Wharton Jones of London &c. I shall endeavour to prove that the doctrine that

Gerlach, Handbuch der Gewebelehre. S 217
——— Zeitschrift für rat. Med. VII Bd S. 75

Schaffner, Zur Kenntniss der Malp. Körperchen der Niely und ihres Inhalts. (Die Same VII Bd P. 345)

blood corpuscles are developed within previously existing cells is a false one, and at the same time to communicate some results which I have been able to come to, as to the mode in which these bodies really originate.

Dr. Gerlach asserts that he finds in the Malpighian saccali of healthy spleens blood corpuscles contained in the cells which develope them. According to him although these cells exist only sparingly at a time, they are of very constant occurrence. He further believes that the saccali are connected with the lymphatics of the spleen, and that the blood corpuscles, as soon as formed, are thrown by them means into the circulation.

These observations, although contradicted by every other anatomist, have been confirmed by Dr Schaffner. He states that in the Malpighean saccali of the Sheep and Cow, he found large cells of about 1/83rd of a Line in diameter, which contained yellowish-green granules and a certain number of perfect blood corpuscles. He also made similar observations in some reptiles.

That these cells containing blood-corpuscles were not identical those alluded to formerly, as being described by Prof. Kolliker, may be concluded from two circumstances.

2

See Pl VIII — Fig 2

Baumgärtner, Beobachtungen über die Nerven und das Blut — Freiburg. 1830.

1st, If they had been, it is scarcely conceivable that the invariably accompanying pigmentary cells, and other indications of extravasated blood could have been overlooked, 2ndly, they cells in question had a different anatomical position from those of Kölliker. I think it more probable that the appearances were fallaciously interpreted, and that their real nature was as follows. Cells, much larger than the rest often occur in the malpighian capsuli, which from the smoothness of their outline and their considerable power of refracting light, remind the observer at once of blood globules, being of course easily diagnosed by the use of reagents. As to the colour, it is a character which is extremely difficult to judge of unless it be well pronounced, and is further liable to lead to fallacy, as almost any corpuscle in the body is capable of assuming a blood tinge from mere intussusception, as occurs very frequently in the Spleen.

I shall next proceed shortly to detail the facts connected with the history of the development of the blood-corpuscle from the earliest period, in which I shall include all the other observations tending to prove that the bodies in questions originate in these cells

According to Baumgartner, the earliest blood-corpuscles consist in the frog of aggregations

Schultz, Systeem der Circulation – S. 35-36.

Lee Recherches – Entwickelungsleben im Wirbelthierreich S. 139, 140.
– Bischoff – Entwick. der Säugethiere – S. 283
– Voit – Annales des Sc. nat. 1844 Avr. P. 207.

of yelk-granules, without any vesicular membrane
These gradually disappear until about the 12th day, -
a perfectly transparent ring is seen round the globular
nucleus, the reddish colour becoming perceptible. A simi-
lar series of changes is described by Schultz the next
observer of any importance, consisting in the transfor-
mation of an embryonic cell containing numerous gran-
ules, by the gradual melting away of its contents into
the oval nucleated blood corpuscle, "the nucleus being
formed by the persistence of one or more of the larger gran-
ules, the smaller ones either blending into it or, by and
by, disappearing. In the chick, on the other hand,
according to the same observer, the nuclei originate
first, in the form of transparent homogeneous-looking
yelk globules. Around these in the course of deve-
lopement, a membrane is formed, within which gran-
ules are deposited. After this, the resulting cell gradu-
ally enlarges and assumes the oval form and chara-
teristic colour, the granules having completely disap-
peared. The whole of this process according to Schultz
is not completed until a late period of embryo-life.

All the more recent observers agree with Schultz
and Baumgärtner in maintaining that the
blood-corpuscle is originally identical with the
embryonic cell (Dotter-Zelle (Reichert) Furchung-Zelle).

They differ however materially in other respects

The question which has been most disputed in relation to the early developement of the blood-corpuscles is that of their connection with the first formation of the capillaries. It is maintained by Schwann, Valentin Reichert Bischoff-Kölliker and others that this takes place by the junction and melting together of branching cells, while Reichert maintains that the first capillaries are mere intercellular spaces. The partial consideration of this question will be almost unavoidably included in the following remarks.

Among the most exact of the recent investigators of the early stages of fœtal life, Prevost & Dumas, describe the first origin of the blood corpuscle as follows. According to them the vascular area, or, as they term it, "hæmoplastic area" of the germinal membrane, is constituted towards the end of the 1st day, before, of course, any blood vessels or corpuscles are formed, of two layers (corresponding to the mucous & serous) composed at this time of globules (globules hemoplastiques) which are described as varying in diameter from 1-1250th to 1-625th of an inch. Between the layers which these globules form, the new blood-vessels are developed, to which, they suppose, the globules themselves afford the material for the developement of corpuscles within them. These last do not appear until

Kölliker. Ueber die Blutkörperchen eines menschlichen Embryo, und die Entwick. der Blutkörperchen bei Säugethieren

Zeitschrift für wiss. Med
III Bd S 122

Remak Untersuchungen über die Entwickelung der Wirbelthiere — S 5-6

the end of the 1st day being gradually formed in a homogeneous fluid at this time existing in the young vessels.

Prof Kölliker gives the following as the result of his researches with reference to this subject "The vessels which are first formed, even when they do not exceed in diameter the future capillaries, are not vessels with a simple structureless membrane. They are all originally solid masses like the heart, and are not divided by any limit from the surrounding parenchyma which is formed of similar Embryonic cells. Gradually however the margins become distinct and at the same time or even sooner, their interior becomes fluid, in consequence of which the central cells become loosened and swim free." These form the first blood-corpuscles, which therefore "originate in the vessels, and are nothing more than central colourless cells of the originally solid vessel-layers (Gefäss anlagen).

The most full and complete view of the whole subject equally valuable from the authors original researches and as including all the results of the more recent observers, is contained in the first part of Remaks great work on developement, now in progress of publication.

According to him, not very many hours after

Op. cit. P 13.

The commencement of incubation, the germinal membrane consists of two layers each of which consists of globules from 1-150th to 1-100th of a line in diameter, those of the lower layer being rather larger than those of the upper. In process of development, these globules in both layers become metamorphosed into smaller bodies, presenting the anatomical peculiarities of cells. Subsequently to this change the superior layer splits into two - namely, a thicker superior and a thinner inferior lamina, distinguishable from each other by structural peculiarities. Shortly after this, the well known shield-shaped thickening of the germinal membrane & the primitive trace begin to be visible. The cells above mentioned are observed to have undergone important changes; both in the upper & middle layer, they have gradually become ~~smaller~~ & smaller & smaller by successive division and at last untraceable.

At a little later period, namely, during the last quarter of the first day, it was observed that the earliest traces of the blood-vessels were visible in the middle layer. These first appear as opaque cylinders from 1-80th to 1-50th of a line in diameter, and possess a reticulate arrangement. On more careful examination they are seen to consist of granular nucleated cells

from 1-300th to 1-200th of a line in diam. "Here and there isolated cells occured of large dimensions with large transparent nuclei, and dense granular contents surrounding them, like those cells which at a later period make their appearance as colourless granular blood-cells in the first circulation."

The walls of the more developed of these vessel-traces consist of a single layer of cells, which project considerably into the central cavity. In those which are situated in the vascular area, towards the End of the 1st day, even before any trace of the heart has shewn itself, numerous partly colourless, partly coloured granular cells (Blood cells) are visible, which on the addition of acetic acid display simple or double nuclei. "How these first blood-cells originate" observes Remak "I cannot speak decidedly; I can only conclude that they owe their origin to cells which exist in the bases of vessel-layers.

At the period at which the action of the heart commences, that is about the 36th hour, a considerable number of corpuscles already exist in the vessels, both colourless & coloured. The former in general contain numerous granules and are more or less spherical. The coloured although many of them are also spherical, are for the most part oval or even sausage-shaped.

In the researches of Remak above detailed, my account of which I have shortened to the utmost extent consistent with clearness, we have probably the best & most accurate description account of the phenomena under our consideration. It will be observed that they are in the main confirmatory of the previous results, as well of Kölliker as of Prevost & Dumas.

During last summer and autumn I made numerous attempts to demonstrate these facts to my own satisfaction, and succeeded in as far as relates to the essential part of the process. If I was not so successful as I might have been, this is, in some measure accounted for by the great difficulty wh attends the successful dissection of the Embryonic structures, even as late as the 2nd day.

From my Examinations during the period referred to (during which alone the primary development of the blood corpuscle fr the Embryonic cell can be studied, as after this it gradually ceases) I arrived at the following results.

1st The colourless cells which are destined to constitute blood-globules, as observed during the 2nd day, are identical with the Embryonic cells which form the tissues or organs which are laid down at the same time in the same position, that is, the heart & vessels. Thus e. g. the heart in its earliest condition consists

wood

See Plate VIII Fig. 1

of cells entirely the same as those destined to form blood-globules.

2nd, I am unable to trace any earlier stage in the development of the cells referred to, than that of transparent perfectly homogeneous looking vesicles

3rdly. As these enlarge, they become distinguishable into a central nuclear portion and a surrounding membrane, — the former appearing as if rising from the surface of the latter.

4thly The nucleus is from the first vesicular.

5thly. During the course of development, the whole becomes coloured and assumes the following characters, as observed on the third day. The cell-membrane is smooth and homogeneous, and is much swollen and rendered almost invisible when water is added, the colour being destroyed. The contents are pretty deeply coloured and contain a few granules of varying size and number floating in a transparent fluid. The nucleus is vesicular and often contains one or two granules. At one period in its history, on the addition of water it displays a very remarkable structure, which is represented in Pl. III Fig 3. Instead of presenting a simple vesicle, a delicate membrane is seen rising from it on one side, which differs from the membrane of the nucleus wall itself in not being so refractive. No such structure is

visible before the addition of water. As to its signification it is difficult to express an opinion, unless it be connected with the mode of multiplication of the corpuscles to be described immediately

I have lately had an opportunity of seeing the very detailed results of Mr. McLeod on the primary development of the blood-corpuscle. As however his observations did not commence until the third day of incubation, and as the development in question is in progress early in the 2nd day, they can scarcely be considered as referring to the same series of changes as those which have been hitherto under our notice. The first stage in the process according to Mr. McLeod may be described as follows.

The blood-corpuscle originates in the form of a small granule which enlarges and becomes clearer in the centre. Subsequently this enlargement still going on, the central clear part becomes dark and finally distinctly granular. the border being well-defined smooth and transparent and the whole retaining its original spherical form.

With respect to the appearances above described I can only say that I have not seen them and cannot help thinking it possible that they may have arisen from other bodies besides blood globules intermixed with them in the specimen examined.

The succeeding stages ~~are~~ however as described by Mr. McLeod are much in accordance with what I have detailed above

of my own observations. He says, "The central part gradually becomes less opaque and ceases to appear granular, the external portion separating at the same time in some degree from the central part" (nucleus). He further states that the corpuscle becomes coloured and at the same time flattened in form, remaining perfectly circular. After this it gradually elongates in both directions and assumes the general characteristics of complete developement.

At a period between the third & fourth day of incubation, and from that time to about the 10th or 12th a different mode of formation of new blood corpuscles, much more easy to trace and consequently ascertained with more certainty begins to be observable. This consists in a multiplication by division which goes on very actively during the 4th, 5th and 6th days and seems gradually to diminish in activity after that time, till at last it can no longer be detected. The appearance presented by the blood when this process is in its greatest activity, I have given in Pl. VII Fig. 1. When a blood-corpuscle is about to divide, it in the first place assumes an unusually elongated form, ~~the constricted~~ part gradually becoming narrow ~~until separation takes~~ and secondly, the membrane becomes gradually constricted across the short diameter, till it assumes an hour-glass form, the constricted part gradually becoming nar-

All these forms are shown in Pl VII F. 1

Remak, Med. Zeitung 1841 No 27 & Schmidts Jahrbucher Bd 33 S. 145.
See also Canstatts Jahres bericht for 1841

lower & narrower until separation occurs. The result is that two new corpuscles are given rise to, which although they at first possess a spherical form, subsequently assume all the characters of the original, from which they were derived. The behaviour of the nucleus during the process seems not to be constant. It sometimes appears to divide previous to the commencement of the constriction, at other times it does not do so, a new nucleus seeming to be developed in one of the newly formed corpuscles.

When I first observed the foregoing facts, I thought they had been undescribed. I find, however, that they are noticed by Remak in the work before alluded to, and it also appears that he had detailed similar observations in some previous researches on the blood-corpuscles of an embryo-fowl. Prof. Kölliker also in the paper above cited, in alluding to Remak's first observations, expresses himself decidedly in favour of a mode of multiplication consisting of "the conversion of a blood-corpuscle as it becomes larger into 2-4 new corpuscles, according to the number of the nuclei leaving it undecided whether this multiplication takes place by division of the cell or by endogenous development."

The structure of the corpuscles, towards the end of the period during which they are observed to multiply by division, differs considerably from that which they presented at their first appearance. The wall of the en-

* See Pl. III Fig 3 — in which the appearances induced by this change occuring in different degrees are shewn

⊙ See Pl. VIII Fig 4 ?

fusicle seems to be divided into two layers. The external is perfectly transparent colourless and homogeneous. The internal, much less resistent than the external, is in immediate contact with the colouring fluid contents. It reminds one strongly of the inner membrane of the plant-cell (primordial utricle), which has a similar relation. That two membranes exist is evident from several circumstances 1st, When the corpuscles are submitted to a fluid whose density is above that of the serum, the inner membrane shrivels up, the outer remaining at first unaltered* 2ndly A similar effect is produced too much greater degree by certain reagents, a clear space being formed all round the inner membrane and between it and the outer. 3ndly, When a corpuscle is extended in the direction of its long axis, the external membrane is often seen stretching like a bridge,° more or less twisted often — between the divided portions of the internal membrane. Similarly it is observed that if a portion of this structure escapes by a rupture of the outer membrane, it assumes a spherical form and swims free in the surrounding serum Extremely resembling a blood-corpuscle.

The nucleus is a colourless space in the centre of the corpuscle of a spherical form, and consists evidently of a delicate vesicle containing a fluid, in which a few granules of extreme fineness float. This the only part of the

cell which does not disappear during spontaneous solution (see Essay p. 4), after which it remains faintly visible as a collection of very fine granules.

In comparing these facts with the appearances presented by the corpuscles during division, I should be inclined to believe it probable that the internal membrane is as much concerned than the external in the formation of the two new corpuscles which result, these being in fact modelled out of the contents of the original, just as the two cells are modelled out of the yelk-mass in the commencement of the process of "cleaving". This would also accord with what we know of the mode of multiplication of the plant-cell by division, of all the circumstances of which we can satisfy ourselves more completely, on account of its larger size.

After the process of multiplication by division as above described has begun to decline, how are the corpuscles reproduced during the remainder of fetal life? This question, on which I have been unable to derive any information from observations on the chick during this period (fr. the 12 day to the termination of incubation), may perhaps be explained by the following results of Prof. Kölliker. From observations on human and mammalian embryos he concludes as follows. "As soon as the liver becomes developed, the multiplication of blood-corpuscles in the general mass of the blood ceases, and in its place is

Collates in op. Sup. Ct. Pp 128, 156.

substituted an active developement of blood-cells in the substance of the liver." This developement consists of a "formation of colourless blood cells round nuclei, which are transformed into coloured blood corpuscles by the formation of colouring matter in their contents,- either directly or after they have first undergone a process of multiplication."

There is no reason to suppose that the colourless cells in question are at all organically connected with the liver, as they bear no relation to any of the normal structures which that organ presents in the foetus. Their connection with it seems rather owing to the circumstance, suggested by Prof. Kölliker, that during a considerable period of embryo life succeeding the developement of the liver, the whole blood of the umbilical vein passes through the liver into the general circulation, and consequently as this blood contains all the nutrient material from the placenta, the developement of blood cells must be supposed likely to goon with great activity in the capillary system of that organ, without it even being necessary to suppose that it possessed any direct influence on the process. Kölliker however believes that the liver has a very decided influence, and compares its function in this respect to that of the lymphatic glands in the adult. Supposing the activity of the

process to be dependent not upon its secreting function, but upon the activity with which, during this period of fœtal life the development of new vessels ~~in the liver~~ takes place

As to the mode of formation of the non-nucleated corpuscles, which gradually increase in frequency towards the termination of fœtal life in the Mammalian Embryo, Kölliker's observations lead to the conclusion that they are formed from the nucleated by a gradual disappearance of the nucleus. What is observed in the Embryo of the chick tends also to the same result. During the latter part of the period of incubation it may be seen that the nucleus, in all the corpuscles, becomes gradually relatively smaller, and although it of course does not entirely disappear, the adult corpuscle in the bird being nucleated, it is obvious that if the same process of gradual diminution were continued, it would eventually do so, as is actually the case in the Mammalian Embryo.

Dr Schaffner has maintained that in the Embryo of the Sheep and other animals, certain cells exist in the liver, in the interior of which blood-corpuscles are developed. This assertion seems to me to be in the last degree questionable. In relation to it I have repeatedly examined the fœtal liver of the sheep, pig and cow at various ages, but always with the result of finding no traces of the existence

See also a paper by Ed Weber "Ueber die Bedeutung der Leber für die Bildung der Blut-körperchen der Embryonen"

Zeitschrift für rat. Med. III Bd S. 160

These observations tend to confirm the results of Kölliker and to shew that in the Liver of the Foetal Chick and of the Frog at certain periods of life, a formation of blood-corpuscles goes on ~~in the Liver~~ &c

of any such structures. I have already alluded to Dr Schaffers similar observations relative to the spleen; it appears possible that these may admit of the same kind of explanation.

Now all the facts which have been considered we may come to a conclusion which is a very important one, namely, that the doctrine of those physiologists is false who maintain that the adult corpuscle is a body different in its signification from the foetal, or that the latter stand in the relation of nucleus to the former as mother-cell. We have seen that, in the chick it is possible to trace from day to day the successive and gradual changes by which the original embryonic cell is transformed, so as to assume the characters of the perfect adult blood-corpuscle. We next proceed as shortly as possible to treat of the mode of multiplication of the corpuscle after these changes are completed that is during adult life.

Almost all observers who have investigated the subject on which we are entering have agreed in supposing the coloured corpuscle as in some way or other dependent on the colourless or lymph-corpuscle for its origin. I wish to shew that facts exist sufficient to throw very great doubt on this doctrine, and for the sake of shortness I shall include in the following pages, no con-

Note, In the development of the pus corpuscle, this can be seen, and the illustration a a good one, as the pus corpuscle differs from the colourless blood-corpuscle in no respect in structure. Numerous pathologists have described the commencement this process as consisting in the aggregation of granules, and in making the observation with high powers, a minute transparent vesicle will be seen, in relation to and around which the granules place themselves and wh. is no doubt precursent to them

deration which is not strictly necessary for this purpose.

The lymph-corpuscle or colourless blood-corpuscle, as it occurs in the blood, exists under two pretty distinct forms - referable to different stages in its history.

Of its primary origin we know little except that it first exists in that part of the vascular system which is in relation with the lymphatic glands. There is no evidence however that it is at any time organically connected with these organs or, in other words, that it ever forms a constituent of their structure, as no cell form can be pointed out to exist in them which corresponds with any stage of its development.

It would appear that it first originates as a transparent perfectly homogeneous vesicle of inconsiderable size, which becomes surrounded with two or three or eventually with numerous granules. This however cannot be demonstrated but seems very probable from the earliest appearances which it presents.

A form corresponding to every early condition of the corpuscle is shewn in Pl. III. f. 2. as occurring in the thoracic duct of a dog. This consists of a cell which contains, besides a number of granules, a vesicular nucleus.

Of the two modifications of the colourless corpuscle which, as above mentioned, occur in the circulating blood, that

See H. Müller. Beiträge zur Morphologie des Chylus und Eiters. Zeitschrift für rat. Med. Bd III - P. 227 & Taf. IV Fig 3a.

Note The clear space towards the vesicular nucleus goes also a very frequently described as the cell-cavity, which is a complete mistake.

which seems to occur most frequently differs but little[20] from the forms just described. At present when not acted on by reagents a granular cell about 1-3000th of an inch in diam. which does not possess very well defined margins. When acted on by water and weak acetic acid, it presents the appearance represented in Fig VII R 3 This reaction is produced with the greatest uniformity and is evidently owing to the production of such a degree of imbibition of the vesicular nucleus, which always occupies the side, not the centre of the corpuscle as to burst the external membrane thus remaining merely as if adherent on one side of the mass of granular contents.

During last summer I had the best possible opportunity of studying the anatomy of the colourless corpuscles in the blood of the boy Finlay in whose they were in such abnormal abundance. They corresponded in general both before & after the action of reagents to the forms above described. After treating them for a long time with water they presented the appearances shewn in Pl VII Fig. 4 in which is most distinctly evident the perfect separability & independence of the vesicular nucleus.

When acetic acid of ordinary strength was added to these corpuscles, they are displayed highly refractive horse shoe shaped nuclei of a form similar to that represented in Pl VIII Fig. 4 To ascertain the relation of these to the

Note. Even in the same individual at different periods different forms are assumed by the colourless blood-corpuscles. This observation I have made not only in the case of others, but most satisfactorily in my own blood in which I have satisfied myself that at certain periods the general mass of the colourless corpuscles was in a more advanced stage than at others.

vesicular nuclei already alluded to. I allowed some of the corpuscles shewn in figs. Pl. IV to be gradually acted on by weak acetic acid, by which means were obtained the appearances shewn in fig 5 Whence it is evident that the horse shoe-shaped nucleus insoluble in acetic acid is placed at that part of the granular contents, which adheres to the vesicular nucleus, and in the burst-corpuscle occupies its concavity, being situate towards the centre. Hence probably this body consists of those granules which constituted the corpuscle in its earliest state, the rest being of later origin and hence more soluble in acetic acid

I therefore conclude that this form of the colourless corpuscle consists of the following parts, viz, 1st An external cell-membrane, 2ndly A cell-cavity containing (a) Granules soluble in Acetic Acid, (b) A granular nucleus insoluble in Acetic Acid; (c) A vesicle (cell-form nucleus — M. Jones). From observations on the colourless corpuscles in other cases similar results are to be arrived at.

In others however the great mass of the corpuscles present a somewhat different appearance, tho at the same time we can easily recognize to be only an advanced form that is, more nearly approaching the period of disintegration, of the same structure. Even the corpuscles when examined without the addition of reagents resemble very much those

See Pl. VI Fig. 1

last described except that they are a little larger. When water is added and subsequently very dilute acetic acid according to the mode recommended by Dr Wharton Jones, the appearance which he describes is presented, the vesicular nucleus ("cellaform nucleus") being displayed, which has now assumed a spherical, instead of the irregular figure presented in the corpuscles previously described.

When treated with the ordinary dilute Acetic acid they display sometimes the horse-shoe-formed nucleus, but more frequently the triple or trefoil nucleus, formerly supposed to be characteristic of the pus corpuscle, which is invisible before such addition is made and is situate between the "cellaform nucleus" of Wharton Jones & the external membrane.

If the above facts be admitted, it will be scarcely necessary to adduce further proof that the coloured corpuscle is not formed from the colourless, as such a doctrine is evidently at variance both the anatomy of the lattice, and the history of its development. I shall however shortly mention the principal special arguments which have been brought forward in support of the doctrine, and the objections with which they may be met.

The theory exists, as maintained by different obser-

Kaisse - Wagners Handwörterbuch. Art. Blut § 196.

Kölliker in op. cit. p 153.

vers under two distinct modifications
According to the first, the colourless blood-corpuscle or lymph-corpuscle is transformed directly into the coloured, most of those who hold this view maintaining that in the process the contents clear up and disappear, while H. Müller maintains that the nucleus become adherent to the external membrane and is permanent.
According the second, the nucleus of the colourless corpuscle is transformed into the coloured, the external membrane and granular contents disappearing.
The arguments in support of the first doctrine are the following.
1st, It is said that direct observations have been made by Rasse proving a gradual transformation of the lymph corpuscle into the coloured blood-corpuscle, each stage in the alteration as regards form & colour having been demonstrated. To this it may be replied that the accuracy of the observations is denied by very many observers, and that from their very nature they are liable to many fallacies
2ndly, It is said that in many coloured corpuscles nuclei occur - indicating a transition stage. This is denied by the great majority of observers and is evidently untrue.
3rdly Prof Kolliker who adopts the theory that the nucleus disappears during the transformation adduces the following facts, viz, 1st, the small lymph corpuscles of the thoracic duct

are usually of the same size, often smaller than the colourless corpuscles. 2nd by their membrane resembles that of the blood corpuscles as to appearance, action of reagents &c, - becomes wrinkled as the chyle is evaporated in the same manner and shews no sign of dissolution. Both these ~~arguments~~ facts may be admitted without in the least proving the doctrine or even rendering it probable. Kölliker further states in contradiction to Mr. Wh. Jones that ~~the~~ colour exists not in the nucleus but in the cell cavity. The very fact of two such good observers make such opposite statements is the best illustration of the unimportance of the observation. Lastly, Kölliker maintains that the lymph-corpuscles possess in a less degree the flattened form of the blood-corpuscles. To this it may be said that many other corpuscles as those of pus are also flattened and that therefore the circumstance proves nothing.

Lastly It is argued from analogy that as in the Embryo an undoubted transformation from the nucleated to the non-nucleated form takes place by the disappearance of the nucleus, so according to Kölliker may it be concluded "obschon nicht mit vollkommenem Sicherheit, doch mit grosser Wahrscheinlichkeit" that in the adult the same thing takes place. In a question like the present analogy affords a very insufficient ground of argument, and besides there is no proof, although we observe

R. Jones. Phil. Trans. 1846
Gerlach, in op. cit.

Le Pl VI fig 1 Explanation

a gradual transition from the nucleated to the non-nucleated form during the later periods of foetal life in the whole mass of the corpuscles, that any such transformation takes place in the individual corpuscles themselves.

The second doctrine namely that the nucleus of the colourless corpuscle is transformed into the coloured is supported principally by the observations of Mr. Wharton Jones. It also is advocated by Gerlach & Remak. Mr. Jones divides the history of the development of the coloured corpuscle into 4 stages, terminating in the formation of the coloured. The first of these is represented by the "coarsely granular" form to which he applies the term of "granule blood-cell. This, he believes, becomes "finely granular by the gradual solution of its contents. After this a nucleus begins to be visible & the form of nucleated cell is assumed. Finally the nucleated cell burst and the cell-form nucleus is liberated, and becomes the coloured corpuscle. All these facts are with the exception of the last, perfectly correct, and may no doubt be demonstrated without difficulty be demonstrated in the blood of some individuals, though not of all owing to the differences before alluded to. The doctrine however that the "cell-form nuclei" are identical with blood corpuscles is evidently untenable. 1st, because many of the coloured corpuscles are much smaller than the smallest

See Müller in op. cit. S. 274

See on this subject Virchow, Die pathologische Pigmente.
Arch. für path Anat &c I Bd S 385
Remak, Diagnostische und pathogenetische Unter-
suchungen. — Berlin, 1845. (Abschnitt II S. 99.)

of the nuclei in question and, secondly, because no transition forms can be detected, which could not possibly be absent, were the theory a correct one. The great resemblance existing between some forms of these nuclei and the coloured corpuscle is generally admitted, nor can it be questioned that they often possess, as Mr Jones has described, a well-marked colour when examined in the mode which he recommends. This latter circumstance however implies nothing, for if water be added to any animal fluid containing blood-corpuscles in quantity, the colouring matter will be dissolved and any cell-structures, of whatever nature which may happen to be present will assume a blood-tinge

Remak was led to a similar conclusion to that of Mr Jones from the result of the following experiment. He took 50 lbs of blood from a horse and subsequently at intervals of several days examined the remaining blood under the microscope. The day after the bleeding the blood contained an unusual number of colourless blood-corpuscles, in many cases as numerous as the coloured. About the tenth or twelfth day, many of these corpuscles which possessed a single or double nucleus, lost their granular contents, and there appeared at the same time, after the addition of water "isolated colourless vesicles of the size of the colourless corpuscles, in which no nucleus was visible

but a reddish coloured round smooth body nearly as large as a blood-corpuscle & compressed laterally in the same manner was apparent as the nucleus, beyond which the clear colourless wall of the vesicle itself projected. Subsequently these nuclei became free and gradually assumed the form of the perfect coloured corpuscle.

The above observations correspond very exactly with those of Dr. Jones and no doubt admit of the same explanation. The fact that after a large bleeding the colourless corpuscles exist in unusual numbers, does not in the least imply that they have any connection with the reproduction of the coloured, it being equally well accounted for, whatever theory we hold as to the constituent of the blood which they are destined to form. I may add that I repeated the experiment of Remak but without any satisfactory result. The horse which I employed was bled successively on the 20th, 23rd, 26th & 29th of November each time to between 60 & 70 lbs. No difference on which any conclusions could be founded, in the structure either of the colourless or the coloured corpuscles, although the animal was under observation until the 15th of December.

The circumstance which, of all others appears to me the most conclusive in reference to the question before us, is that which was alluded to above viz. that numerous coloured blood-corpuscles exist in healthy blood which

are by far smaller either than the colourless corpuscles or their nuclei. These miniature corpuscles, are of such uniform occurrence and present so well defined a structure that there can be no doubt that they are in reality normal constituents of the blood. They occur however in greater frequency in some individuals than in others. During the last 4 months I have been observing them in the blood of a man, Henry Smith a patient in the Richmond Infirmary who, though suffering from internal aneurism is otherwise in tolerable health. In this man they exist in great frequency varying from 1-6700 to 1-4000 the of an inch in diameter. They are among the few objects which cannot be satisfactorily examined without an object-glass which will define well with a magnifying power of from 500 to 600 linear.

We have already seen that it is impossible to attribute the origin of the coloured corpuscle to the colourless. We have also seen that it is impossible to assign it to any organic constituent of the liver, spleen or other organ. We are therefore shut up to the conclusion that it is developed by a process in which itself is alone concerned, but of the nature and seat of which we are as yet ignorant. If the facts related above be admitted to be correct, we seem to have in them an indication of the direction which we ought to follow in our future enquiries.