three of the chief museums here—to wit, the Hunterian, the University College, and St. Thomas's. The particulars of the first twenty are given in my book on Tumours. The nature of these thirty-four is set forth in the following table:

Simple papilloma, 25 cases (one of the above proved to be associated with cancer, and two or three with myoma); myoma, 4 cases; epithelioma, 2 cases; carcinoma, 1 case; sarcoma, 2 cases—total, 34 cases.

But in all these cases papilloma was the chief and the distinctive element. In two instances it was found associated with myoma; in two or three with "lymphoid cells;" in one with cancerous deposit; and in one with commencing cartilage, suggesting an exceedingly rare condition known here as "chondrifying sarcoma."

Now papilloma, unless very largely developed, yields no sign of its presence to the "*toucher rectal*," and none to the exploring sound. Its presence can only be demonstrated by *débris* under the microscope, and then the characteristic structure is sometimes beautifully distinct. The first act of micturition, or, if not, the first washing of the bladder, may produce an atom of translucent material, which shows under a quarter-inch object-glass a papilloma with its central blood-vessel, and the long prismatic epithelium ranged round the extremity of the papilla, assuring the surgeon of the presence of a growth which makes exploration wholly unnecessary. If this fails, a flat-bladed lithotrite may remove a fragment, and so produce the irreproachable witness. But if by none of these means can you produce the needful evidence, and the history is manifestly that of vesical growth, the kidney being acquitted of all participation in the evil, then I have no hesitation in advising that a little *boutonnière* should be made, and a finger be introduced into the bladder, and the question settled beyond dispute. And this can be easily done in nine cases out of ten.

And here, again, the original source of misapprehension shows itself. Professor Guyon doubts the possibility of examining the bladder thus, and adduces the small effect of finger-manipulation in the bladder when operating by the "*taille*," and further states that the age at which tumours of the bladder appear is the age "*des périnées épais et des prostates volumineuses.*"

Quite so; that is true as regards the cases of cancer, but is less applicable to cases of papilloma; and as I operate only for papillomata, an enlarged prostate is not often encountered; papilloma occurring at all ages, but commencing at 25 years of age and upwards.

Now let me here repeat a statement I have often made, and with great deliberation, that in at least nine cases out of ten it is quite easy to examine the whole surface of the bladder if the tip of the index reaches the cavity. This can be done by making firm pressure above the pubes, provided only that the anæsthetic is given to a sufficient extent to overcome all opposition from the abdominal muscles—a proceeding about which we have no difficulty or hesitation whatever in London, with our skilled specialists in the administration of anæsthetics. In that condition, the whole surface of the bladder is easily brought down to the end of the finger so placed, which can readily detect even a very small papillomatous growth. I have demonstrated that fact so often to my *confrères*, both native and foreign, that it is beyond a doubt; and I am ready to repeat it without stint for any serious inquirer.

Well, supposing by means of such an exploration, I discover a single polypoid growth of papilloma; I find the question of operation is at once before me. Supposing, after full examination, I feel that it is not difficult to put in the forceps and remove it at once; why not? *Voilà tout.* If it is large or not easily placed, I give up the preceding idea, and do the suprapubic operation, as happened to a case about two months ago, in which, after exploring by the perineum, I encountered a large tumour springing from the top of the bladder. I did the high operation at once (the senior surgeon of the Royal Infirmary at Glasgow being present) removed the growth, and that patient accompanied me to the Clinical Society a month afterwards; he was then perfectly sound, and was seen there by the members at the meeting already referred to.

Then it is, perhaps, worthy of remark that almost all my best and enduring recoveries have been those of cases in which the simple perineal opening alone was performed. My first by that method (performed November 6th, 1880) is at this moment well, and living in London, and has had no return. It was a single pedunculated papilloma.

I am ready to avow that I do not necessarily advise all beginners to follow that method of operating. On discovering a tumour, whether by digital exploration or otherwise, one who is not highly practised in the extraction of foreign bodies from the bladder will act more safely, I doubt not, by performing the suprapubic operation. It requires great facility and experience with instruments in a bladder to nip off safely, with one or two bites of the forceps, a polypoid growth by the perineal route. When intending to do this, I always spend some three or four minutes in examining with my finger the exact position and relations of the growth; and, having thoroughly ascertained these, I rarely fail, on introducing a light handy forceps, in going at once to the spot, and in bringing it away complete, or nearly so. If I am not content, or find a more difficult task than expected, I can still proceed to the high operation.

But I am tempted now to ask where are the papilloma cases in Paris? There are only two among Guyon's fifteen cases. Are they less frequent with you than with us, or have you still to find them? Some of them have been regarded here in former times, I have no doubt, as cases of renal hæmorrhage, and have been only identified as vesical tumours in the latest stage. It is quite evident you have not yet begun to deal with them surgically. Nevertheless, they are the most desirable to find and to treat. Little can be done by operative interference for the cancers. There is more chance in dealing with epithelioma, not of accomplishing a cure, but of offering a reprieve, of lengthening a life inevitably doomed; yet the papillomata will far better repay the skill and enterprise of the surgeon.

But it is time to close. There are many other things I should be glad to add, but am compelled to be brief. One of my chief objects in making this communication is to show that there never was any ground for supposing that there could be any difference between Professor Guyon and myself as to the inutility of making an exploring operation for a tumour, the presence of which can be verified by the "*toucher rectal*"; and that, if an attempt is to be made to remove such tumours, the high operation, and not a perineal one, is the only desirable route. On the other hand, I record my profound belief that they are better let alone.

I have never performed an exploring operation except in the absence of all signs of physical change in the rectum; and when I thus discover a tumour of any kind in the bladder, I decide, after carefully examining it, by what means I can most safely and efficiently remove the growth. In my opinion, each surgeon must judge for himself in what way he can best attain the desired object. No uniform and absolute rule can be prescribed to him by authority however high. Personal predilections and personal qualifications must always count for much in determining a decision in all pursuits which partake of the nature of a practical art; and, assuredly, among the highest and finest art must be ranked all the achievements of modern surgery.

AN ADDRESS
ON
THE HÆMATOZOA OF MALARIA.[1]

By WILLIAM OSLER, M.D., F.R.C.P.,
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Our knowledge of the animal parasites infesting the blood has been of late enriched by observations which show that certain of these hæmatozoa, as they are called, are more widely distributed and more important than we had hitherto supposed. Parasites belonging to the spirozoa, and to the nematode and trematode worms, have long been known to occur in the blood of various animals. Recent investigations prove that the flagellate protozoa are also not uncommon blood parasites, and it is possible that they may be the pathogenic organisms of certain diseases. I propose in this communication to give an account of the hæmatozoa which have been found in persons suffering with the various forms of malaria.

Historical.—Our knowledge of the blood-changes I am about to describe, dates from the researches of Laveran, in Algiers, which were communicated to the Paris Academy of Medicine in 1881 and 1882, and which were finally embodied in a large work on the malarial fevers, published in 1884.[2] He found, as characteristic elements in the blood of persons attacked with malaria, (1) crescentic pigmented bodies; (2) pigmented bodies in the interior of the red corpuscles, which underwent changes in form, described as amœboid; and (3) a pigmented flagellate organism. These forms were looked upon as phases in the development of an infusorial organism which he regarded as the germ of the disease. Richard[3] confirmed these observations. A

[1] An address delivered before the Pathological Society of Philadelphia.
[2] *Traité des Fièvres Palustres*, Paris, 1884.
[3] *Comptes Rendus*, 1882.

more general interest in the question was aroused by the publications of Marchiafava and Celli,[4] who found in the blood of malarial patients at Rome the bodies described by Laveran. They figured carefully the alterations of the organism in the interior of the red corpuscles to which they gave the name Plasmodium malariæ. Councilman, of Baltimore, has more recently confirmed these observations.[5] The pigment granules so numerous in the interior of the red corpuscles in cases of "comatose pernicious fever," and which appear to be included in a hyaline mass are, according to Marchiafava and Celli, and Councilman (who had previously described them[6]) these amœboid parasites deeply laden with altered hæmoglobin.

Technical Details.—The finger pad from which the blood drop is taken should be thoroughly cleansed, and, if the examination is made during a paroxysm, the sweat which may exude after the friction and drying should be removed. Attention to these, apparently trivial, details will secure specimens of blood free from small particles of dirt, and facilitate considerably the search for pigmented bodies. The layer of blood beneath the top cover should be very thin and uniform, the corpuscles, as far as possible, isolated and not aggregated in clumps or in rouleaux. It is well to surround the cover with paraffin if the examination is prolonged. No reagent of any kind should be added. Cover-glass preparations may be made and stained in methyl blue or fuchsin, and mounted in balsam. Osmic acid preparations may also be employed. Although these bodies may be seen with a power of 500 to 600 diameters, it is essential for the satisfactory study of the changes to use higher powers. I have uniformly worked with the $\frac{1}{12}$ homo. immersion of Zeiss, and the $\frac{1}{15}$ im. of Reichert. Stricker's warm stage will be found useful.

Description of the Bodies.

1. *The Forms which Exist within the Red Corpuscle.*—(*a*) The most common alteration in the blood of malarial patients is presented by a pigmented structure inside the red corpuscle. The attention of the observer will most likely be first attracted by the presence of a few dark grains in the stroma, and a careful study of a suitable specimen will soon lead to the conviction that these are not scattered loosely, but are enclosed in a finely granular or hyaline body in the interior of the corpuscle (Fig. 1). The red discs in which

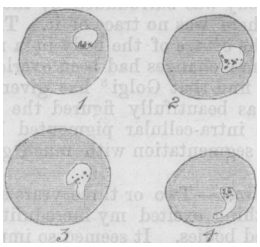

Fig. 1.– Amœboid body in red blood-corpuscles. The sketches were made at intervals of five minutes.

they occur are usually larger, look flat, and are very often paler than normal; they may, indeed, exist only as colourless shells. The number of corpuscles so affected varies extremely in different cases. In some instances they are readily found after a search of a moment or two, but, in other cases, a prolonged examination may be necessary. Only one is usually present in each corpuscle, but two or three, or even four, may occupy the stroma. They vary greatly in size, the smaller ones not occupying a fourth of the corpuscle, while the larger ones may almost fill it. A delicate contour line can usually be seen separating the body from the stroma; at times this is very indistinct, particularly if the illumination is very bright. The substance appears hyaline, or very finely granular, and the pigment grains are scattered irregularly in it. They may be very numerous, and give a dark aspect to the body, or they may be scanty. They frequently present rapid Brownian movements. Occasionally a vacuole may be seen in the interior of the body. In several instances the bodies appeared to be enclosed in a clear space—vacuole—in the stroma. When first seen they are more or less spherical, but, as already stated, the outline may be indistinct. The pigment granules may be seen to alter their position in relation to each other. If the margin of the body is carefully observed, slow changes can be seen, which gradually bring about alterations in shape. These movements, which appear to be amœboid in character, can often be traced with great ease. They are well represented at Fig. 1, and, better still, at Fig. 2. Changes in position of the body in the corpuscle result from them. They are decidedly slower than the amœboid movement of the colourless corpuscle. I have not seen any evidence of migration from the corpuscle. In dry pre-

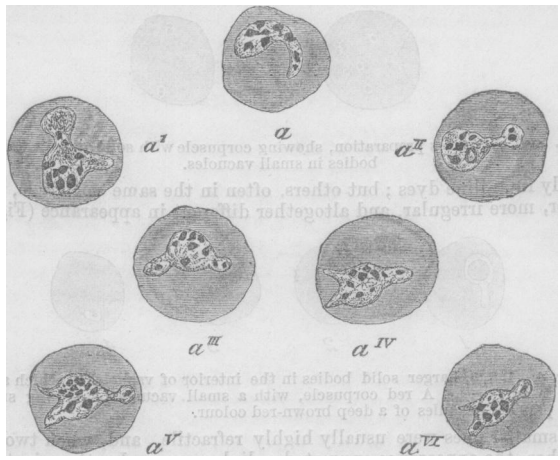

Fig. 2.—Case VI. Pigmented body in red blood-corpuscle; outlined with camera ($\frac{1}{12}$ Zeiss, C eye-piece), by Dr. J. P. C. Griffith; illustrating some of the changes during an hour and a half's observation. *a*, at 11.45, slow alterations in outline, and the pigment-granules are in active dancing motion. a^{i}, 12.15. a^{ii}, 12.25, body has rotated as well as altered its shape. a^{iii}, 12.30. a^{iv}, 12.40. a^{v}, 1 o'clock. a^{vi}, 1.02.

parations these bodies stain deeply with gentian violet or fuchsin, and present a granular stroma, in which the pigment grains are imbedded. (Fig. 3.)

Fig. 3.—Cover-glass preparation of blood stained with fuchsin. The amœboid bodies stain deeply in the corpuscles. Some of them are not pigmented.

(*b*) In seven cases peculiar hyaline structures existed in the interior of the red corpuscles, which differ from the bodies just described, in the absence of pigment and in the much greater activity of the changes. Fig. 4 illustrates the appearance and the alterations in outline. These

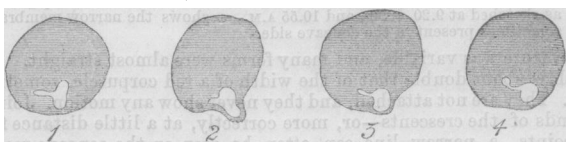

Fig. 4.—Sketches of the alteration in form of one of the hyaline bodies; 1, at 7.8 P.M.; 2, at 7.12; 3, at 7.15; 4, at 7.20.

bodies are devoid of structure, and the corpuscles in which they are present are not so pale as those with the pigmented forms. Marchiafava and Celli, who have given an excellent plate of these bodies,[7] regard them as the initial forms of the pigmented bodies. One does occasionally see appearances indicative of commencing pigmentation, but they have not, as a rule, the solid aspect of the pigmented bodies. In three cases I have seen the following remarkable changes. The hyaline body, while actively changing shape, suddenly burst from the stroma, and disappeared, or formed only a few granules. Thus, in a red corpuscle, there were, at 3.40 P.M., two hyaline, irregular-shaped bodies, which were changing rapidly in outline. The alterations were so marked that the physicians present at the time had no difficulty in seeing them. The stroma of the corpuscle was of full colour. At 3.50 P.M., as I was carefully watching these forms, the corpuscle suddenly ruptured, and gave exit to two distinct masses, which quickly broke up into ten or twelve spherical bodies. No change took place in these after twelve hours, except that they became pale and indistinct. The stroma of the corpuscle became quite colourless. On two other occasions a similar phenomenon was witnessed, but in one no trace could be seen of the extruded material. This is evidently a physical change, and I think these very pale hyaline bodies must be carefully distinguished from the pigmented forms, though possibly associated with their early development.

[4] *Fortschritte der Medicin*, Nos. 14 and 24, 1885.
[5] Paper read before the Association of American Physicians, June, 1886. Councilman amd Abbot, *American Journal of Medical Sciences*, April, 1885.
[7] *Fortschritte der Medicin.* 1885. No. 24.

(*c*) In seven cases there were vacuoles in the red corpuscles containing solid-looking bodies of various sizes and shapes. Certain of these structures resembled micrococci very closely (Fig. 5), and stained

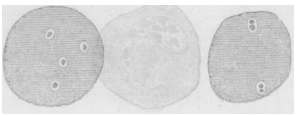

Fig. 5.—Cover-glass preparation, showing corpuscle with solid, deeply stained bodies in small vacuoles.

deeply in aniline dyes; but others, often in the same corpuscle, were larger, more irregular, and altogether different in appearance (Fig. 6).

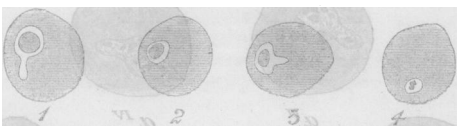

Fig. 6.—1, 2, 3, Larger solid bodies in the interior of vacuoles (?) which alter in outline. 4, A red corpuscle, with a small vacuole containing small pigment-granules of a deep brown-red colour.

The smaller ones were usually highly refractile, and, when two were together, the appearance suggested a diplococcus. In three instances these bodies had a deep brown tint, as if composed of pigment. The larger bodies were homogeneous, very variable in size and shape. No movement was noticed in them, but the outlines of the spaces in which they lay sometimes changed actively. In Case 29, these bodies were very abundant, and for days formed the only noticeable alteration in the corpuscles.

2. *The Free Forms.*—(*a*) Pigmented crescents. These bodies, which were found in eighteen cases, present remarkable features in appearance and structure. The form was usually that of a beautiful crescent (Fig. 7), with rounded or gently tapering ends; but the degree

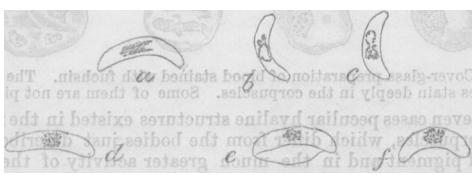

Fig. 7.—Crescents, *a*, *b*, *c*, show the slow alterations in the form of the pigment, as sketched at 9.20, 10.40, and 10.55 A.M. *e* shows the narrow membrane sometimes present in the concave side.

of curvature was variable, and many forms were almost straight. The length is about double that of the width of a red corpuscle, sometimes more. They are not attached, and they never show any motion. Joining the ends of the crescents—or, more correctly, at a little distance from the points—a narrow line can often be seen on the concave margin (Fig. 7, *e*). The body of the crescent appears made up of a structureless, homogeneous material, in the centre of which is a prominent collection of pigment granules. This, with the peculiar form, makes these bodies very easily recognisable in the blood, even when closely surrounded by the corpuscles. The pigment is very dark in colour, distinctly granular, and varies somewhat in its arrangement. As a rule, it is central and aggregated, either in a heap, or assumes the form of a band placed transversely to the axis of the crescent. In some instances it is more scattered, but I have never seen it at either end of the body. Although the most careful examination fails to detect any movement in the hyaline substance of the crescent, yet the existence of such may be inferred from the very positive movement which the pigment granules undergo. Fig. 7, *a*, *b*, *c*, represents these alterations; changes in form are exceptionally seen, as shown at Fig. 8 (1, 2, 3). A crescent became, within an hour, an ovoid body.

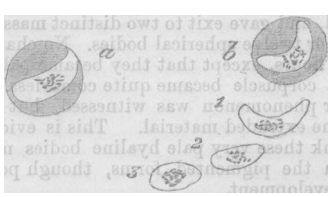

Fig. 8.—*a* and *b* show crescents in the interior of red corpuscles; 1, 2, and 3, changes in a crescent.

Sketch 1 was made at 9.40, 2 at 10.10, and 3 at 10.30 P.M. The outline of these bodies is very clear and defined. Ovoid, elongated and rounded forms of identical structure are also met with, but the crescents predominate. The number is variable, from one or two in a slide, to six or eight in the field of the 1-12th im. Though almost always free, they occur sometimes in the interior of a corpuscle, indicating, doubtless, the mode of development (Fig. 8, *a* and *b*).

(*b*) *The Rosette Form.*—In six instances there were rounded bodies, a little larger than red corpuscles, with a dimly granular protoplasm, and in the centre a rosette of pigment (Fig. 9). Some of these ap-

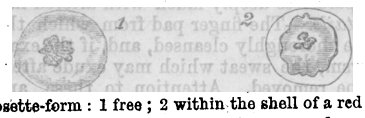

Fig. 9.—Rosette-form: 1 free; 2 within the shell of a red corpuscle.

peared to be enclosed in a delicate membrane, others were free. In six cases remarkable changes were seen in these forms, of the nature of segmentation. Thus Fig. 10, *a*, represents one of these as seen at

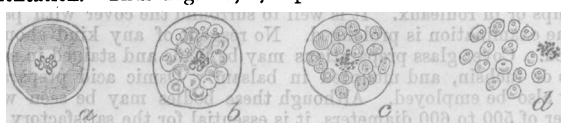

Fig. 10.—Segmentation of a rosette-form: *a* at 6 P.M.; *b* at 6.10, segmentation proceeding; *c* 6.30, segmentation complete; *d* 7.40, small free bodies.

6 P.M., September 4th. At 6.10 (*b*) there were distinct indications of segmentation in the finely granular protoplasm. At 6.30 (*c*) this had resulted in the formation of twelve or fifteen rounded bodies clustered about the central pigment, and still enclosed in the sheath. At 7.40 (*d*) the shell had burst, and given exit to the small corpuscles, which presented a tiny speck at or about the centre. At 10.40 they had not undergone any material change. In Case 60, one of quartan ague, this phenomenon was repeatedly observed. The development of the rosette form can, I think, be traced from the intra-cellular pigmented bodies, which increase in size until the entire corpuscle is filled. In some instances the body was surrounded by the remnant of the red corpuscle, in others there was no trace of it. The pigment granules gradually collect in the centre of the body in a more or less distinct rosette. I thought these changes had been overlooked by the writers on this subject, but I find that Golgi[8] has given a very full description of them, and has beautifully figured the development of the rosette form from the intra-cellular pigmented bodies. He has followed the process of segmentation with much greater detail than I have been able to do.

(*c*) *Flagellate organisms.*—Two or three years ago, when I first read Laveran's papers, nothing excited my incredulity more than his description of the ciliated bodies. It seemed so improbable, and so contrary to all past experience, that flagellate organisms should occur in the blood. The work of the past six months has taught me a lesson on the folly of a scepticism based on theoretical conceptions, and of preconceived notions drawn from a limited experience. Flagellate bodies were seen in seven cases, never in great numbers, usually only one or two in a slide. They are smaller than red blood-corpuscles, often not more than half the size. A specimen in one case was equal in one diameter to a red corpuscle lying near it. They are round, ovoid, or pear-shaped; the protoplasm finely granular, and in every instance contained pigment, usually central, which often displayed rapid Brownian movements (Fig. 11). The flagella are variable in

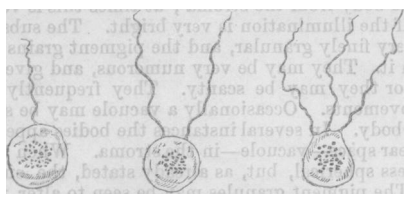

Fig. 11.—Flagellate forms.

number; one, three, and four were noted in different specimens. The length, as closely as could be estimated, was two or three times that of the body. They are exceedingly delicate, gently tapering, and, except in one instance, I could not determine the existence of a small terminal knob, figured by Laveran. The movement is exceedingly active, and the lashing of the long filaments may be sufficiently

[8] Sulla Infezione Malarica, *Archivio per le Scienze Mediche*, vol. x, No. 4, 1886.

strong to drive away the corpuscles in the vicinity. The undulatory movement caused by the play of the filament over the surface of a group of corpuscles may attract the attention of the observer before he sees the cilia. The motion does not persist long; in none of the specimens which I examined, for more than half an hour. In one instance, the flagella disappeared in the short interval between two observations, but I could not determine what became of them. I have not seen the free-swimming cilia described by Laveran, but Dr. Councilman tells me that he has confirmed this observation. I have not been able to discover either nucleus or vacuoles in the flagellate organism. Slight, irregular changes in outline occur, due to slow movements in the protoplasm.

(*d*) Small, round, pigmented bodies, from one-fourth to one-half the size of a red corpuscle, were not uncommon in some cases (Fig. 12).

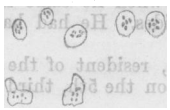

Fig. 12.—Small free pigmented bodies, some of which show amœboid movements.

Usually, they remained unchanged, but, in several instances, they showed amœboid movements. The smaller ones about equal in size the products of subdivision of the rosette form.

Before proceeding to discuss the nature of these bodies and their relation, I will briefly refer to the condition of the blood-corpuscles.

The red corpuscles showed no other notable alteration save that already described. The pigmented organism evidently destroys the vitality, and consumes the hæmoglobin, for the affected cells become pale, often spherical, and, finally, are reduced to the condition of mere shells; except in cases of pronounced anæmia, the variations of the corpuscles in size and outline were not great. The colourless corpuscles were in some cases increased in number, and in very many instances contained dark granules. In several specimens, they were observed to contain the pigmented organisms. In Case 40, a crescent had been included (Fig. 13), and, in Case 51, the process of inclusion

Fig. 13.—A colourless corpuscle containing a crescent.

of two free pigmented bodies was watched during half an hour (Fig. 14). The blood-plaques were, as a rule, scanty, even when the anæmia was pronounced. No pigment was seen in them.

Types of Malaria Studied.—Of the seventy cases examined, a majority were instances of ordinary intermittent fever, chiefly quotidian and tertian, with two quartan cases. There was one case of remittent fever, one of comatose pernicious malarial fever, and the remainder were cases of malarial cachexia or chronic paludism, with occasional outbreaks of fever, with or without chills. In all of the cases, with the exception of seven, one or other of the forms above described was found in the blood.

Relation of the Forms to the Varieties of Malaria.—The pigmented amœboid bodies are met with in both acute and chronic cases, but they may be said to be specially characteristic of the more acute manifestations of the disease. In recent examples of quotidian or tertian ague which had not been under treatment, the amœboid intra-cellular forms were almost invariably present. I will refer subsequently in detail to the cases in which they were not found. The hyaline non-pigmented forms, and the vacuoles containing solid bodies, also occur in the acute cases; indeed, these latter forms were the only alterations noted in several instances. Thus, in Case 29, a man aged 48 was admitted to the Philadelphia Hospital September 27th, in a chill. He had had a paroxysm ten days before, and had suffered with malaria several years previously. The blood examined during the hot stage showed no pigmented bodies, but numerous corpuscles containing the vacuoles shewn in Figs. 5 and 6. The chills occurred on the 28th, 29th, 30th, and October 1st; and each day the blood was carefully examined, without finding other bodies than those in the vacuoles or hyaline spaces. On October 1st, the patient began with ten grains of quinine twice a day, which was continued for five days. He had no chill after October 1st. On the 7th there were crescents in tolerable numbers, which persisted until the 27th, the date of the last examination.

The crescents appear to be associated with the more chronic forms of malaria, or with acute cases which have been under treatment for some time. Of eighteen cases in which they were present, in twelve there was a history of infection lasting from six weeks to six months. In many, the cachexia was marked, and the spleen greatly enlarged. In six instances the attacks were recent—under a month; but in every one of these cases quinine had been taken. As a rule, the crescents occurred alone in the blood; but there were cases observed in which the pigmented amœboid bodies, the rosette form, and the flagellate organisms, were also present. I did not find the crescents in any recent cases of intermittent fever which had not been under treatment.

The rosette form, with its peculiar segmentation, occurred in six cases, and always in association with the amœboid intra-cellular bodies. Case 31: tertian ague, examined in fourth attack; no medicine. Case 33: quotidian for seven days. Case 37: quotidian for six weeks, anæmic, and had a large spleen; took quinine one day. Case 39: quotidian for seven days. Case 58: quotidian, on and off, for six weeks, then stopped; now daily chill for a week. Case 60: quartan for three weeks. I have noted these details, as this form has not been much studied, and as Golgi seems inclined to ascribe to it an important connection with the development of the paroxysm. It was only observed in acute cases which had not been under treatment.

The flagellate organisms were present in seven cases, six of which were chronic forms, and one an acute case of three weeks' duration.

The small free pigmented bodies were very variable in numbers; they seemed more abundant in the chronic forms with cachexia.

Relation of those Forms to the Paroxysm.—Very many observations were made with a view of determining whether these organisms bore any definite relation to the remarkable periodic attacks which characterise acute malaria. For this purpose, in typical cases, examinations were made in the intervals of, just before, and in each stage of, the paroxysm. The results may be thus stated: there were instances, particularly if recent, in which the amœboid organisms were decidedly more numerous and larger before and during the paroxysms than in the intervals; there were others in which the number during the chill and hot stage was so small, that examples were very hard to find; in others again, slides taken before the attack and during each stage were negative, and yet in subsequent paroxysms the bodies were present in the blood. I think, on the whole, that the pigmented bodies in the red corpuscles are more numerous before and during an attack, but the difference is by no means striking, and I have repeatedly had to search long in slides prepared during a paroxysm for a single example. In acute cases which have lasted some weeks, and have had no medicine, the amœboid bodies have seemed to be quite as abundant at one time as another. Nor have I been able to see any special difference in the form of the bodies just before or during the chill, though in the early days of the attack they may be small and less distinctly pigmented, or indeed may present, as in Case 29, already referred to, the appearance of vacuoles containing small solid bodies.

The remarkable segmentation of the rosette form was in each instance met with during the paroxysm, and Golgi claims to have traced in five cases a series of changes corresponding to the stages of the attacks. In the intervals, the pigmented bodies gradually increase in size until they fill the affected red corpuscles, and finally the pigment collects in the centre, as shown at Fig. 9. The process of fission coincides with the onset and course of the paroxysm, and by the time of its conclusion the rosette forms disappear. In Case 60—a quartan ague—an attempt was made to follow these changes, with the following result. The patient, a lad of 18, had had malaria, on and off, for a year, but for three weeks before admission the chills had been recurring with regularity. On Saturday, the 6th, the blood was examined in the chill. The red corpuscles contained many large pigmented bodies, and the rosette forms were numerous, many in process of subdivision. On the 7th and 8th, he was free from fever, and the most careful examination of the blood failed to detect any forms but the ordinary pigmented intra-cellular bodies. They did not seem more numerous on the evening of the 8th than they were on the 7th. On the 9th, hourly examinations of the blood were made between 11 A.M., when the fever began, and 4 P.M. In the first two slides, there were very many pigmented bodies with the granules becoming concentrated, some with typical rosettes and a few in course of segmentation. In the specimens taken during the afternoon, the process of division was readily traced, and there were many of the small bodies in the field. On the 10th the note is: "No free bodies, all intra-cellular, tolerably numerous; no rosettes; no segmentation." On the 11th, several examinations were made, and the note reads, "absolutely none, save pigmented forms in the red." On the 12th, the slide at 8 A.M. showed large number of pigmented bodies, some with the granules irregularly arranged, other with distinct rosette. Fever began at 12 A.M.

Throughout the paroxysm, hourly examinations were made; rosette forms were abundant, and segmentation active. On the 13th and 14th, the ordinary forms were present, and in the paroxysm of the 15th, the segmenting bodies were again seen. The development of pneumonia interrupted the observations. It is worth noting that in this case the onset of the paroxysms was marked by an outbreak of the most intense urticaria. Blood and lymph from the wheals did not show any special changes.

Certainly the segmentation seems associated in some way with the paroxysm in these cases, but unless our observations have been faulty or very incomplete, there are many others in which there are no such changes in the attack. It is a point, however, to which the attention of observers should be carefully directed.

The crescents appear, as already stated, to be confined to the more chronic cases, or to those which have had treatment. They may persist for weeks or months. Thus in Case 56—a patient had irregular fever with what he called dumb chills, which had lasted for a month—for three weeks there was fever without chills, the temperature rising on some occasions to 103°. The crescents were numerous, and were not associated with other forms. With this his general condition was good, and he did not look anæmic. Under arsenic he improved, and the fever subsided, but the crescents were still in his blood six weeks from the date of the first observation.

Genuine paroxysms may occur in these chronic cases without the development of other forms than the crescents. This observation was repeatedly made in Case 25, a man with irregular malaria of many months' duration and occasional severe chills. The flagellate organisms did not seem to have any special relationship to the paroxysm, but they were so rarely seen that my observations on this point are not of much value.

Influence of Medicines on the Organisms.—Quinine invariably caused the pigmented bodies to disappear. In acute cases, which were usually studied during two or three paroxysms before the administration was begun, this observation was repeatedly confirmed. In a few days the corpuscles were entirely free; in several instances, the crescents appeared before the blood became normal. For example, Case 46 had his first chill on October 1st, and a daily recurrence until the 10th, when he came under observation. The pigmented bodies were abundant, and continued so on the 11th and 12th, when the temperature rose in the paroxysm to 105°. Quinine (twenty grains) was given on the morning of the 13 h (which broke the chill), and repeated on succeeding days. The bodies were present on the 13th, and a few on the 14th. They were not found on subsequent days. In less acute cases the action of the quinine did not seem to be so prompt, and the crescents did not disappear so rapidly under its use. Certainly, in recent cases this medicine acts as a positive specific against these organisms, just as it does against the malady itself. Arsenic does not appear to influence the pigmented intra-cellular bodies. In a chronic case, without chills, but with irregular fever, the crescents persisted for over five weeks, although the patient had improved in general health and vigour, and was no longer anæmic. Thallin and antifebrin were given in some cases without any noticeable results. As is well known to practitioners in malarial regions, there are cases of intermittent fever which subside without special treatment. I have had several patients in whom, without any quinine, the chills stopped or recurred very irregularly. In Case 66, the crescents appeared in the blood, which at first contained only the intra-cellular forms.

Cases examined with Negative Result.—As before stated, there were eight instances of apparently true malaria in which the organisms were not found, and to these I shall now briefly refer. I would remark, in the first place, that we cannot always rely upon one, or even two, examinations of the blood for these bodies. They may be very scanty, or they may be present at one examination and absent at the next. For example, Case 41, a young man, aged 26, was admitted with a temperature of 104°. He had been cranberry-picking in New Jersey, and had been ill for a week with fever and indefinite pains, but no chills. He was so very dull, that as the fever persisted, typhoid was suspected, although, as a cranberry-picker, malaria was first thought of. The blood was examined on three occasions with negative results, but on the fourth observation, five days after admission, and when the temperature had fallen to normal, crescents were found, which continued in the blood until he was thoroughly cinchonised. The cases are as follows:

Case 10. Child, aged 5; chills and fever in Maryland nine months ago, occasional chills since, the last two weeks ago; spleen 4 inches vertical diameter; had taken quinine, none recently. One examination.

Case 11. Man, aged 19; never malarial before. Four distinct paroxysms. Slides examined from fifth and sixth, taken in cold, hot, and sweating stages. No quinine. I did not see the case subsequently.

Case 20. Man, aged 40. First attack six months ago. Chills on and off for past three months. Blood examined three days after last chill. Had taken quinine for two days. Spleen enlarged.

Case 21. Man, aged 28. Examined on 17th, first chill on September 6th; four since. On 14th, took quinine grs. xxx, and has had gr. x t. i. d. since.

Case 26. Man, aged 35. Chills for three weeks, at first quotidian, latterly tertian. Had taken medicine, but did not know the nature of it. Was admitted on 24th. Two examinations, negative; pigment in white corpuscles. On 25th quinine was given. Three subsequent examinations, without result.

Case 28. Man, aged 60. Admitted on 14th. Well-marked chills for eight weeks; had one when he came in, and four after. Blood examined on 28th, two slides. He had had quinine gr. xx each day since admission.

Case 38. Man, aged 70, resident of the almshouse for six years. First chill on 2nd, second on the 5th, third on 6th, when blood was examined, two slides.

Case 52. Man, aged 25. Chills and fever for six days. Blood examined in chill, and on the following day. Had had quinine.

Thus, in five of these cases quinine had been taken, and they may be counted out. In Case 10, the child was brought from the country, and only one examination was made. Case 11 was undoubtedly a case of quotidian ague, and the examination of slides taken from each stage of the fifth and sixth paroxysm was negative. I did not see the patient, and further examinations were not made. In Case 38, the bodies were not found on two occasions. This man also could not be followed, and I do not know his subsequent history.

The importance of excluding other causes for the paroxysmal chills was well illustrated by a case under the care of my colleague, Dr. J. H. Musser, which we regarded as one of malaria, but in which the pigmented bodies could not be found. The man had had chills on and off for several years; of late, the attacks had been more frequent and recurred more regularly. Quinine in medium-sized doses had no influence, but very large doses appeared to control the paroxysms. Their recurrence excited suspicions, and the discovery of pus in the urine, with decided pain on deep pressure in the lumbar region, indicated a more probable cause for the irregular chills.

Nature of the Organisms.—It is very evident that we are dealing here with structures unlike any others which have been described in human blood, and with bodies which have no relation whatever to the spirilla, micrococci, and bacteria of certain acute diseases. I would call attention to the remarkable unanimity in the description of these parasites by Laveran, Richard, Marchiafava and Celli, Councilman, Golgi, and myself. Laveran's original description is well-nigh complete, and subsequent workers have done little else than confirm his results, though to Marchiafava and Celli is due the credit of insisting upon the amœboid character of the intra-cellular form. Before discussing the relation of the forms to each other, it will be necessary to take a brief review of cognate organisms occurring in the blood, upon which recent investigations throw an important light.

It has been known for some years that hæmatozoa exist in the frog; one form, a flagellate organism, the Trypanosoma sanguinis, described by Gruby in 1843, is a well recognised monad; a second, the Drepanidium ranarum, of Lankester, is evidently a gregarine, possibly a larval form, as he suggests.[9] Having been long familiar with these bodies,[10] which were very abundant during several winters in the frogs in my laboratory at Montreal, I was at once struck with an apparent similarity to them of the forms found in malarial blood. The crescent-shaped body in particular resembles strongly certain of the gregarines, and I thought it possible that we had here an instance of a sporozoon becoming flagellate at one stage of its development as Rivolta affirms may be the case. I soon discovered, however, that there were other observations on hæmatoza which bore more directly on the subject, and rendered possible a more likely explanation. Mitrophanow,[11] in 1883, announced the discovery, in the blood of the carp and of the mud-fish, of parasites belonging to the flagellate infusoria. A description of these forms need not detain us, further than to note that they were polymorphic, and one stage was represented by an amœboid body without flagella.

In a report published by the Punjab Government, December 3rd, 1880, and in the *Veterinary Journal*, London, 1881-82, my friend, Dr. Griffith Evans, described a new and very fatal disease known as *surra*, which prevailed among horses, mules, and camels in India, and

[9] *Quarterly Journal of Microscopical Science*, vol. xxii.
[10] *Canadian Naturalist*. 1883.
[11] *Biologisches Centralblatt*, Bd. iii, p. 35.

in which he discovered a parasite in the blood during life. At first Evans believed it to be a spirillum, but subsequently came to the conclusion that it was a much higher organism. His observations have an important bearing on the question of the parasites in malaria. In 1885, Veterinary-Surgeon Steel published "An Investigation into an Obscure and Fatal Disease among Transport Mules in British Burma," which also proved to be *surra*. A careful clinical investigation of the disease led to the conclusion that it was a true relapsing fever, very similar to recurrent fever of man. Steel found the parasite described by Evans in all cases, and determined that it appeared as the temperature rose and disappeared in the intervals between the paroxysms. He regarded it as a true spirillum, and named it Spirochœta Evansi. Both Steel and Evans found the disease readily communicable to dogs, horses, and mules, either by inoculation or by ingestion. Recently, on the return of Dr. Evans from India, he placed material from the *surra* disease in the hands of Dr. Crookshank, who has made an elaborate report,[12] confirming Dr. Evans's view that the organism is not a spirillum, and states that the parasite is morphologically identical with the hæmatozoa described by Mitrophanow in the carp and mud-fish. In 1879, Lewis[13] described certain parasites in the blood of rats in India; and, again, in 1884,[14] he more fully discussed the question, and spoke of the identity of the organism with that found in the *surra* disease. Crookshank, in the paper just mentioned, gives the results of his investigations on the blood of European rats, 25 per cent. of which he finds infested with Lewis's parasite. It is a flagellate organism, with an undulating fin-like membrane, and is highly polymorphic. Crookshank has distinguished "globose, angular, non-filamentous, bi-flagellate, semi-circular, and disc forms;" the latter represent the encysted stage. This organism is believed to be morphologically identical with the *surra* parasite and with Mitrophanow's hæmatozoa.

In the *Biologisches Centralblatt*, 1885, Professor Danielewsky, of Charkoff, makes an important contribution to the subject. He states that Trypanosoma, the well known flagellate organism of frog's blood is polymorphic, and occurs in an amœboid form, and also produces spores; and, further, he has found in the red blood-corpuscles of birds a pigmented protoplasmic body, which subsequently appears in the plasma as a pigmented flagellate organism. In a later communication,[15] he suggests the identity of the pathogenic blood parasites of man with the hæmatozoa of healthy animals, and refers specially to the similarity of the forms which he has found in birds to certain of those described by Laveran in malaria.

With this information, we are in a better position to discuss the relation of the forms described to each other, and the zoological position of the organism. It is evidently closely allied to the hæmatozoa just spoken of, and the facts which we know of their life-history enable us to assert, with greater confidence, that we are here dealing with the varieties of a highly polymorphic species, and not with two or three different organisms. The flagellate form is doubtless the adult condition; and it is interesting to note, in contrast to the hæmatozoa of the rat and of the *surra* disease, the comparative infrequency of its occurrence. Laveran met with it ninety-two times in four hundred and thirty-two cases, and Councilman eleven times in eighty cases. The steps in development remain to be worked out. It seems clear, however, that the pigmented amœboid form may become transformed into a sporocyst (represented by the rosette form and its changes), or into an encysted body (resting form), the crescent. The gaps in our knowledge relate specially to the form and manner of entrance of the parasite into the red corpuscle. Do the solid particles contained in the vacuoles (Figs. 5 and 6) represent the earliest stage? I think it highly probable that they do, and that they, with the hyaline unpigmented bodies, are the immature forms. The spore-like structures which result from the segmentation of the rosette form do not resemble the small solid bodies seen in the red corpuscles, but are rather like the tiny free pigmented forms which, in some cases, were abundant in the plasma. Of the latter, various sizes are found, and it is possible that from them the adult flagellate bodies arise. Golgi suggests that the spores, resulting from the segmentation, pass to the spleen, and there attack the red corpuscles, in which they develop into the amœboid forms. As at present the data are not available for a final decision, a further consideration of these points need not detain us. There is sufficient evidence to show that the various forms are only phases in the life-history of one of the flagellate protozoa, belonging to the order Flagellata-Pantostomata. Mitrophanow suggests a new genus, Hæmatomonas, to include the monad hæmatozoa; but Crookshank, who has carefully worked out the affinities of the parasites of the rat, the fish, and the *surra* disease, has referred them to the genus Trichomonas. The organism here described has not, however, the characteristic marks of a Trichomonas; for it lacks the undulating fringe on one side and the caudal filament. Nor does it agree with the features of a Cercomonas; so that, meanwhile, until the true affinities are determined by an expert, its proper place seems to be the genus Hæmatomonas of Mitrophanow, which conveniently includes all monads parasitic in the blood. Thus: genus, Hæmatomonas; species, Hæmatomonas malariæ. Definition: Body plastic, ovoid, or globose, no differentiation of protoplasm, which contains pigment grains; flagella variable, from one to four. Highly polymorphic, occurring in (1) amœboid form; (2) crescents, encysted form; (3) sporocysts; (4) circular, free, pigmented bodies. The name designates the natural affinities of the parasite, its habitat, and the conditions under which it occurs, on which grounds it seems preferable to that of Plasmodium malariæ, suggested by Marchiafava and Celli.

Relation of the Parasites to the Disease.—The same difficulty meets us here as in so many affections in which micro-organisms have been found: Are they pathogenic, or are they merely associated with the disease, which in some way furnishes conditions favourable to their growth? As evidence of their pathogenic nature may be urged, with Laveran, the constancy of their presence, their absence in other individuals in malarial regions, the destructive influence upon the blood-corpuscles, and their abundance in the graver forms of the disease. But even these considerations, weighty as they may appear, will not carry conviction to all, in the absence of experimental demonstration such as can be afforded in the case of certain pathogenic schizomycetes. Attempts to isolate and grow these hæmatozoa outside the body have failed. Marchiafava and Celli have shown that the inoculation of healthy persons with blood taken from a case of malaria is followed in a variable time by genuine ague paroxysms, in which the blood contains the parasites; but in regions where malaria is prevalent such experiments are not wholly free from objections. A series of negative observations on undoubted cases of malaria would be convincing. I lay no special stress on the three cases in which I did not find the parasites, as the patients were not followed from day to day with the accuracy necessary to give any value to the observations. It must be borne in mind that hæmatozoa are not uncommon in animals, and, as in the rat, do not appear to interfere seriously with the health of their hosts. Under these circumstances, the association of a specific form with a definite disease in an animal makes it all the more probable that the species is pathogenic. A further study of the *surra* disease is particularly to be desired with the new light which Evans and Crookshank have thrown upon it. The conditions under which the disease occurs, combined with its paroxysmal character, are so similar to those of malaria, that a full explanation of its pathogeny would have a very direct bearing upon the present question.

To my mind, two facts in connection with these hæmatozoa point significantly to their etiological association with malaria. First, the positive anatomical changes which can be directly traced to their action, changes upon which one at least of the most marked symptoms of the disease depends; I refer to the destruction of the red blood-corpuscles, which can be followed in all its stages, and is as well-defined an alteration of tissue brought about by a parasite, as any of which we know. The second fact is the action of quinine upon the parasites. The simultaneous disappearance of the symptoms of the disease and the hæmatozoa suggest that the specific influence of the medicine is upon the parasites, though it may be urged that the quinine, while curing the disease, simply removes the conditions which permit of their growth in the blood.

Practical Considerations.—An interesting practical point is the diagnostic value of the presence of these bodies. There were six or eight cases in which the examination of the blood proved of great service in determining the existence of malaria. Some of these are worth mentioning. One of the first was a man aged 37, who had been under observation on three or four occasions with anæmia and an enlarged spleen. He had had three attacks of hæmatemesis. There was no history of malaria, and, from the gravity of the case, I was led to regard it as one of severe splenic anæmia. On his fourth visit, however, a careful examination of the blood revealed the presence of the parasites, and I gave, in consequence, a more favourable prognosis in the case, which has since been justified. In an instance of pernicious malaria admitted to the Philadelphia Hospital, under the care of my colleague, Dr. J. H. Musser, the diagnosis rested on the discovery in the blood of the characteristic changes in the corpuscles. To a third case, No. 41, I have already referred, and there were four or five other instances of chronic malaria in which the nature of the dis-

[12] *Journal of the Royal Microscopical Society.* 1886.
[13] *Quarterly Journal of Microscopical Science.* 1879.
[14] *Quarterly Journal of Microscopical Science.* 1884.
[15] *Centralblatt f. die Medicinischen Wissenschaften*, Nos. 41 and 42. 1886.

ease was determined by an examination of the blood. On the other hand, in many cases of suspected malaria, the absence of these bodies led to a more careful examination, and to the discovery of the cause of the chills and fever. Four of these were cases of phthisis with ill-defined physical signs; in a fifth, after several negative blood-examinations, the ague-like paroxysms were found to be due to a septic pneumonia; in a sixth and seventh, renal disease was discovered. I feel confident that, in malarial regions, the examination of the blood will prove, in skilled hands, a most valuable aid in the diagnosis of many obscure cases.

Melanæmia.—These researches on malaria throw light on the formation of pigment in the blood and various organs in the chronic cases. Evidently the primary change is in the red blood-corpuscle, which is gradually destroyed by the amœboid form of the parasite. Every stage of this process can be readily traced, and these observations bear out the more recent views on the origin of the pigment in the blood itself. The pigmentary degeneration of the red corpuscles noticed long ago by Frerichs and by Kelsch,[16] was no doubt the same as here described. The gradual accumulation of the granules in the spleen, liver, and bone-marrow leads to the characteristic melanosis of these organs. I sought carefully for evidence of active interference with these parasites on the part of the white blood-corpuscles, but on only

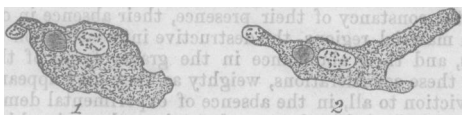

Fig. 14.—A colourless corpuscle studied for an hour and a half, during which time it had, as shown at 1, included a pigmented body, and was about to take another 2.

two or three occasions was this seen. Once a crescent was found inside a colourless corpuscle (Fig. 13), and again, as shown at Fig. 14, a corpuscle gradually enclosed two free pigmented bodies. The greater portion of the pigment resulting from the destruction of the monads is picked out by the cells of the spleen and bone-marrow, which also, no doubt, as in health, remove the effete red cells and their remnants. Pernicious malaria, common enough when Stewardson[17] wrote his well-known article, has now become very rare in Philadelphia. In these cases, Marchiafava and Celli have found the capillaries of the various organs filled with corpuscles containing pigment-grains which appear enclosed in a hyaline matrix. Councilman and Abbot[18] have described the same change, and I am indebted to Dr. Councilman for the specimen from which the accompanying sketch was taken (Fig. 15). It represents a small brain-capillary filled with corpuscles, in many of which are pigmented bodies which stain deeply, and, so far as can be

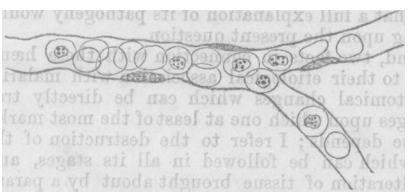

Fig. 15.—Sketch of a capillary vessel of grey matter of brain. Case of pernicious comatose malaria—Dr. Councilman. The red corpuscles are seen in outline, and in five there are pigmented bodies.

ascertained, are identical with the pigmented organisms met with in the red corpuscles during life. Only one instance of fatal malaria came under observation, a man aged 70, admitted to Dr. Musser's wards on October 25th. He had been on the Isthmus of Panama and in Georgia, and had chills and fever in both places; last chill was three days before admission. He had also had hæmaturia. He was very anæmic, the spleen was slightly enlarged, the temperature, 101.3°. There was great stupor, and he was roused with difficulty; the tongue was dry. The temperature became subnormal on October 27th and 28th. Examination of the blood showed many pigmented bodies in the red corpuscles, numerous free circular forms, a few crescents, and several flagellate organisms. The stupor deepened to coma, and he died on the night of October 28th. The spleen and liver showed typical pigmentation, and the bone-marrow was also very dark. The spleen-pulp contained free pigment and many large cells, some of which were filled with dark granules, while in others there were bodies identical with the small pigmented forms so abundant in the blood during life. The marrow presented similar changes. The number of red corpuscles containing the pigmented bodies was not great, nor were the capillaries of the liver or the brain stuffed with them, as in the instances of pernicious malaria just referred to. Probably this was an instance of severe malarial cachexia of many months' duration, and scarcely should be grouped with the pernicious comatose form.

To my colleagues, Drs. Curtin, Neff, and Musser, I am indebted for the privilege of examining the malaria-cases in their wards; and to my resident physicians, Drs. Donohue, Albertson, and Westcott, for assistance which materially lightened my work.

[16] *Archiv. d. Physiologie*, 1875.
[17] *American Journal of Medical Sciences*, 1851.
[18] *American Journal of Medical Sciences*, 1885.

AN ADDRESS
ON
THE INADEQUATE TREATMENT OF ANÆMIA.[1]

By Sir DYCE DUCKWORTH, M.D., F.R.C.P.,
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None amongst us can doubt that there is everywhere a great deal of untreated anæmia. I observe it quite as commonly in healthy rural districts as in the large towns. An out-door life, in pure air, is by no means preventive or curative of this state. I have a strong impression, indeed, that many cases, anæmic in the country, improve under the conditions of the more intense life of big cities, provided the ordinary hygienic conditions are favourable. It is common to find the contrary affirmed—that country girls often become anæmic in the large towns. This is quite true, but the facts of each case must be brought out in order to explain the cause in each case. The causes of anæmia, ill-understood as they are, are certainly not uniform. For instance, I am as convinced of anæmia due to nervous influences, as I am of anæmia due to bad air, bad food, and imperfect solar influences; and for successful treatment regard must be had to all such matters. It is not difficult to follow the onset of the disorder in a young girl who comes from healthy farm-service in the country, to work as a scullery-maid in the dungeons of Belgravia, or to sleep in the stifling attics of Mayfair; but it may be asked why this state should so often supervene in young girls sent from home to schools where, now-a-days, even in Germany and France, attention is paid to diet and to active open-air exercise. The causes may be, and probably are, not far to seek in each instance, but they are, at any rate, as I have said, not uniform.

In this communication I wish to express my belief that many cases of anæmia are insufficiently or incompletely treated. I propose to discuss neither the very large subject of the etiology, nor the nature of the particular disorder in question. I refer to cases which are very common in all ranks of life, and more especially frequent in young females, to what is known as essential anæmia in its non-pernicious variety.

The term chlorosis is especially applied to the aggravated form of this in women, and it is a good one, and worthy of retention on all accounts. I suppose the ordinary conception of chlorosis is that of a case of severe anæmia in a young woman accompanied by amenorrhœa. The relation of the latter to the anæmic state has been interpreted in two ways; first, that the amenorrhœa is the cause of the anæmia; and secondly, that the amenorrhœa is the consequence of the anæmia. With the latter view I am disposed to agree. Menstrual disturbance is common, and chiefly in the direction of scanty and pale flow, the latter being perhaps as often met with as total cessation of menstrual effort. Of course, I exclude cases where menorrhagia is the cause of a truly hæmorrhagic and non-essential anæmia.

It is a matter of fairly common belief that chlorotic women are especially liable to gastric ulcer, and to the worst accident of such a lesion, namely, perforation; and in this belief I share.

The association of menstrual derangement, itself the result of the anæmia, with gastric ulcer, is too obvious to escape recognition, and there is no other disorder so frequently associated. The ulcer itself, once formed, probably suffers from nutritional defect by reason of the impoverished state of the blood, which prevents the formation of resisting tissue around it. The risk attending gastric ulcer in an anæmic female is certainly great. Amongst other evils and dangers

[1] Read in the Section of Medicine at the Annual Meeting of the British Medical Association at Brighton.