

THE ETIOLOGY
of
MALARIAL FEVERS
A
THESIS

for the Degree of M.D. EDIN.

by

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*Submitted with *
J.M.C.*

Plate I.

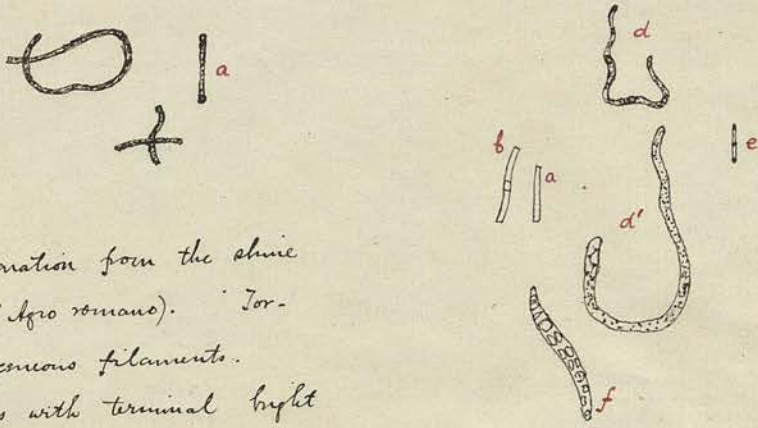


Fig. 1. Preparation from the slime of *Capsulace* (*Agro romano*). Irregular homogeneous filaments. a, a bacillus with terminal bright granules.

(Arch. f. Pathol. u. Pharm. Bd. 81.)

Fig. 2. Same preparation. a, homogeneous bacillus. b, homogeneous filament with transverse division. d, filament containing several bright granules, d', same filament two hours later. e, small bacillus with median & terminal granules. f, fusiform cell not in series. (36.)

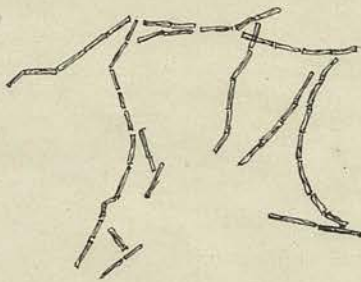


Fig. 3. Same preparation, two days later. Homogeneous articulated protoplasmic filaments. (loc. cit.)

Plate III.



Fig. 1. The parasite in first stage of development; - from blood of spleen. (Article by Dr. Laveran.) (Journal d'Hygiène, Ann. 257, Août, 1881.)

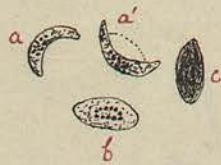


Fig. 2. The parasite in first stage of development. a, a', elongated form with median pigmentation. b, oval form; c, same after osmic acid. (Same article.)

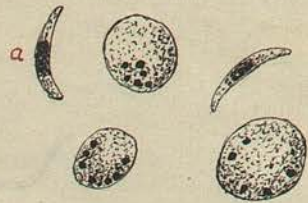


Fig. 3. The parasite in first stage. (Same article.)

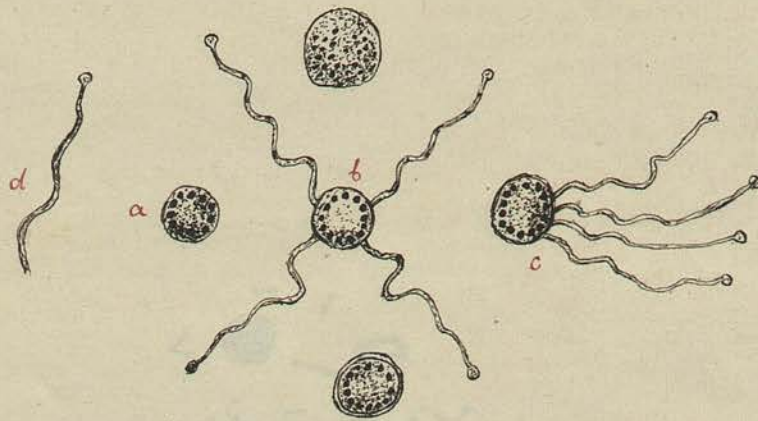


Fig. 4. a, parasite in second stage of development, motionless. b, same with movable filaments. c, same, showing organism in motion. d, a free filament. (Same article.)

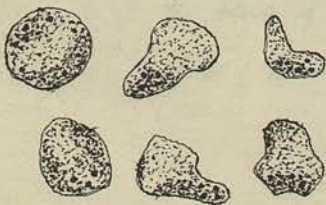


Fig. 5. The parasite in its third stage of development, organisms more or less deformed. (Same article.)

The Etiology of Malarial Fevers.

Within the last two years the subject of malarial fevers has attracted more than usual attention not only on the Continent and in America, but also in this country. The increased interest has been due to a further development of the hitherto unconfirmed question as to the immediate cause of such fevers and to more exact and comprehensive investigations into the nature of their specific poison.

In view of the recent experiments of Professors Klebs and Tommasi-Bondeli I wish in the following paper to trace the history of the researches into the nature of the malarial poison, to endeavour to verify from chemical investigation the accuracy of such researches, and to throw some light, from an examination of the blood, on some of the graver symptoms of pernicious ague.

The views that malarial fever is due to the influence of cold on the system, a view brought forward by some observers, or to some peculiar, probably electrical, conditions, of the atmosphere, a view held by others, need only to be mentioned to be at once rejected. There can be no doubt that the disease is caused by a specific poison, a statement proved when we consider the nature of the disease, its restriction to certain limited districts, and the fact that the only remedies which have any influence on the course of the disease are of a specific nature.

The first writer on the subject of intermittent and remittent fevers was an Italian called Lancisci, whose book "*De nocivis paludum effluviis*" was published about 1695. He attributed the cause of malaria to the decomposition of vegetable matters in marshy places and named the disease "Marsh miasm." His view of the origin of the disease held its ground for long, and in part does so still, but from a wider

knowledge of the geographical distribution of the disease it is seen that something more than vegetable decomposition and a marshy soil is necessary to explain the cause. In proof of this it will be well to adduce some of the more important characteristics of the disease.

A very small part of the earth's surface is free from the appearance of malarial fever, and that part, to speak generally, consists of the polar regions, the sea and large lakes, parts of mountain ranges devoid of vegetation, and deserts. Malarial fever appears as an endemic in certain districts, these districts being either of a marshy nature, or if not so, the subsoil is found to contain a quantity of moisture, so that when the sun has dried the hard superficial crust which becomes cracked and fissured, a moist marshy soil is exposed. Still in all districts of such a nature malaria does not necessarily arise. In districts not of a marshy nature but in which malaria appears, it is

known that the subsoil contains a certain quantity of moisture which has been prevented from draining away, either from the low-lying position of the ground or from the compact non-porous nature of the deeper layers of the soil, and which even excessive sun-heat has not been able to dispel. Such a district if exposed for long to excessive heat, so that all moisture is removed, is, for the time being, deprived of the power of giving rise to malaria; but, if protected from the power of the sun by abundance of woods, so that the moisture is not entirely abstracted, its power is still retained. Or, if after complete drying, the soil be exposed even to a single shower of rain, the ground at once asserts its power of developing malaria.

Working in combination with a moist soil for the development of malaria is vegetable decomposition. It is not to be supposed that vegetable decomposition is of itself sufficient to give rise to malaria, a theory which at one time received attention,

for there are many districts in all parts of the world where such continually occurs and where malaria has never developed. Abundance of woods gives rise every where to decomposition from the falling of the leaves, and in malarial districts these by their decomposition will certainly accelerate the appearance of intermittent fever, but removal of the woods aids in rendering the district less diseased, in as much as it allows the full influence of the sun to bear on the soil and thoroughly dry it. Anything which favours the decomposition of plants favours the development of the disease. Sea-water, for instance, overflowing a low-lying coast on which vegetation of any kind is active, seems to be a common source of malaria, and it acts by destroying the fresh-water plants which begin to decay as soon as the sea-water has receded. Similarly, on the banks of rivers which are periodically overflowed there occurs extensive destruction of vegetable matters, and if the overflow be followed by excessive heat decomposition soon sets in. Old beds

of rivers, drained lakes and ponds, deep excavations in a clayey soil give rise to similar results, namely, a soil or subsoil with a certain degree of moisture.

The last source, excavation of the soil, is worthy of special note, for one of the most fruitful sources of malaria is newly turned up soil, especially virgin soil, and this is due to the fact that the malarial poison does not occur in the superficial dry layers of the soil, but in those which are more deeply situated and are moist. In marshy districts in which malarial fevers occur as an endemic, the number of cases increases or decreases according as the conditions for the decomposition of vegetables are favourable or unfavourable.

Thus, though vegetable decomposition and a marshy soil aid in the development of malaria, yet its production is not necessarily connected with the presence of marshes, ponds, rivers or rank vegetation, for it as often occurs in dry arid soil denuded of vegetation.

Further, for the development of malaria there is necessary a certain temperature for it is found that a temperature below 60°F . is sufficient to prevent the outbreak of the disease or arrest its progress. Thus it happens that in cold seasons malarial districts are free from fever.

Lancisci, in describing the nature of malarial fever, called it a marsh miasm, but this name must now be considered somewhat inappropriate. Malaria does not appear in all marshy districts, — for instance, it has never appeared in the bogs of Ireland, — besides it is not necessary that the ground in malarial districts be distinctly marshy; in fact, large watery expanses, popularly called marshes, would be sufficient to prevent the spread of the poison even in malarial regions. It is quite true that marshy districts are the favourite seats of intermittent fevers, yet it is also true that if these districts become covered to a sufficiently high level with water, the spread of the disease is at once arrested.

Malaria is found also in districts quite free from marshy ground, but in such cases the subsoil is of a moist nature or is subject to occasional overflows.

From what I have already said it will be ascertained that when a malarial soil is covered by a sheet of water or an unbroken crust of earth, the poison is inert. This shows clearly that the atmosphere must gain access to the malarial poison before it has the power of developing. This is known to be a very important element in the causation of malarial fevers. If a district in which intermittent fever occurs be covered with good earth, a thing which sometimes happens as a result of earthquakes, then the disease no longer appears in that district. This buried malarial bed is perfectly harmless, even if it remains moist in the warm season of the year, as long as this covering, (what the Italians call "il terreno di colmata") remains sufficiently thick and compact. The

poison soon springs to life if this subsoil is separated from the atmosphere merely by a thin layer of loose earth, or if the covering is destroyed by excavations or clefts. In some of the malarial districts of China it has been found that the disease can be arrested by covering over the poisoned soil by some non-porous material as concrete.

Thus, a moist soil on which decomposition of vegetable matter may or may not be taking place, a high temperature of the atmosphere, not below 60°F ., and a free access of air to the soil, though necessary factors for the production of intermittent fevers, are to be considered only as adjuvants. If all of these three conditions be not present malaria cannot arise.

The nature of the malarial poison is still a matter of question. Judging from the decided peculiarities of malarial regions one might naturally infer that the poison was of a chemical nature

developed from the decomposition of plants. But this idea must be set aside in as much as it fails to explain how the fever arises in districts possessing those conditions of moisture, high temperature and free access of air, and does not arise in districts of an exactly similar nature. Some of the facts relating to the manner in which malarial fevers spread bear more directly on the nature of the poison. The specific gravity of the poison keeps it near the surface of the earth, the poison rising only from two to three yards above the ground. It is not, however, confined to low-lying districts for instances of intermittent fever have occurred at a considerable height, 1600 ft. Persons living in the upper part of a house, or in the higher ground of a valley, may escape when those on a level with the ground become affected. The miasm spreads more rapidly in a horizontal than in a vertical direction, and its onward course is often broken by such obstructions as a group of trees or large stone-

walls. All these facts point to a corpuscular nature of the poison, for it is impossible for a gaseous product of decomposition to diffuse itself in such a manner.

During the last twenty years frequent endeavours have been made to discover a specific germ in malaria. The first investigations on this subject were made by Dr. Salisbury of Ohio in 1866. In a paper published by him (Amer. Journ. of Med. Scin. Jan. 1866) he attributes malaria to the entrance into the system of the cells or spores of a species of Alga of the genus Palmella, to which he gave the name of Gemiasma. He describes four forms and to each he ascribed a distinct fever-producing power, viz. G. rubra, G. alba, G. verdans, and G. protuberans. On examining microscopically the saliva, expectoration and urine of persons living in reputed malarial districts he came to the conclusion that the only object constantly present was the Palmella or "Ague-plant," and he

proved that these spores were not to be found in the excretions of persons living at a higher level or in districts where malaria had not previously existed. The fact that lead him to believe this plant to be the poison of malaria was that two young men became affected with the disease, having slept for one night in a room in the window of which was placed a frame containing some earth in which these plants were growing. The house was situated some distance (5 miles) from any malarial district and no person but those in that room contracted the fever. But it may very properly be objected to such a conclusion that the young men who contracted the fever may have visited unhealthy districts and been exposed independently to the action of the malarial poison; and also that the earth in the frame may have contained other plants than the *Palmella* to which D. Salisbury attributed the essential power. No other American writer has

confirmed these observations, nor has Prof. Salisbury since brought forward more convincing proofs of the correctness of his previous experiments.

A few years later D. Harkness discovered the same species of Alga as that described by D. Salisbury in the excretions of many people who were living in malarial and non-malarial districts, and they have been found by other observers even on the Alps.

Later other investigators have discovered different germs, each of which in turn was believed to be the specific malarial poison. Safford and Barlet described the microzome *Hydrogastrium granulatum*, Archer found one to which he gave the name of *Chytroblastus aeruginosus*, and Burgellini discovered the *Palmogea micrococa*. Prof. Eklund of Stockholm, on examining microscopically the soil of the Isle of Skeppsholm, discovered an organism which he called *Dinophysis hyalina*, and which, he states, after injection into animals produced febrile attacks some-

what periodical. None of these spores has received confirmation from other writers tending to show their connection with malaria, and all have since been found in healthy soil which was moist enough for their development. There is no doubt that they are merely accidental occurrences in the excretions of malarial patients, and in no way connected with the essential poison of the disease.

In 1869 D. Balestra (Archivio di Med. Chirurg. ed Ig. di Roma, An. 1. 1869) described an Alga to which he subsequently gave the name of *A. miasmatica*, believing it to have some connection with the development of malaria. But the proofs which D. Balestra brings forward are far from conclusive. He subjected liquids containing these fungi to the action of sulphate of soda, arsenious acid and sulphate of quinine, and noticed that thereby the growth of the plants was arrested and their structure destroyed. But it has long been known, as Binz proved, that quinine has a poisonous action on a number of organisms which have nothing to do with malaria. He

also for eight hours inhaled from a bottle which contained some marsh-shine in which these plants were growing and became affected with malarial fever. Still this is only one proof of the poisonous action of the plant, and it must be remembered that D. Balista, at the time of his experiments, was living in an unhealthy district, and being engaged in collecting materials for his experiments was much exposed to the influence of the poison.

Again, Griffini collected dew from marshy fields in malarial districts and injected it into dogs and rabbits, but his experiments were far from decisive. The injections raised the temperature of the body, but no characteristic febrile attack was produced, there was no enlargement of the spleen, and examination of the blood revealed no multiplication of these organisms presumed to exist in the dew. The plan of Griffini was followed a few years later (in 1870) by Lanzi and Ferrigi and with more success (*Il miasma vegetale o malarico ed il clima di Roma.*) In the dew which they injected they discovered a germ to which they gave the name of *Bacteridium brunneum*, and

on making autopsies on some of the animals which had died after the injections they found black pigment in the spleen, liver and blood. These observers have since confessed themselves in error, and state that the *Bacteridium brun-nemum* is nothing more than the particles of pigment found in the blood of malarial patients.

The most recent investigations on this subject are those of Prof. Tommasi-Bondelli of Rome and Prof. Klebs of Prague which were first published towards the end of 1879 (*Studien über die Ursachen des Wechselfiebers u. der Malaria, Arch. f. Exper. Pathol. u. Pharmac. Bd. XI.*) and which tend to prove that the special cause of malarial disease is a low vegetable organism.

I wish to bestow a more minute consideration on the investigations of Profs. Klebs and Bondelli as they seem to prove with a high degree of probability the existence of a specific malarial poison, — or, as they themselves assert, — It is possible to reproduce malarial infection in every form in rabbits in which it is known in man, and that the malaria produced artificially

in animals is generated by organisms existing in the malarial soil at the time when the outbreak of the fever has not yet taken place. After a careful study of the characteristics of intermittent fevers and of the previous investigations on the subject, Profs. Klebs and Bonelli, before the commencement of their experiments, seem to have decided for themselves that there was a special poison to be discovered and that it was of a corpuscular nature. They first made watery extracts from the marshy soil or slime of the Pontine Marshes. These they injected into rabbits and produced in them a disease similar in all its features to intermittent fever, and the animals, on examination after death, presented pathological appearances characteristic of that disease.

Before entering on an examination of the experiments of Profs. Klebs and Bonelli, it will be well to consider what are to be recognised as the characteristic signs and symptoms of malarial fevers, so

that we may be able to estimate how far the experiments tend to show that the experimental malaria corresponds with the fever as it occurs in man.

The two most distinctive characters of the disease are the regular intermittency of the febrile attacks, and the enlargement of the spleen occurring independently of any inflammatory process. There are two other signs, believed by some to be pathognomonic of malaria, and which I will merely mention for the present, viz., the preservation of the body weight during the febrile attack, and the occurrence of particles of pigment in the spleen and marrow of bones and sometimes also in the blood.

The first of these characteristics of malaria is the regular intermittency of the febrile attacks; but it is not a constant feature in malarial fevers. It is a well-known fact that instances of intermittent fever occur where the intermittency is quite absent, and the fever assumes either a somewhat continuous type or is irregularly remittent. A malarial fever of a continuous type, *Febris intermittens continua vel subcontinua*, often resembles ty-

plus fever, and has a somewhat peculiar course. As a rule such a case begins with a high temperature, preceded by a slight rigor, a headache, or merely a feeling of malaise, or there may be no initial stage whatever. The patient feels warm and oppressed, suffers occasionally from headache. The temperature may remain high for a few days liable to an occasional slight decrease, sometimes the body is moist, but is seldom covered with profuse perspiration. Gradually the headache disappears, there is still no sign of periodicity in any of the symptoms, until after a few days there may be a fall of the temperature. Again there is a sudden access of fever, this time of shorter duration, when the temperature again falls. This may occur several times, the patient becoming weaker and thinner, until the fever assumes a distinctly intermittent type.

A very good instance of this type of malarial fever came under my notice in the Royal Southern Hospital, Liverpool, and the temperature charts of the case I have annexed to this paper. It is the case of C. C.,

a Swedish sailor, who was admitted to the hospital suffering from chronic eczema. His history states that he was first affected with intermittent fever nine years previously while living on the west coast of South America, and had had no recurrence of the febrile attacks since that time. During the first fortnight of his residence in hospital he showed no symptoms of ague, when one evening he had a slight rigor accompanied by nausea, and his temperature gradually rose until, on the following afternoon, it stood at $104.6^{\circ}F$. For the following three days the temperature remained almost continually high with only very slight irregular remissions, the patient suffering at first from headache, and having occasional slight perspirations; there was no delirium. On the morning of the fifth day the temperature had fallen to 101.2 , and for the next eight days there was a daily occurrence of fever, but without any appearance of rigors or initial symptoms of ague attacks, the patient being quite free from headache, and perspiring at irregular intervals. The rise of temperature

reached its height at a later period each day, gradually postponing but in a very irregular manner, the attack assuming the character of a quotidian remittent fever. On the 14th day from the rigor there was no indication of febrile attack and the patient became convalescent.

Another irregularity in malarial fevers is the pernicious form, but this form does not differ so much from the simple form of the disease as the continuous form, in as much as the pernicious paroxysm is generally preceded by one or two paroxysms showing regular intermittency. It is certainly the most dangerous form of malarial fevers, head symptoms being the most prominent feature, evidenced by coma or delirium. I shall best illustrate this form by referring to the case of O. L., a patient in the Royal Southern Hospital, Liverpool. He was a sailor and contracted the disease in Savannah, North America. On admission to hospital, one month after his first attack, the patient was very anaemic, felt

very weak and complained of pain in the joints in walking; the temperature standing at 101.4. The same evening he became somewhat stupid and confused, and at midnight was quite comatose, perspiring profusely, the pulse being strong and regular. Exactly 12 hours after admission the temperature had fallen to normal, but soon commenced to rise, remaining between 101 and 102 for the next two days. During that time the patient had been quite unconscious, not roused by any stimulus, and only recovered consciousness on the third day after admission, the temperature having fallen to 99.4. For the next two days, though conscious and answering questions when roused, he remained in a sleepy drowsy state, the temperature keeping a little above normal. He recovered completely, the disease ending immediately in convalescence. There were no subsequent attacks of fever, but the patient was extremely weak for some time. It is interesting to note that in this case the action of emiprasins and blis-

ters was very much delayed, for after an application of mustard for 24 hours to the calves of the legs there was not even reddening, but subsequently the skin sloughed where the emipism had been applied. I append the temperature chart of the case, and that also of a very similar case which I need not relate in detail.

These varieties of malarial fever require to be noted when experiments are made on animals with a view to ascertain what the malarial poison is, for we must not expect to find every case of ague, even when produced artificially, to be of a regularly intermittent type.

The second characteristic of malarial fevers is the splenic enlargement. Many acute diseases are accompanied by swelling of the spleen, - and especially septicaemia - but in such cases the characters are very different from those which occur in ague. The spleen, on examination after death from septicaemia, is found enlarged, the edges and corners rounded, and the substance

soft and friable, a condition very different from the ague-cake, which exactly resembles the healthy spleen except that it is uniformly enlarged in every direction and the substance is harder. In the spleen of ague there is no rounding of the edges or corners, and the surface of section is usually of a slate grey colour, facts which serve to distinguish it from any other form of splenic enlargement. In amyloid disease, if the whole spleen is affected with that form of degeneration, the organ assumes a form which is nearest in appearance to the ague-cake, but the anterior border is more rounded, and the surface of section is quite different in colour.

Another important point in the diagnosis of malarial fevers, one which by some is considered pathognomonic, is the occurrence in the spleen and marrow of bones and sometimes also in the blood of black pigment particles. These are found not only in the pernicious form but also in the simple forms of the disease when of long duration. The first who drew attention to the

presence of pigment in the blood was Meckel, in cases of melanaemia. The particles occur in the form of black scales or granules or of irregular, somewhat angular, fragments, and the scales not infrequently assume exactly the shape of discoid red-blood corpuscles, as has been shown by Dr. Marchiafava (*Commentario clinico di Pisa, Gennaio, 1879*). The same writer has found these particles in the marrow of the bones of a child three years old, which died from ague, from three to four hours after death; Prof. Klets and Bondeli have observed them under similar circumstances; and I have seen them in blood taken from patients suffering from intermittent fever; so that these bodies cannot be considered as post mortem products. They more probably result, during the febrile attack, from the decomposition of the haemoglobin. The pigment certainly contains iron from the blue colour which arises by the action of hydrochloric acid and ferrocyanide of potassium.

The fourth important diagnostic point, one upon which Drs Klebs and Bondelet lay great stress, is the fact that the weight of the body is not diminished during the febrile attack in spite of the high temperature, and it is only after the fever has lasted for some time that there is any decrease in weight. This certainly distinguishes ague from other acute febrile diseases, for in the latter the body-weight diminishes from the commencement of the attack.

These signs, the intermittency of the fever, the characteristic enlargement of the spleen, the preservation of the body-weight, and the presence of pigment in the blood and tissues, are to be recognised as sufficiently pathognomonic of the disease, and it will be necessary in the experimental production of the disease to produce similar characteristics.

I will now return to the investigations of Profs. Klebs and Bondelet. Their aim was to endeavour to discover what was the nature of the malarial poison,

for their previous studies on the subject had led them to believe, first, that the poison was of a corpuscular nature, and secondly, that it was to be looked for in the soil of affected districts. They made watery extracts of soil obtained from different parts of malarial districts in and about Rome, and these on examination microscopically were found to contain numerous organisms, Diatomaceae, Desmidiaceae, Hyphomycetes, micrococci and bacteria. It soon came to be noticed that, though the variety of organisms in each extract was very great, some species were absent in one that were present in another, but that there was universally to be found in the extracts one special form, or rather series of forms, of segmented fungi, which evidently belonged to the genus *Bacillus*.

Experiments were also made with the air overlying malarial soil, and this same genus was discovered. The air was drawn up through a specially constructed ventilator so that the corpuscular elements of the air

were obtained on a glass plate covered with a mixture of glycerine and isinglass, and when the specimen was examined there was found, in addition to the coal-dust, threads of wool and linen, and various organisms, round and rod-shaped, the Bacillus in its different forms as obtained from the watery extracts of the soil.

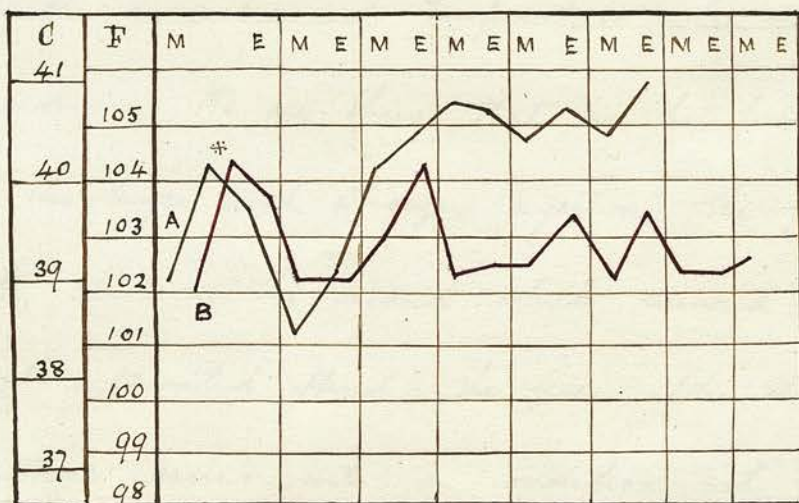
With a view to obtain the Bacillus in an isolated form, a thin layer of earth from malarial soil, in which it had been already demonstrated that the organisms were present, was placed in a porcelain air-bath, which was kept heated by gas. This was kept at a regular temperature and water was from time to time supplied, so that the conditions of moisture and temperature necessary for the outbreak of malaria were exactly imitated. As a result of this it was noticed that first the Diatoms died, that the Hyphomycetes developed no further, and that there was no clonidium or mould-formation on the surface. The microscope also

showed that the different forms of the Bacillus developed to a great preponderance over all other organisms. Prof. Klebs then applied a method which he had already successfully used for the isolation of numerous pathological organisms, that of fractional cultivation, "fractionirte cultur." A single drop was taken from the fluid obtained after destruction of most of the organisms and put into a pabulum, and only those organisms developed which found this a suitable medium. From this another drop was taken and put into fresh pabulum, until, by a repetition of this process the Bacillus was obtained in isolation.

Having thus obtained the organisms isolated in a pabulum Prof. Klebs and Landeli next endeavoured to establish the connection between the Bacillus and intermittent fever by experiments on animals.

The experimental investigations of Prof. Klebs and Landeli were all made on rabbits. First two healthy rabbits were killed by strangulation in order to determine

exactly the normal size of the spleen. The normal temperature of the rectum was next determined as 39.5°C (103°F). Following this two other rabbits were taken and into one of them was injected subcutaneously a syringe^A (Prava's syringe, containing 1.5 cc.) of water which had rested for three days in a thin layer over the shine on the bank of Lake Kaprolace; and into the second the third part of a syringe^B (0.6 cc.) of one of the prepared liquid cultivations from the shine of the same lake. In both animals fever of a distinctly intermittent character appeared, as may be seen from the accompanying temperature-charts:—



Temp. four hours after injection.

In both the temperature rose within four hours of the injection. In the first after a normal, or rather subnormal, temperature on the second day, the temperature rose slightly on the third day and on the evening of the fourth there was a rapid rise, and the temperature remained high for the following three days when the animal was killed. In the second animal, after a rise of temperature on the day of injection there was no fever on the second and then a rise of temperature on the third day, and from the fifth to the seventh there was only a slight rise with daily remissions, on the eighth a normal and on the ninth a subnormal temperature when the observations ceased. We see thus that in the first case, which received the larger and stronger injection, the fever became continual, and in the second, which received a small injection of cultivated fluid, the fever after the second rise of temperature passed into a condition not far from health. The post mortem examinations of these two

animals also give important results. In both there was an absence of pus at the seat of injection, the spleen was enlarged to about three times the normal size, and organisms, similar to those in the fluids which were injected, were found at the seat of injection and in the spleen and lymphatic glands. At the point of injection filaments containing spores were found, but in the internal organs spores alone were seen, and these on cultivation developed within 24 hours into filaments containing spores. There was no decrease in the weight of either animal.

A third rabbit, into which an injection containing the organisms collected from the air over malarial ground and cultivated in urine, developed fever of a quartan type passing into the quotidian form and revealed on post mortem examination all the characteristics of intermittent fever.

From these three experiments it is at once seen that the injection of fluids containing these organisms

obtained from the malarial slime or from the air overlying it, were followed by febrile attacks of an intermittent character, and having made certain that the rise in temperature was not due to any inflammatory process, as was shown on post mortem examination, it is reasonable to conclude that these organisms were the essential cause of the fever. In the first rabbit it is seen that an injection from a thin layer of water lying on malarial slime produced an intermittent febrile attack: an injection was then made with water from a lake (Capros-lake), the bottom of which was shown to be rich in malarial poison, and no fever was produced. A double injection was then made with the water of the lake into the same rabbit, but there followed merely a single but well-marked rise in temperature, which gradually sank to the normal standard. From this we may draw a very important conclusion, viz., that water resting on slime which is rich in malarial poison does not contain the poison.

The watery extracts, or the natural fluids themselves, which were used for experimental purposes, were obtained in different places where malaria was known to exist, and it was found that equal quantities of different specimens acted with different strength, that is to say, the poison was more abundant in some malarial districts than in others. This fact, after an investigation had been made into the exact constitution of the soil from which each specimen was obtained, led Profs. Klebs and Grassmann to form the conclusion that a soil suited for the development of malaria loses this property the more copiously it is permeated by the natural effluvia of man and beast, or the more carefully it is cultivated and manured; and that methodical cultivation of the soil, even in districts notoriously unhealthy, produces a decrease in the production of malaria.

In the experiments on animals the form of intermittent fever produced varied greatly. Thus a simple tertian might result and continue as such, or the fever

might commence as a quartan and pass into a quotidian; but it is to be noticed that the poison in all is the same. It is possible that the form which the fever assumes depends to a great extent upon the amount of poison which the system receives at the time of infection.

In order to prove more thoroughly that the results obtained from the injection of extracts known to contain these organisms were not merely accidental occurrences, Prof. Klebs made an infusion from the garden-soil of the pathological laboratory of Prague, a district which is not malarial, and injected it into rabbits. In some the injection produced a temporary febrile state which soon passed off, while in two symptoms of septic poisoning appeared from which both rabbits died. Post mortem examination of the two last revealed pus in different parts, and entire absence of pigmentation of the spleen or tissues; but there was enlargement of the spleen. The splenic enlargement, however, was different from that occurring in malaria, the substance being quite soft

and friable and the normal configuration destroyed.

Having given all these experiments a careful study one feels compelled to conclude that Profs. Klebs and Tomdali have succeeded in demonstrating the presence of an organism in malaria, and in proving that it is the essential cause of the disease. While all who have studied the condition of the blood in most febrile diseases admit the frequent presence of bacteria, the difficulty has been to assign to these organisms their pathological importance. Before the germ theory of a disease is established it is necessary to prove, first, direct observation of organisms in the blood or tissues of those subject to a special disease; secondly, that those organisms are always found in that disease, and are not found when the disease does not exist; and thirdly, that inoculation of these organisms produces the same disease in other persons. In regard to the *Bacillus Malariae* Profs. Klebs and Tomdali have, I believe, fulfilled these conditions.

I will now give a description of the life-history of the *Bacillus Malariae*. The most simple forms of the *Bacillus* arise from homogeneous filaments, often tortuous or twisted, which, when cultivated in isinglass, albumen or urine, divide into segments and produce spores in their interior both before and after division. The segments are called "Dauersporin" by Klebs; and the position of the spores in the segments varies. Sometimes they are found at the ends of the segments, sometimes there is only one spore in the centre, and sometimes there are both terminal and median spores. Some of the cultivations demonstrate extremely well the filamentous development of these spores when they have become free. The spores when liberated are oval in shape and have a high refractive power. One of the ends of these capsules elongates and forms a filament, which separates itself and soon becomes converted into a rod-shaped bacterium—a deanso-bacterium or bacillus. A reference to the series of drawings given in the article by Profs. Klebs and Cru-

deli, and a copy of which I have made in Plate I., will best elucidate the characters of the organism. The first figure shows filaments, homogeneous, tortuous in shape, found in the cultivation of the skin of Caprolace (Agro romano) and prepared in gelatine. Among the filaments is seen a bacillus inclosing a bright granule at each end. At a later period the same cultivation showed a homogeneous bacillus without indication of division, one with a transverse division; a filament containing several bright granules which, two hours after, had greatly increased in size, and a small bacillus with one median and two terminal granules. The fusiform cell does not belong to the series of developing fungi. In this same cultivation, two days after its preparation, were seen articulated filaments of homogeneous protoplasm. In the fourth figure is seen the Bacillus as it is found in the spleen of those suffering from intermittent fever, and in fig. 5 as it exists in the blood of the veins of similar patients

before the febrile attack is at its height. The last drawing represents the Bacillus as it is almost always observed in the blood of malarial patients during the cold stage (with a power of 750 diameters.) Prof. Cordeli adds that this last figure, where the filaments are so much less in diameter than that of the spores contained in the filaments, represents the first stage of the breaking up of the Bacillus, which leads later, in the warm stage, to the complete liberation of the spores in the blood.

Since the publication of the results of the researches of Profs. Allet and Cordeli the subject has engaged the attention of other observers, and it will be well to turn to their views for a short time to see how far they agree in confirming or refuting the investigations made at Rome.

In April 1881 D. Burdel of Virzon read a paper on the Etiology of Malarial Affections before the Academy of Medicine, which has been published in the official journal of the Academy. He states that, since the publication of the

results of Profs. Klebs and Cordeli, he has made investi-
 gations into the nature of malaria, and opposes very strongly
 the parasitic origin of the disease. At the end of the paper
 he says, " Je termine en rappelant qu'il y a longtemps que j'ai
 signalé ce fait, que j'ai été heureux de voir être confir-
 mé et appuyé par mon savant confrère le prof. Vermeil,
 c'est qu'en tous lieux ou tous pays, mais plus souvent
 cependant dans les régions où les conditions telluriques do-
 minent, qu'elle que soit la saison et l'époque d'année, on
 voit les pertes abondantes de sang, les grands traumatismes
 chirurgicaux et accidentels, tout ce qui enfin apporte un
 ébranlement considérable dans le système nerveux de la
 vie organique, produire des accès de fièvre intermittente les
 mêmes caractérisés, tributaires de la quinine, et très fré-
 quemment aussi des accès de perniciosité les plus redou-
 tables. Et alors, quel est donc le rôle des algues et des
 schyzomycètes bacillés que l'on ne rencontre que dans l'eau et
 la boue des lacs? " It is thus seen that D. Cordeli falls back
 for an explanation of malaria on the condition of the ground

and on that alone, for he also says "..... j'ai acquis la conviction que le sol plus ou moins humide, mais réchauffé par l'ardeur des rayons solaires, était le seul et unique foyer d'où naît la cause simple ou complexe à laquelle, depuis des siècles, on a donné le nom de Malaria." Dr. Burdel repeated the experiments of Profs. Klebs and Boudeli but was unable to decide that any special microzyme was universally present in malaria, and that numerous organisms were invariably found. He injected watery extracts of malarial soil into himself and a friend without producing the slightest febrile movement. He points out also that in his experiments on rabbits the rise and fall of temperature after injection of extracts from malarial soil were in no way regular or intermittent. In this last statement Dr. Burdel fails to recognise that intermittency is not a constant sign of malarial fevers, for it is often wanting in the graver forms of the disease (perniciosa ague.) Dr. Burdel, it seems to me, brings forward no direct proof of the non-existence of a specific Bacillus Malarial, and the conclusions which he draws are not al-

ways logical. His investigations and their result would rather indicate that the experimental inquiry into this subject is one of great difficulty.

A second series of experiments, also in part adverse to the views of Profs. Klebs and Gendeli, has been made by Dr. George Sternberg at the request of the National Board of Health of Washington. Dr. Sternberg conducted his experiments on a marshy ground in the neighbourhood of New Orleans. On examining the soil of malarial districts and the air in its proximity he found numerous algae and bacteria, and among the latter certain which had an almost perfect resemblance to the *Bacillus Malariae* of Klebs and Gendeli. Adopting the method of Klebs in isolating these organisms, he subsequently injected the solution containing them under the skin of rabbits and produced febrile attacks, but, he adds, he has not yet proved that the resulting fever was analogous to intermittent fever as it occurs in man. The conclusion which Dr. Sternberg comes to as a result of his in-

investigations is that the etiology of marsh fevers has certain direct or indirect relations with the presence of proto-organisms or their germs in the air or water of malarial districts. Such a decision, from one who is in a position to study the subject with many facilities, is very important and goes far to corroborate the views of Klebs and Grudeli. It would be absurd to expect that observers in all parts of the world would produce exactly similar results; for this purpose the different observers must be in precisely similar conditions.

Another recent paper on the question of the malarial poison comes from the pen of D. Laveran. In the majority of the cases investigated by M. Laveran the disease had been contracted in different parts of Algeria and Tunis. As a result of his studies he comes to the conclusion that malaria is a parasitic disease; but still he differs from Prof. Klebs and Grudeli as to the characters of the specific organism. His views may be

shortly summarised as follows:- In the blood of those
 subject to malaria are found pigmented parasitic ele-
 ments which present three principal forms. These pa-
 rasitic elements of the blood in their three forms pro-
 bably represent only three phases in the development
 of one and the same parasite, living in a state
 of encystment for a part of its existence. These pig-
 mented parasites are found in the blood of those only
 who are suffering from intermittent fever, and disap-
 pear on administration to the patient of sulphate of
 quinine. They are of the same nature as the pig-
 mented bodies so abundant in the vessels of all or-
 gans of those who have died of pernicious ague, and
 which have been hitherto described as pigmented leuco-
 cytes, "leucocytes mélanifères." Dr. Laveran gives elaborate
 drawings of the organism in its three stages of develop-
 ment. In its first stage it has the appearance of a
 white blood corpuscle, but rather less in size (about $\frac{1}{3000}$ in)

enclosing a few dark brown pigment particles; or it is semilunar in shape, tapering at the ends, and on the concave side a fine line is sometimes to be traced uniting the extremities of the crescent; the pigmentation in the latter form is confined to the centre. Some of these bodies as taken from the spleen are represented in Fig. I. of Pl. 3. In its second stage of development the parasite is round and the pigment particles are arranged regularly near the surface. It is furnished also with four filaments, about three or four times the length of the organism, and these filaments, each provided with a terminal swelling, possess motion and have also the power of changing their point of attachment to the parent organism. As long as the body is at rest the pigment granules retain their regular arrangement, but sometimes they seem to move about freely within the organism and then lose all regularity in arrangement. M. Laveran believes the parasite in its second stage to

be a form of animalcule which exists at first in an encysted stage and then becomes free with moving filaments. (vid. fig. 4 Pl. 3.) Lastly the parasites lose their filaments, their regular shape, and the symmetrical arrangement of pigment, and appear very much as they are described in their first stage of development.

The description of the organism as given by D-Laveran with great minuteness, and on close examination it will, I think, be found to agree in part with the investigations of Klebs and Bonelli. First, in regard to the pigment particles, it has been long known that they are not parasites and are produced by the gradual deoxidation of the red blood corpuscles. The particles, as I mentioned before, when treated by ferrocyanide of potassium and hydrochloric acid, become blue, for they contain a part of the iron of the haemoglobin, a fact traced by Klebs and Bonelli in their first paper (*Sulla natura della Malaria*). Speaking of this black pigment in the blood D. Jannasi-Bonelli

writes that its production is an effect of the action of the malarial ferment; that its appearance is very probably due to the great activity displayed by that ferment for the oxygen existing in the red blood corpuscles; and that of all vegetable parasites hitherto known that called the *Bacillus Malariae* is the one which shows the greatest avidity for oxygen.

D. Laveran was not the first to suppose these pigment particles to be the specific organisms of malaria, for, as I mentioned before, Dr. Lanzi and Terrigi previously described them under the name of *Bacteridium brunnescens*. Again, the filaments observed by M. Laveran are very probably the filaments of the *Bacillus Malariae*, which are sometimes to be seen surrounding the blood corpuscles. One hesitates greatly before accepting all the details of M. Laveran's description. The symmetrical arrangement of the pigment granules, and the peculiarly adaptive powers of the filaments, are questions of extreme doubt. Such appearances I have never seen, nor have I read of others having done so; but one frequently

observers in the blood of patients suffering from ague large irregular granular corpuscles containing particles of pigment, and also homogeneous filaments lying between and round the corpuscles. There is no doubt that M. Lavesan has had the *Bacillus Malariae* under examination, and his observations will with some modification strengthen the views of Profs. Klebs and Gendeli.

More direct confirmation of the results of Klebs and Gendeli has been given by the recent researches of Dr. Marchiafava and Buboni. Their work has been of an entirely clinical nature. They found that on examining the blood of persons during the cold stage of the fever, with a power of from 600 to 700 diameters, the parasites figured in the drawings I have already given (vid. Pl. III) were seen. And they add that if the blood is examined in the warm stage of the fever, the rod-shaped bacteria being destroyed, we see only the spores, and that these might easily be confounded with the numerous forms of micrococcus to be found in the blood even in a

state of health. Dr. Marchiafava has been able to demonstrate the spores and Bacilli in the spleen, the marrow of bones, and the blood of three persons who died of pernicious ague, showing the same characters as those observed by Prof. Klebs and Conrad. Dr. Sciamanna also, by a method which he uses for extracting blood directly from the spleen without any injury to the patient, has proved that in the blood of the spleen the spores of the Bacillus Malariae are constantly found during the acme of the fever, and cultivation of these spores always gives rise to the developed Bacillus, sometimes in very large quantities.

I will now put together en resumé the leading facts of the investigations into the nature of malaria.

In the soil, and the air overlying the soil, of malarial districts in and about Rome a distinct organism, the Bacillus malariae, is universally found; this organism is never seen in healthy soil, or in any district where it is known malaria does not exist; the Bacillus Malaria has been found and

described by numerous independent observers; when fluids containing these organisms, obtained either directly from the soil itself or the air over it, or prepared by cultivation, are injected into rabbits, febrile attacks distinctly intermittent are always produced; rabbits into which are injected fluids, which do not contain the *Bacillus Malariae*, may develop febrile attacks which are, however, only of a slight nature, are not intermittent in character, and are due to the operation of injection; post mortem examination of the rabbits which developed malarial fever revealed all the characteristics of malaria in the spleen and blood; the *Bacillus Malariae* has been found in the spleens of persons who have died from pernicious ague, and on cultivation showed the same characters as the *Bacillus* found in the soil of malarial districts. It is thus evident that there is a high probability of the connection between the organism which has been called the *Bacillus Malariae* and the development of intermittent fever, for the investigations conform to all the conditions necessary for the establishment of the germ theory of a disease.

First, the *Bacillus malarialis* has been observed in the blood and tissues of individuals suffering from malarial fever; secondly, it has always been found when that disease existed (at least when produced artificially) and is not found in the absence of the disease; and thirdly, its injection into animals produces intermittent fever.

The accuracy of these facts relating to intermittent and remittent fevers can also be determined clinically, and I will now record some observations I have made on patients who came under my notice. The cases of ague which I have had the opportunity of examining were sailors who had contracted the disease in North or South America or in Africa. As a rule before their arrival in England quinine had been administered to them in varying doses on board ship, but it frequently happens that sailors arrive in port suffering from malarial fever, both in the simple and pernicious forms, who have had no treatment whatever.

On examining the blood of persons who are suffering

from malarial fever for the first time, and only in a mild form, I find that in the period of intermission the blood contains nothing worthy of notice, it presents the characters of healthy blood. Should the person, however, have been subject to the disease for many months, or be suffering from the disease in its worst or pernicious form, a change is readily seen in the blood. The red blood corpuscles are markedly diminished in number, the blood presenting the characters of the blood in anaemia, and particles of pigment, varying in size from small granules to about $\frac{1}{2000}$ th of an inch, are frequently seen. If the blood be examined at the commencement of the cold stage, the period of invasion, then there is universally to be found the specific germ, the *Bacillus Malariae*, as it is represented in the diagrams I have already given. A drop of blood, removed from the finger of the patient and examined under the microscope with a power not under X700, shows the *Bacillus*,

of different sizes, and consisting of short rods articulated together or occurring singly, and containing bright granules at their ends, the diameter of the granules being slightly greater than the breadth of the filaments. These organisms are to be seen moving about freely, dipping down in the thin layer of blood so as to be lost sight of for a time and again appearing. An individual Bacillus is seldom larger than the breadth of a red blood corpuscle. As a rule the size varies from a $\frac{1}{4}$ to the breadth of one red blood corpuscle, from $\frac{1}{12000}$ in. to $\frac{1}{3000}$ in. (0.002 mm — 0.007 mm.)

When the blood from the same patient is examined a second time, but towards the end of the cold stage, the organisms are still to be seen, but their form is somewhat altered. The terminal granules or spores of the Bacillus are still of the same size and high refracting power, but the connecting filaments are extremely small. Even at this time the germs are

still active and move freely about in the field.

During the hot stage a change occurs. On examination of a drop of blood the Bacilli are no longer to be seen, in fact as bacilli they do not exist. A careful exploration of the field will reveal a number of bright granules which are probably the spores of the Bacillus liberated by the disappearance of the fine connecting filaments. It is an extremely difficult question to decide that the objects under observation are really the terminal granules of the Bacilli as seen in the cold stage, for the blood even in a state of health, and certainly in all acute diseases, frequently contains similar bodies.

An examination of the blood in the sweating stage reveals nothing more than a diminution in the number of those bright granular bodies, a fact which of itself points to the certainty of many of the granules being the liberated spores of the Bacillus. Examination of

the secretions and excretions gives on the whole unsatisfactory results. The saliva and perspiration contain so many corpuscular elements that I have never been able to determine the presence of the Bacillus in any of its stages in them. The urine, however, on microscopic examination is found to contain bodies, similar in character to the liberated spores, but the examination of that fluid, even after its concentration, requires so great a time, that the fact of the spores not being found in any particular case I should consider no proof of their non-existence in that secretion.

Such are the facts that can be made out in regard to the life history of the Bacillus Malarial from a study of the blood of those suffering from intermittent and remittent fevers, and I will now give in detail a few of the cases which I have studied with a description of the blood at each time of examination.

I. A. M., a sailor, aet. 22, six weeks before his admission

to hospital, while in Savannah, North America, was first attacked with intermittent fever, the rigors occurring daily for about ten days when they entirely ceased. He then left Savannah, and a fortnight afterwards was re-attacked by the fever, the rigors occurring daily as before, ceasing, however, a few days before his admission to hospital. There was no enlargement of the spleen. On the fifth day after admission the patient had a slight rigor at 5 p.m.; Temp. 102.4.

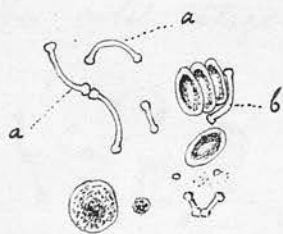


Fig. 1.

The blood was examined at 5 p.m. and the following was observed. (vid. Fig. 1.) The *Bacillus Malariae* was readily seen, a, moving freely about in the field. At b is

seen a *Bacillus* enveloping the blood corpuscles, a condition very similar to that which D. Laveran describes (vide supra pp. 44-45), the individual *Bacillus* here representing the free moving filament with club-shaped end, separated from the parent organism (vid. Pl. III.) The filaments are here

slightly less in diameter than the terminal spores, showing that even at this period, the commencement of a rigor, the organism has considerably advanced in development, or rather retrogression, for Profs. Klebs and Boudeli consider the Bacillus in its perfect form as seen in special cultivations, the body of the organism being of the same size as the terminal spores.

Examination of the blood at 5.30 p.m., the patient still in the cold stage. Bacillus still present and still active.

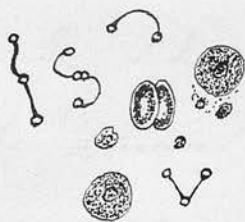


Fig. 2.

The filaments are now extremely thin, the terminal and median spores being of their ordinary size. This

condition is believed to represent the final stage in the life-history of the Bacillus, the filaments becoming gradually smaller until they give way and the spores are set free.

8 p.m., patient in the warm stage; the Bacilli are no longer to be seen; innumerable small round granules, the spores of the Bacillus.

Blood at 11.30 p.m., the patient perspiring; the granular bodies are still present, but less numerous; the blood otherwise normal. The urine which had been passed during the night, when examined next morning with the microscope, showed a small number of small, highly refractive granules, the spores of the *B. Malariae*. This patient had no further attacks of fever, convalescing rapidly under the use of quinine, his blood examined microscopically presenting at all times a perfectly normal appearance.

II. J. J., a sailor, admitted to hospital in an extremely depressed state, answering questions with difficulty; had been attacked with fever for the first time 7 weeks previously, rigors occurring very irregularly, always very slight; present attack was the most severe the patient had had. It was evidently a case of pernicious ague.

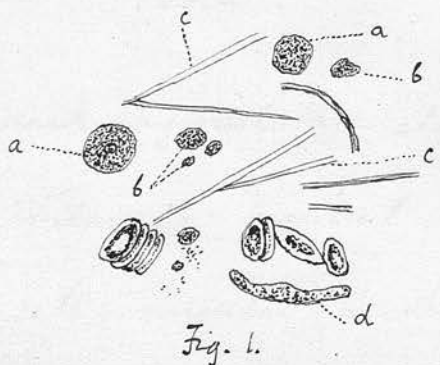


Fig. 1.

Blood examined at 10.30 p.m. T. 100.2.

(a) White corpuscles apparently normal in amount; (b) a number of small granular corpuscles; scattered among

the corpuscles are fine homogeneous, unsegmented filaments (c), the first stage of the developing *Bacillus Malariae*; and a long irregular cell (d) containing bright granules, probably also belonging to the same series, but further advanced.

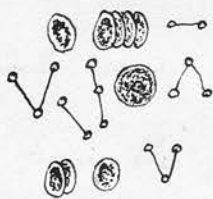


Fig. 2.

Second day; blood examined at 1 p.m., Temp.

103.6. The *Bacillus malariae* seen in great quantity, as represented in Fig. 2;

no movement noticed; filamentous part of the organism very narrow. The filaments connecting the spores are perfectly straight, a position they seem always to assume when the organism is dead.

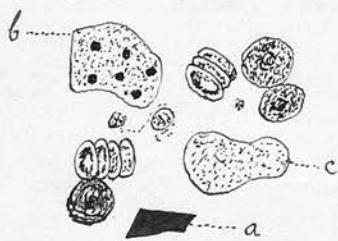


Fig. 3.

Third day; blood examined at 1.30 p.m., Temp. 98.6. White blood corpuscles increased in number; no trace of malarial organisms; a large mass of

dark pigment (a), also a brownish-black granular cell containing pigment granules, and a similar granular cell, irregular in shape and non-pigmented, (b. & c.)

In the first of these two patients, H.M., nothing abnormal is noticed in the blood with the exception of the *Bacillus Malariae* in its later stages of development; but the man had only a very slight attack of fever, and was in a fairly healthy condition otherwise. The second patient was a weak anaemic man who had been suffering from the fever for about two months and had been gradually getting weaker until the pernicious attack occurred. The blood of the latter when first examined showed fine branching filaments, which greatly resemble the earliest stage in the history of the malarial organism as described by Klebs and Conrad. The state of the blood on the third day of the attack (vide Fig. 3) is of great interest. It reveals first large flakes of pigment free in the blood, a condition which is believed by many to be the cause of the serious head symptoms in pernicious ague, the pigment particles becoming fixed in the smaller blood-vessels of the brain and giving rise to local thromboses.

Secondly, there are two large granular cells, one somewhat symmetrically pigmented; similar bodies I have not observed in healthy blood, and only in this case of ague. They correspond almost exactly to the bodies described by M. Laveran as occurring in those suffering from intermittent fever. They are the malarial organisms of M. Laveran in their third or retrogressive stage of development (vid. Pl. III.)

Although it may now be considered a matter of certainty that the *Bacillus Malariae* is the essential cause of intermittent and remittent fevers, there are still many points on the subject of malaria which require elucidation. The questions still to be investigated in regard to malarial fevers are, — In what tissues do the malarial organisms accumulate, — What causes their liberation from these situations, — How do the organisms act on the body to produce the symptoms of ague, — and, How are we to explain the variations in the durations of the intermittencies in this fever.

From the researches of Dr. Sciamanna and Cuboni we learn that, though the blood in the cold stage of ague contains the *Bacillus Malariae*, this organism is found in greatest abundance in the spleen and marrow of bones. These, therefore, would seem to be the chief foci, and it is there also that we find the chief pathological changes in ague. If we set aside the staining of the tissues generally, and the occasional capillary thromboses which occur in ague, as secondary to the condition of the blood, then the only characteristics of ague to be recognised on post mortem examination are the enlargement of the spleen, and a discoloration and slight condensation in the marrow of bones. In the latter situation there is said to be distension of the lymphatic vessels and sometimes annular cirrhosis, tending to become chronic. The clinical fact, also, that necrosis of bone is not an uncommon sequela of ague,

points to the marrow of bones as one of the chief seats of disease in that fever. D. Laveran suggests that the liver also may be a nidus for the malarial poison when latent, on account of the numerous pigment granules to be found in the small blood vessels of the liver after an attack of the fever. In one or other of these situations the *Bacillus Malariae* lodges, and seems to be capable of remaining there in a latent form for an indefinite time. It is well-known that persons may have an attack of ague, although they have had no opportunity of becoming re-infected for as long a period as 20 years; and during that time the organism must have lain dormant in the body. The *Bacillus Malariae* is probably in an encysted form in these different nidi.

What causes the discharge of the *Bacillus* from these nidi is merely matter of conjecture. Persons who

have had ague, and who, after many years of freedom from the disease, again suffer from it without a second exposure to the infection, are usually in a low state of health at the time. Such a person may be suffering from another disease, or have received some injury during the treatment of which he has become much debilitated, when suddenly ague reappears in him. Whether it is that the cyst-wall enclosing the malarial colony suffers with the constitution of the patient, breaks down, and allows the organisms to escape into the blood; or whether the Bacillus is rendered more active at that time from an insufficient supply of oxygen and pierces the cyst-wall, are matters of conjecture.

The variations in intermittency in the attacks of ague may be due to either of two causes, - first, to the quantity of poison received by the system at the time of infection; or secondly, to the nature of the

soil from which the *Bacillus* arises.

As to the mode of action of the malarial organisms on the system Dr. Kundeli suggests that the febrile attack does not take place until the discharge of the parasites from their special nidus has gone on to such an extent as to accumulate in the blood a vast number of these organisms, and that the chills are produced by the simultaneous irritation of the vaso-motor nerves by the organisms (*Practitioner*, Nov. 1880.) The *Bacillus Malariae* finds in the blood all the conditions necessary for its rapid development, a high temperature and nourishment in the form of oxygen in the red-blood corpuscles.

It will be acknowledged that the discovery of the *Bacillus Malariae* is a great acquisition in our knowledge of the causation of malarial fevers, and offers an explanation which corresponds with what is

already known of these fevers. There are still many
gaps in the natural history of malaria, and it merely
requires continued methodical investigation to fill up
those blanks.

John Merritt Chisholm,

M. A. Ed. 1875, M. B., G. M. Ed. 1878.

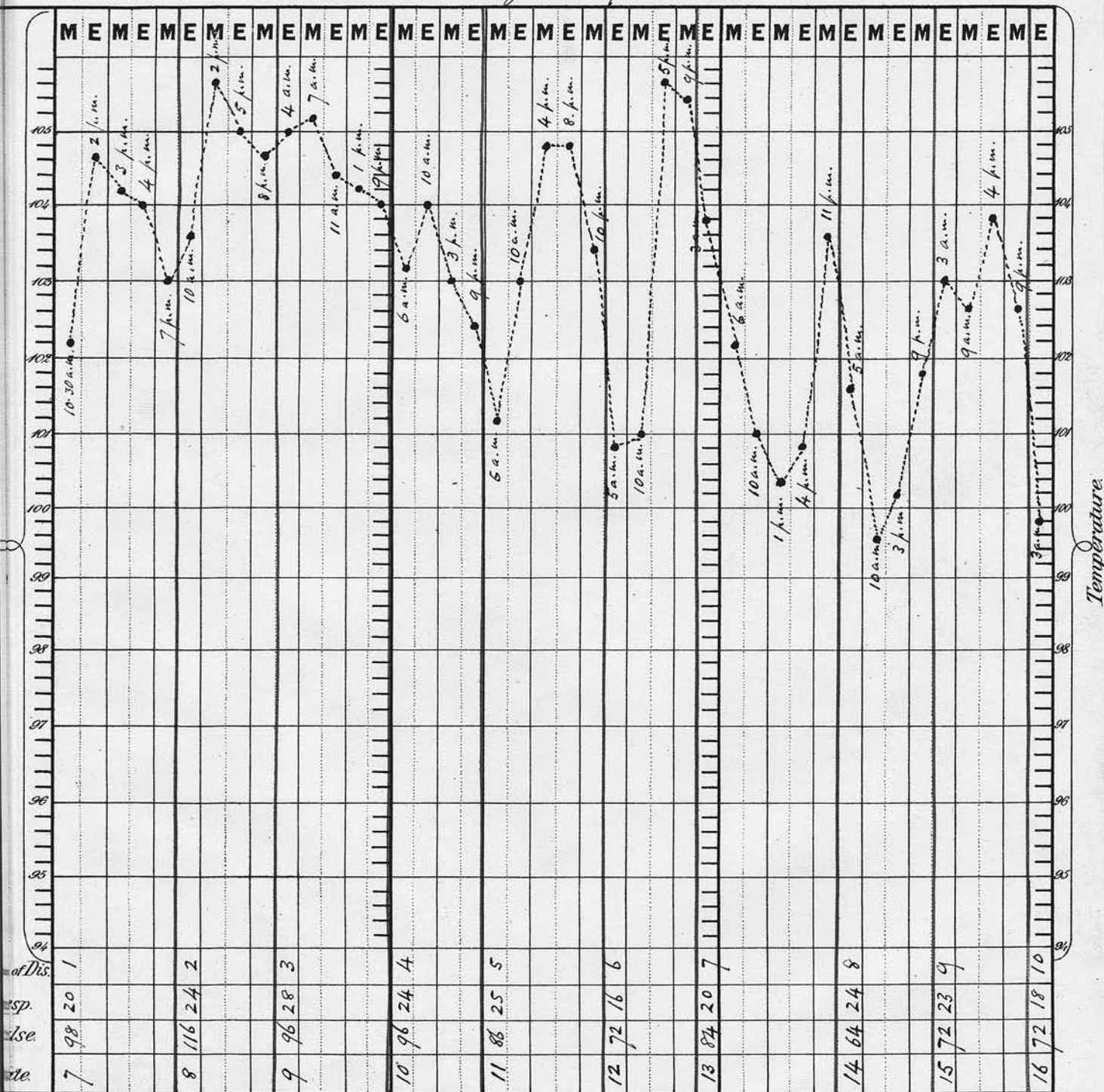
24th April 1882.

Case I.

Name *C. Christensen*

Age *27*

Disease *Tr. intermitt. subcontigua*

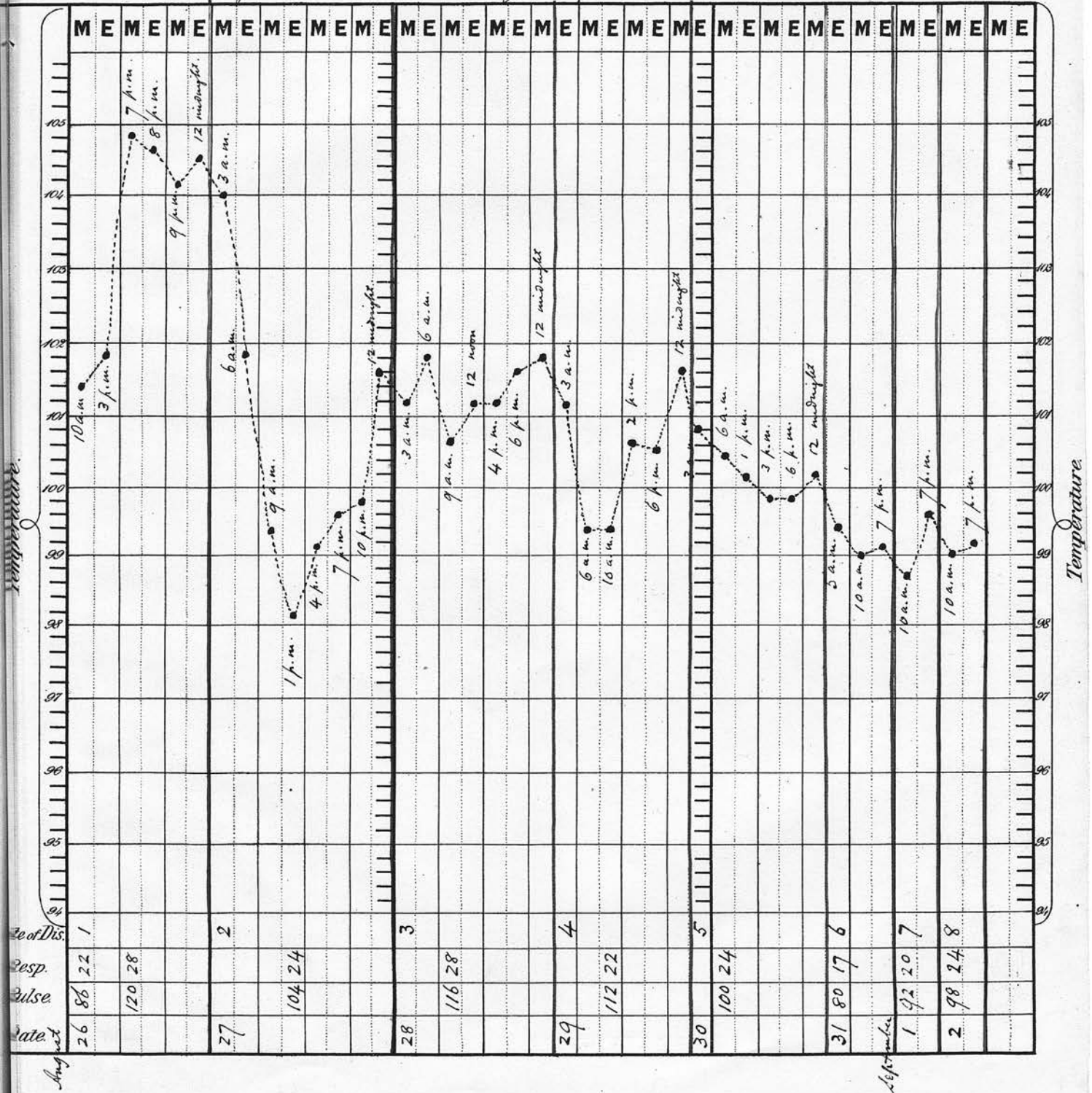


Case II.

Name *Olaf Lindorholt*

Age *17*

Disease *Feb. intermittens*



Case III.

Name John Jones Age 29 Disease *Fbris interm. pernicios.*

