TABLE D.—*Appearance of Blood in one case of Quartan Ague.*

Serial No.	Duration of disease prior to observation.	Result of Examination of Blood.		Remarks.
		During paroxysm.	During interval.	
33	One year	.....	Echinoid ...	Very anæmic; no plasmodia visible. No phagocytes to be seen.

TABLE E.—*Appearaace of Blood in a case of Remittent Fever.*

21	Two weeks. Date of observation—			
	27th February 1891, 3-30 P.M. ...	T. 103·8° Echinoid.	.....	Phagocyte cells full of spores.
	2nd March 1891, 10-30 A.M. ...	T. 100° Plasmodic.	.....	After quinine and arsenic mixture.
	11-45 A.M. ...	T. 99·4° Echinoid and plasmodic.	.....	.. ...
	1 P.M. ...	T. 100·8° Echinoid. Plasmodic.	.....	.....
	1-35 P.M. ...	T. 101·4° Echinoid.	.....	Free plasmodia and flagellate monads.
	3-30 P.M. ...	T. 101·4° Echinoid. Plasmodic.	.....	Free spores.
	3rd March 1891, 10 A.M. ...	T. 99·4° Plasmodic.	.....	*Quinine and Arsenic.* Many phagocyte cells charged with spores.

In connection with this paper the following will be found to be of interest in connection with one or other of the points now brought forward. To economise space I cannot do more than refer to the various papers with a general indication of their purport.

Roman Malarial Fevers.—Celli, Marchiafava, Weyl (Berl. Klin. Woch of November 3, 1890.)

Organisms of Ague.—Vandyke Carter. Sc. Mem. by Officers of Indian Army, Part III, 1880.

Hæmatozoa of Ague.—Laveran-Journal des Connaissances Medicales, January 8, 1891.

Parasite of Quartan Ague.—Golgi, Zeitschrift für Hygiene, Vol. X, p 137.

Parasite of Irregular Malarial Fevers.—Sakharoff. Annales de l' Inst. Pasteur, July 25, 1891.

Experimental Malarial Infection in Man and Animals di Mattei. Reforma Medica, May 30, 1891.

Postpaludal Pneumonia.—Hadji-Costa. Revue de Med., November 10, 1891.

Alkalinity of the blood in disease.—Rumpf. Centrl. f. Klin Med., No. 24, 1891, and Centralbl. f. d. Med. Wiss No. 41, October, 1891.

Methylene blue in Malaria.—Lava, Gazz. Degli Ospitali, November 29, 1891.

Methylene blue in Malaria.—Guttmann and Ehrlich. Berl. Klin. Woch., September 28, 1891.

Indications for Quinine.—Manquat. Lyon. Med., October 25, 1891.

An epitome of most of these papers will be found in the Epitome of Current Medical Literature of the British Medical Journal for 1891.

RECENT GERMAN RESEARCHES ON MALARIA: ITS TREATMENT BY METHYLENE BLUE.

WITH INTRODUCTORY REMARKS.

BY SURGEON-MAJOR G. M. GILES, M.B., F.R.C.S.

THE etiology of malaria is a study of paramount importance to the practitioner of tropical medicine. In different regions, the intensity of the poison may, to some degree, vary; but in India, from Karachi to Sudia and Sirhind to Cape Comorin, malaria is the cause of a greater total of sickness than perhaps all other diseases combined. Few of its inhabitants get through twelve months without an attack of fever or other indication of malarial infection. This is well shown by the prevalence of splenic enlargement which is generally recognised as the best test of the comparative malariousness of different localities. In the Punjab, [78]* it is quite common to find 20% of the population so affected and percentages of 35·1 for adults and of 71·4 for children are recorded; while, at the opposite end of the country, in Assam, the writer met with a case in which 37% of a body of labourers (mostly adults) shewed more or less enlargement

* These numbers placed [so] in brackets refer to bibliographical references given at the end of the article. Most are from the paper by Plehu.

of the organ. Save under the assumption that the researches which will be placed before the reader, contain the solution of the question, it cannot be said that we know anything whatever of the essential nature of malarial infection.

Hitherto, we have been content to refer malaria to that favourite refuge of the destitute etiologist, climate. Doubtless climate has something to say in the question, but hitherto no one has been able to define what particular elements of the numerous factors that go to constitute a climate are the most important in the matter. Peshawar and the Terais of Lower Bengal and Assam are, *e.g.*, localities equally notorious for being intensely malarious; yet no two climates could well differ more entirely in all points. Whatever then be the cause of malaria, it is evidently capable of flourishing under most diverse climatic conditions; and until we know more how climate acts in the matter, it will be well for us to concentrate our attention on the changes going on within the patient. Our barometers and well-gauges must necessarily remain useless till we know something of the essential nature of infection which their fluctuations influence. From the time that we have gained any clear notions on the connection between disease and parasitic organisms, the extraordinary periodicity of malarial affections has rendered them, *a priori*, a most favourable field for the bacteriologist.

It seems hard to imagine that they can depend upon aught else than the growth and reproduction of successive crops of parasitic organisms; but in spite of this, the results of bacteriological investigation have been here most disappointing. About 12 years ago, Tommasi-Crudeli announced the discovery of a *bacillus malariæ* which was confidently advanced as the infective agent of the disease—and at this period, I more than once thought I had, as the diatomists say, "glimpsed" such an organism. I failed, however, to stain it, and have long since learned to refer the appearance to the effects of coagulation. At the time this view was supported by other Italian observers, but it has, I believe, been long since abandoned, even by its originators who now appear to be all converts to the protozoal character of the malaria parasite. Such changes of opinion illustrate most forcibly the difficulties and uncertainties of the investigations, which are indeed such that no one need shrink from altering their interpretation of the appearances observed under the microscope.

In 1880, too, Laveran [41] announced the discovery of protozoal parasites in malaria, and has since followed up the subject by a series of papers which have continued to appear at intervals since this date. His opinions, however, have made so little impression in England, that the scanty notice they have received from our Medical Press rather gave me the idea that they had shared the fate of the Tommasi bacillus, and Selileu's [79] malaria coccus. In this latter case the bodies seen were probably the same as those now described as protozoal, Celli [80] and Marchiafava attaching the same interpretation to the appearances. Under these circumstances I was much astonished when, recently, chance brought to my notice what a mass of literature and experience have accumulated in favour of this view.

A few weeks back, however, I received from Surgeon-Lieutenant-Colonel Temple Wright, of Shahjehanpur, a letter most generously offering me translations he had had made of some recent German papers on this subject.

A relative of his had recently been treated in England for chronic malarial symptoms by the new German methylene blue treatment.

His attention being thus drawn to the matter, he went to considerable expense to obtain translations of Erlich and Guttman's paper on this subject, and of others on that of the etiology of malaria. The subject is one which, as he justly remarked, ought to be promptly tested in India, but which, nevertheless, can hardly be advantageously taken up by one who hopes to retire very shortly to a land where happily malarial material is comfortably scarce; and knowing the interest I take in animal parasites, though I have never had the pleasure of meeting him, he most kindly offered them to me.

After reading over the papers, I began to realize more keenly than usual how much the isolation of our life in *partibus infidelium* shuts us off from current professional thought even on points that most vitally concern us.

On the continent, at any rate, the dependence of malaria upon protozoal parasites seems quite accepted. The translations which in this way came into my hands, furnished a very complete view of modern researches on this subject, and it seemed a mistake that the trouble and expense of translation should be wasted on an individual.

Had an adequate knowledge of their researches been current among us, I feel sure we should have had in the Indian Medical Press numbers of papers in which their accuracy was discussed. Most of us, however, like myself, are quite incapable of translating the interminable sentences in which the Teutonic scientist loves to veil his ideas; and of the few who can do so, an even smaller minority are likely to hear of the publications in question.

Under these circumstances with Dr. Temple Wright's concurrence, I have succeeded in persuading our editor to depart from general rules and to reproduce for us selections from the papers in question.*

* We regret that the great pressure on our space at present forces us to postpone the publication of these somewhat voluminous papers to future issues.—Ed.

Being the work of a German physician (Dr. Hophirk, M.D., Jena) and moreover not intended for publication, the translations are hardly suited for publications as they stand, though they bear the impress of scrupulous exactitude. They have accordingly been largely re-written, with the view of converting them into what I hope will be found tolerably plain English.

The more important portions are reproduced *in extenso*, but, when possible, without endangering a clear elucidation of this subject. I have economized space by giving merely an abstract. It must be confessed that the credit of the profession here in India is concerned in subjecting these views to the most rigid tests, and only the widest diffusion of information of the subject can enable it to be taken up by a sufficiently large body of observers.

The Home Medical Press are only too ready to sneer at our "leaving such investigations to foreigners." If at home they vaguely recognize that we may not be able to buy a thermostat in the next bazar, the man at Peshawar has surely only to step across the street to Calcutta or Bombay to find a well-equipped laboratory at each street corner.

Of the difficulties with which we are beset at every turn in any attempt at investigation, folks at home have not the least idea, but this should not deter the numerous competent microscopists, to be met with in and out of the service, from each contributing his mite to the solution of the question. For the adequate study of these bodies a tolerably high power is requisite, but they are recognizable enough under Zeiss E. ($\frac{1}{10}''$). The only other requisite for the study is a constant temperature chamber for the microscope. Unfortunately all the usual appliances of this sort require gas for their regulation, and so cannot be worked in India except in one or two towns. Even in Calcutta continuous work is impossible owing to the gas being turned off during the day, *i.e.*, unless one incurs the expense of a private gasometer. The apparatus, too, must be one which can be installed close to the wards of the hospital. It is evident, therefore, that the ordinary apparatus will have be modified to our needs, and that a paraffin lamp is the only practicable source of heat. A suitable regulator for paraffin heat is to be found in Salili's regulator, described and figured in the Royal Microscopical Society's Journal for 1886, p. 1058.

The valve of this apparatus works by the pressure of ether, and so might give trouble in the plains; and a more suitable apparatus is perhaps to be found in Bordin's paraffin heat thermostat described on page 810 of the volume for 1889 of the same Journal.

The Telegraph Maintenance Co. at Calcutta constructed for me an incubator working on this principle; and though it did not work very well, this was mainly due to the constant trouble caused by the mercury regulator which I was obliged to make myself.

My experience indeed is that the regulator figured is not workable. I afterwards found, however, that there is an electrical contact thermometer actually in the market which entirely gets over this difficulty.

Surgeon-Major Warden had one in constant use in his laboratory at Calcutta for testing the flashing point of petroleum. The bulb of this instrument is not so bulky as to prevent its being included within the warm case that holds the microscope in Plehu's apparatus, so that simplicity might be obtained by working the regulator directly by the air temperature of the chamber. Hints as to the construction of the warm box may be found in the figure of Sach's apparatus in page 314 of the same volume of the Journal (1887). I have gone into some detail as to where hints may be found on the construction of an apparatus suitable to our needs, as I am convinced that Plehu is absolutely right in his dictum, that observations conducted otherwise than at the temperature of the blood are utterly worthless. It is only thus that one can prevent the appearance of "echinoid" forms and other sources of fallacy.

Naturally enough, the reading of these papers has led to my making a few preliminary observations on my own account.

Made as they are, without a proper warm stage, and few in number, I attach little value to them. I think, however, I may say that bodies resembling those described, are really to be met with in malarial blood.

Some of them indeed I described and figured more than ten years ago, though I imputed to them an entirely different significance.

In 1881, when serving on the Punjab frontier, I discovered in the sputa of tissues, in cases of the epidemic pneumonia of the district, certain bodies which are now well-known as "Friedlander's" pneumococcus. This was of course before Friedlander announced the discovery; but owing to the tardy way in which official publications see the light, my paper in the Army Medical Reports on the subject did not appear till some time after his results were published. I found also that bodies generally resembling the pneumococci were present also in the blood; but these have never been noticed in pneumonia in Europe, a discrepancy I am now at last able to understand.

As is the case with all diseases in India, malarial complication is well-nigh universally present in Frontier pneumonia; and my recent examinations convince me that the bodies I described were what are now spoken off as the parasites of malaria.

In the meantime, however, finding that the results of examinations of pneumonia blood in

Europe were uniformly negative, I had come to the conclusion that I had been mistaken and that the appearances were the result of imperfect methods of examination. I was further confirmed in this view when I found that similar bodies cropped up in the majority of blood examinations in India.

I have hitherto found no suitable opportunity notifying this modification of my original position on the question of the infective agent of pneumonia, and am, it must be confessed, gratified to find that I was merely misled as to the etiological significance of what I saw, and not the mere dupe of fallacious *post-mortem* appearances in the blood.

It may be well, however, to warn such as have had but little experience in blood examinations that no branch of microscopy is more fraught with fallacious appearances.

With the greatest care it is never easy to pronounce what is abnormal and what the mere unforeseen results of *post-mortem* change.

The least touch of a foreign body [83] will start all sorts of appearances, and the addition of even any of the so-called "indifferent" media is absolutely fatal. Moreover, besides parasites, several other bodies than the red and white corpuscles are to be found in the blood. In health we meet with "plaques" [81] and "phantoms" in disease, and especially in all pyrexial states various irregular bodies resulting probably from the breaking down of cellular elements of blood and tissues, as well as fatty particles introduced by the lymph.

The liquid paraffin method introduced by Plehu, is a great technical advance. Even without an incubator I have occasionally found specimens so prepared uncoagulated after many hours. The bodies I have seen and stained belong to the category of large "plasmodia" and oval bodies. In stained preparations, too, I can make out round flagellate bodies. Once in a halting attempt with a conduction warm stage, I thought I observed some of the flagellate bodies in motion. I have as yet been unable to satisfy myself of the existence of the endoglobular form.

The results of observations of living blood should always be checked by staining. If what one sees is not the result of some mere trick of refraction on the constituents of a rapidly changing fluid, it ought to be possible to demonstrate their existence in dry preparations.

Doubtless a too great value is often attached to the effects of stain. Some microscopists are fond of dignifying these rather uncertain and probably merely adhesive phenomena as "microchemical reactions," but the fact that each of them has his own "method" or "modification," shows that none of the definiteness of the chemist's test tube attaches to these effects. The fact is indeed that trifling and unperceived differences in manipulation may result in producing very different effects with the same stain, and it is in practice very difficult to get a number of similar cover lens preparations from so many smears of the same organic fluid.

Moreover, the same cell may behave quite differently to stains in different stages of nutrition. A good instance of this is the absurd controversy that has raged round the so-called "eosinophile" leucocyte, to which all sorts of mysterious pathological imports have been imputed and denied by the combatants.

None of these controversialists seem to have recognized that leucocytes are actively engaged in the trophic work of the organism of which they form a part, and that they will hence stain differently according to the stage of the process. Naturally enough such differences are more marked when trophic changes are altered and exaggerated as they are in many diseases; but it is now known that these bodies may be generally demonstrated in healthy subjects. A similar instance is to be found in the peptic cells of Heidenhain, which stain very differently according to the stage of digestion going on in the stomach at the time the animal is killed. With such reservations staining processes are of the greatest importance; but it is absurd to assert that same particular mass of protoplasm is a protozoon or a protophyte, merely because it stains well with some particular dye.

Assuming, however, that the existence of protozoal parasites in the blood in malaria be ultimately established, it by no means follows that they are its cause. Our knowledge of the protozoal hæmatozoa is in its infancy; but new species are often discovered, and it seems quite likely that most of the higher animals occasionally harbour them.

Those that are best known, too, seem quite harmless, and the numbers in which they are found in malaria "2 or 3 to a field" seem quite inadequate to account for the mischief wrought [84]. To suggest that fever merely predisposes us to be invaded by them would of course be absurd and contrary to our general knowledge of parasitism; but we have yet to hear of any extensive series of observations on the blood of healthy inhabitants of malarious regions, and it is possible that they may so commonly harbour the parasites as to explain their presence in the fever-stricken. Most parasites have a geographical as well as a specific distribution, and it may be that the surroundings which predispose to malaria favour also the free stage of protozoal parasites, which may none the less be harmless.

I speak with the greatest diffidence as to the value of the casual observations I have been making, but I am tolerably certain that I demonstrated exactly similar bodies to those I find in malarial blood, in a patient suffering from scabies.

The boy, it is true, was pale and may possibly have recently undergone an unnoticed attack of fever. Another reason for maintaining a sceptical attitude as to the malarial parasites is that the protozoa seem to be coming into fashion, *vice* the bacteria become a trifle stale. We have, *e.g.*, quite recently been introduced to a cancer protozoon. We must await farther particulars, but the discoverer does not appear to have observed the organism while alive; and until its behaviour while living affords grounds for considering the body to be a parasite, I fail to see any reason for considering the masses of protoplasm so described as aught else than the results of the endogenous multiplication of the carcinomatous cells. The appearances are not hard to demonstrate, and would certainly have been so interpreted up to the present time.

Returning to the *technique* described in the papers that follow, I may note,—

1*st.*—That the solution of eosin and methylene blue recommended by Plehu has an awkward mode of precipitating after a few days, so that only a little at a time should be made up.

2*nd.*—A strip of celluloid film is better for spreading the blood smears than even the piece of mica he uses. (This material is a photographic requisite.)

3*rd.*—The lobe of the ear is preferable to the finger as a site from which to derive the blood for examination. The skin of the finger is hard, indelibly grimed with all sorts of impurities, and is the most sensitive spot in the body. That of the lobe of the ear is soft, comparatively easily cleansed and singularly insensitive.

I can hardly close these prefaratory remarks without reference to Surgeon-Major Ranking's paper which has appeared in this Journal since I commenced the work of editing these translations for the Press. I could wish he had given us more details of the cultivations he mentions, as Plehu is so very emphatic as to the impossibility of cultivating the malaria parasite. Like Celli and Marchiafava he appears, too, to prefer to consider them micrococci rather than protozoa. In stained and dead preparations, of course, there is nothing to distinguish between them. I have not the least doubt, however, that we have been observing the same bodies, the appearance he speaks of as "chained spores" being well marked in many of my specimens. This appearance is quite distinct from anything described by Plehu, and, if confirmed, would go far to prove the distinctness of tropical from European malaria.

The first paper to which I wish to draw attention is one entitled "Ætiologische und Klinische Malaria-studien" by Dr. Frederick Plehu of the "Moabit" Hospital, Berlin.

It is a masterly exposition of the protozoal hypothesis of the etiology of malaria, and gives so complete a view of the history of the question, that little other reading save perhaps of the works of the rival school of Laveran is necessary. As his paper iucludes a very complete bibliography, the reader can pursue the literature of the question to any extent he may consider desirable.

(*To be continued.*)

A NOTE ON THE PATHOLOGY OF KALA-AZAR OR BERI-BERI OF ASSAM.

By Surgeon-Capt. J. F. EVANS, M.B., I.M.S.

The interest that has recently been taken in the condition known in Assam as kala-azar or beri-beri must, I think, be attributed to its high mortality, and to the increase of the disease, which has of late years arisen, tending to give it an almost epidemic character.

So far as can be ascertained, however, a disease quite similar in type, but of much less general occurrence, has existed in Assam for many years.

Its clinical characteristics have been well recognized, and the relation established, which the disease bears to similar conditions in Ceylon, Burmah, the Dutch Colonies, etc., yet its etiology still remains obscure. The term Beri-Beri has been used in many instances to denote two conditions, in one of which the disease consists in peripheral neuritis affecting generally the lower limbs, while in the other progressive pernicious anæmia, accompanied by dropsy, constitutes the complaint. Comment has frequently been made as to the incongruity of linking diseases apparently so different under one common designation; but were it demonstrated, that both diseases are probably the manifestation of one pathogenic agent, such incongruity would disappear.

It is this view of the question which has prompted the writing of the following notes; for having studied one type of the disease in Burmah and the other in Assam, I have arrived at the conclusion that both have a common origin in the blood-poisoning produced by malaria.

It will be shewn that the result of the inoculation of lower animals with cultures of malarial organisms is to produce two types of disease, in one of which death is brought about by lesions of the nervous structures, while in the other it follows debility and marasmus.

It is interesting also to note that there are two diseases common among horses and mules, one of which, surrah, is analogous to the dropsical form of beri-beri, while the other, kumri, in many points resembles that form of the disease characterised by nerve lesion.

During 1887, in Upper Burmah, I devoted much time to the examination of the blood of