

Malaria and fundus changes / by Freeland Fergus.

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MALARIA AND FUNDUS CHANGES.

By FREELAND FERGUS, M.D.

THE part which is played by constitutional taint in the production of certain maladies affecting the structure of the eyeball and of the optic nerve is well known to all ophthalmic observers. Without noticing such changes as may be produced by acute or by chronic infections, *e.g.*, by pyorrhœa alveolaris or gleet, producing an acute iritis, two constitutional conditions which stand out prominently in the mind of most ophthalmic practitioners are syphilis and tuberculosis. The ravages which are made by syphilis on the organ of vision are only too well known. There is scarcely a tissue in the eyeball which may not be affected. Crude tuberculosis is not nearly so frequently found, but it is now established beyond doubt that many of the diseases of the choroid such as choroiditis disseminata are associated with tuberculosis. Probably also most cases of phlyctenular ophthalmia are due to the same infection. In addition to these we may have actual tubercular growths or ulcerations such as tubercular formation in the iris, the ciliary body, the choroid and the eyelids. It is generally now admitted that perhaps twenty-five per cent. of all cases of interstitial keratitis are due to tuberculosis.

One infection producing constitutional conditions and sometimes affecting the eye possibly does not bulk so largely in the mind of the practitioner in the United Kingdom as perhaps it ought to do. We refer to malaria. Two cases which have recently come under observation seem to be of this nature, and as the matter is of extreme interest especially to those practitioners who have had and will have to an even greater extent in future to handle a large number of soldiers coming from the East we feel that no apology is required for bringing the matter before the notice of ophthalmic surgeons. That malaria can cause disease of the eye has been

perfectly well known for a considerable number of years. Thus in the enumeration of the varieties of optic neuritis given in the last edition of the classification of diseases issued by the Royal College of Physicians, mention is made of malarial optic neuritis, and we shall show here that it has been recognised for a considerable time that other structures of the eyeball may be affected in malarial conditions. Thus for example the choroid has been found to suffer from this disease. The retina also sometimes is involved and not infrequently there are opacities in the vitreous humour. I may be wrong, but I think most practitioners in the United Kingdom who, like myself, have not practised at all in the East, generally speaking, when they find changes in the choroid think instinctively of syphilis or of tuberculosis and almost never of malaria. Still there are numerous instances of such diseases of malarial origin mentioned in the literature of ophthalmology, and I venture to record two which have come before my notice in the hope that other practitioners whose opportunities are more extensive than mine may add further to our knowledge of this subject. One of the patients with whom the present contribution deals is a civilian, a gentleman who for many years has been actively engaged at work in India. The other is a soldier recently invalided home on account of defective eyesight from an hospital in Malta where he was located on account of an attack of malaria. In the first patient there can be no doubt as to the absence of syphilis. His own statement was positive on the point and although I know the gentleman well and would trust to any statement made by him still I thought it right to have a Wassermann done, for sometimes a man contracts syphilis without being the least aware of his being liable to such contagion. The Wassermann in this particular case was negative.

My first interview with the patient, whom we shall call Mr. Z, was on the 5th December, 1914. At that time he complained of dimness of vision in his left eye which

defect he compared to seeing through a veil of smoke. His visual acuteness amounted to seeing letters of 6/6 and that with ease. Apart from this slight complaint the patient was in robust health. He never suffered from headache nor from vomiting, the pupils were found to be slightly contracted and did not respond readily to differences of light. In addition to the smoky sensation he complained of seeing black spots in front of the left eye which spots were stated by him to have been present for some few years. Bjerrum's types showed quite distinctly a very defective light sense for the left eye, the right being normal. On ophthalmoscopic examination at that time the disc of the left eye appeared somewhat hazy. There was no distinct swelling of the disc itself but the veins were enormously distended, the margins were slightly blurred and the whole condition was that of hyperæmia of the optic nerve with dilatation of the veins. At that time I could find no other changes in the fundus. The fundus of the right eye was in all respects healthy. There was absolutely nothing to remark in it except a slight hypermetropia. In the right eye he had visual acuteness of 6/6 clearly and distinctly, and he made no complaint of that organ. Under these circumstances I felt inclined to come to a diagnosis of retrobulbar optic neuritis. The fields of vision were carefully taken and were found to be considerably contracted for red and for green both in the right eye and in the left. Moreover for the two colours just specified the outline of the fields were irregular, sometimes interlacing with each other. But the remarkable thing which struck me about this case at that time was that although the right eye was to all appearance perfectly healthy its colour field was considerably disturbed; notwithstanding that the visual acuteness was as in health and Bjerrum's light sense test had failed to discover any abnormality. On the 23rd December, 1914, I specially took the field of vision for the right eye, and give what I found to be the extent of the field for the four cardinal points:—

| | | | White. | Red. | Green. |
|-----------|-----|-----|--------|------|--------|
| Upwards | ... | ... | 60 | 25 | 25 |
| To left | ... | ... | 85 | 25 | 5 |
| To right | ... | ... | 55 | 30 | 16 |
| Downwards | ... | ... | 60 | 5 | 10 |

The examination was made several times on that occasion and these figures indicate the average of the readings.

Unfortunately I have not kept a copy of the field for the left eye except for one or two points, and these are as follows :—

| | | | White. | Red. | Green. |
|-----------|-----|-----|--------|------|--------|
| Upwards | ... | ... | 50 | — | — |
| To left | ... | ... | 50 | 25 | 0 |
| To right | ... | ... | 80 | 50 | 20 |
| Downwards | ... | ... | 40 | — | — |

I cannot give the figures for red and green upwards and downwards. There was thus evidence of disturbance of the fields in both eyes, particularly in that of the left. The question of diagnosis therefore was rather increased in difficulty. It was evidently a condition involving the left and also to some extent the right optic nerve. I have already given reasons for discarding the idea of syphilis. It occasionally crossed my mind that we might be dealing with a tumour beginning to press somewhere on the optic tract of the left side, but the fields were not hemianopic, and after consideration I put that out of the question. Tuberculosis was a possibility although an improbability. The patient was 42 years of age, was in the enjoyment of robust health and there were no signs or symptoms of any tubercular lesion, if the eye condition were excluded.

Having carefully considered the case from the above points of view I felt strongly inclined to attribute it to malaria from which he informed me he had suffered severely. That seemed to me then and seems to me now the likely explanation of the whole affair. Although there are numerous mentions in ophthalmic literature of

malaria affecting the optic nerve, the retina and choroid, yet it is a possible explanation of many conditions which has perhaps not received from practitioners in the United Kingdom, who have never practised in the East, sufficient attention.

At the time of Mr. Z's first visit I put him on mild doses of iodide of potassium and nothing more. Presently I shall have something to say as to the propriety of giving arsenic in such cases. The only other item which perhaps may be added to the reports of the year 1914 is that about the middle of December of that year he had an attack of ague, and on that account he missed a consultation which had been arranged. In a communication to my patient of date 10th December, 1914, I definitely said: "It is quite possible that all the trouble you have in your optic nerve is due to ague but it would help me to determine this matter if you can let me know if the trouble in the eyes began before or after the attack of ague." From his reply I learned that he had suffered from ague, and that with considerable severity, for a matter of 12 years.

Perhaps a digression in this place may be permitted as to my views of the treatment of a case such as I was here dealing with by means of arsenic. Personally I would be much averse to giving that remedy in any disease in which I found disturbance in the optic nerve structure. It has often a very deleterious effect and may produce disastrous results in the way of nerve atrophies when employed even in doses which are usually considered quite legitimate. That arsenic will often produce nerve atrophy is a perfectly well known fact. The arsenical preparation called soamin, a much vaunted remedy, caused optic nerve atrophy in a considerable proportion of the cases where it had been exhibited. *Timeo Teutonos et dona ferentes*. In one case which came under my observation I am of opinion that the newer remedy neo-salvarsan did the same thing. The patient was a man getting up in the twenties and who

had undoubtedly on his own showing contracted syphilis. He had paralysis of the external rectus of his right eye. The diplopia was quite well marked and quite characteristic. He was put on mercury both by the mouth and by inunctions, and he made a rapid and good recovery. That was a matter of perhaps ten or even more years before the introduction of neo-salvarsan. On its coming into use he heard of it and sought other advice. Naturally, he consulted a practitioner who is justly regarded as an authority on this drug. A Wassermann was first done and it was found to be positive. The drug was duly administered, and two years afterwards he turned up in my consulting room absolutely blind of the left eye from optic atrophy. He informed me quite distinctly that the left eye had been tested and had been found excellent as to its visual acuteness almost immediately before the drug was given. Within a short time of its administration he began to feel the sight of the eye blurred.

In fact my experience with neo-salvarsan has been so disappointing that, while I will not prevent any patient who may wish it having the drug in proper therapeutic doses, I will never advise any of my clients to have it. In the treatment of eye diseases it very soon became apparent that neo-salvarsan was without effect in all those cases of interstitial keratitis which a Wassermann reaction proved undoubtedly to be due to syphilis. My friend and colleague, Dr. Manson, gave it to several children under my care, and in not one of them was there the slightest manifestation of any good effect from its administration.

Nor in other patients have I been more successful. In one case I detected a slight optic neuritis and said to my patient's medical man that I believed it would almost certainly turn out to be syphilitic. His medical adviser confirmed the opinion by telling me that some years before he had attended him in a secondary attack. This patient I advised to have the remedy, and it was adminis-

tered to him by a gentleman of considerable experience in this line of practice. No restriction whatever was put on the administrator. The patient was pronounced to be better. He left Glasgow for his home and returned in five months with as acute a specific iritis as I have ever seen. Fortunately he made a fairly good recovery under the administration of mercury. A third case was equally unsatisfactory. It was that of an officer who had contracted specific disease and who attended me on account of specific iritis. It began to improve under the usual remedies of atropine and mercury and he certainly was improving steadily. He had, however, heard of this new remedy and was very anxious to have it tried. I offered no objection, and accordingly it was given to him by the same gentleman who had administered it in the previous case; thereafter the Wassermann was found to be negative, but six months later he turned up again in my consulting room. The Wassermann was now found to be positive, and he had developed acute shooting pains in his legs which seemed to me as possibly foreshadowing the onset of locomotor ataxy.

I must say that I will give arsenic in any form with great reluctance when I find a pathological condition of nerve structure. It was for that reason that I did not administer any arsenical compound to the patient who is the subject of the first part of this brief memoir.

In the month of January, 1915, I left Glasgow for a month and Mr. Z. was attended during that time by Dr. McMillan. In a note addressed to me by Dr. McMillan of date 5th February, he mentions Mr. Z. and states his opinion that the case is distinctly one of optic neuritis, for the disc was found to be hazy and the colour perception particularly defective on central fixation. By this time Mr. Z. could not see green at the centre of the field. He called it grey. The only change he noted in the fundus oculi was the nerve condition. In February Mr. Z. was seen by a physician of high repute who, after my return from the South towards the middle of February,

told me that he had formed the opinion that the whole condition was due to specific disease. I had already made up my mind that it was not, that it was due to ague, but I thought it right when so definite an opinion was given that a Wassermann reaction should be taken. This was done and the result as already stated was found to be negative. A letter which I addressed to the physician here indicated, of date 21st February, 1915, is perhaps of some interest. "The visual disturbance is certainly due to some interference with the conductivity of the optic nerve, and the only indication which we get on ophthalmoscopic examination is dilatation of the veins of that nerve. In addition to that there is a contraction of the field of vision for colour chiefly in the affected eye and to some extent in the other. I feel almost inclined to attribute the thing to a form of peripheral neuritis associated with ague. He has suffered considerably from ague, and I know that it does cause certain forms of peripheral nerve disturbance. I may be wrong but that seems to me the likelihood."

Mr. Z. left this neighbourhood for some considerable time but in the month of May I received a very interesting communication from a colleague in another town. I had not examined my patient's fundus for some time and therefore cannot tell what were the appearances in the eye at the beginning of May. The gentleman of whose services he availed himself found some spots in the choroid of the left eye, and on this basis he formed the opinion that the case was essentially one of tuberculosis. On seeing Mr. Z. subsequently I found no reason to alter my opinion. There were certainly one or two roundish spots in the left eye considerably outside the macula, but there was nothing like tubercular formation. One spot was more like a melanosis than a tubercular infiltration. There was no swelling or other inflammatory sign. I could not for a moment recognize any similarity between the spots which I now saw and those of choroidal tubercle. They had some resemblance

although not a very close one to some of the appearances occasionally seen in choroiditis disseminata. But if that were the explanation one would have expected to find fresh patches of exudation and the accompanying metamorphopsia. Now the question came to be, were these spots present at previous examinations and had they by any chance escaped observation? The fact remains that he was seen in India by a gentleman of great ability who had examined him most carefully with the ophthalmoscope and had diagnosed him as a case of mild optic neuritis. I myself had repeatedly seen him and had examined him very minutely with dilated pupils but had not seen any such appearances, and lastly, my colleague, Dr. McMillan, a man whose examinations are always extremely accurate, had also examined him in the month of February. He diagnosed an optic neuritis, but did not mention in his notes which he submitted to me any fundus condition other than that of an optic neuritis.

On receiving the letter giving a positive diagnosis of tuberculosis and also insisting that Mr. Z. be put on tuberculin, I at once communicated with Dr. McMillan who wrote to me on the 12th of May to say that when he had seen the patient in February he had formed an opinion similar to my own, that the case was purely one of optic nerve trouble, but he also stated that he was unable to come to a conclusion as to the direct causes.

Now in view of these facts I think we are justified in saying that these spots in the choroid did not appear at the soonest till the month of April, 1915. I think it unlikely that the doctor in India, who had devoted much attention to the case, that Dr. McMillan, who had examined Mr. Z. with great care, that I myself, who had gone over him several times, would have all missed these spots had they been there at an earlier stage of the case. But even if we admit that they were present there were other features which rather refuted the diagnosis which had been arrived at and on which treatment was to be

pursued. I have not got very full notes of the condition on the 14th of April, on which day I saw him, and I do not think the fundus was examined at that time. Previous examinations by myself and by Dr. McMillan had left no doubt in my mind as to the optic nerve being involved. The disc was blurred, the surface of the nerve was hazy, and the veins were greatly dilated. He was, however, tested as regards his field of vision, and it was found to be even more restricted than at the first examination. By this time, on the nasal side of the field of the left eye, the red was not seen beyond 5 degrees from the fixation point and the green not at all. At the visit of the 14th April it was found for the first time that the visual acuteness was slightly less. In writing to the gentleman whom he had seen I again expressed my opinion that we were facing some condition brought about by malaria. Mr. Z., however, came back to Glasgow with definite instructions that he was to get tuberculin. I thought the diagnosis on this occasion was as far astray as that of syphilis, and as I did not wish to treat a patient for a disease which I was tolerably confident he had not got I passed him on to a colleague for treatment.

One or two factors made me unwilling to accept the diagnosis of tuberculosis. In the first place the gentleman was in robust health, he had not lost weight and his eye condition apart from the light sense and the defects in the colour fields was excellent. He had 6/6 of vision in the affected eye. It was only in the month of April, 1915, that it fell to 6/9.

But another very important consideration arose from the fact that both eyes were involved so far as the colour fields were concerned. It would be very difficult to attribute a defective colour field on the right side to a tubercular choroiditis on the left. The pigmentation in the choroid was not very dissimilar to patches of pigmentation which are seen in choroiditis disseminata, a disease which the researches of Hill-Griffiths have shown to be

very frequently associated with tuberculosis. Such patches, however, do not appear in the adult, they are essentially formations in the early years of life. In crude tubercle of the choroid, such as is not infrequently seen in adults, the symptoms are very different from what they were in this case. So far as our experience goes there is always very great diminution of the visual functions, and very generally there is effusion into the vitreous humour and not uncommonly there is separation of the retina. It seems to me quite impossible to predicate tuberculosis of the choroid in an adult 42 years of age with 6/6 visual acuteness in the diseased eye and without any effusion in the vitreous humour.

To epitomize the facts mentioned above, the features of the case were these :—

On the left side an optic neuritis which had been diagnosed before he left India for home, congestion of the retinal veins, particularly of the left eye, and defects in the fields of vision both in the right and left eyes. Viewing the matter broadly it seemed to me quite impossible to accept a diagnosis of tuberculosis.

The general features of this case were much more in consonance with what we know of the occasional manifestations of malarial disease in the eye. As already indicated a good deal of literature exists on the matter but at the time of seeing the patient I happened to remember two papers, one which we read in our student days by Poncet, which appeared in the year 1878 in the *Annal. d'Ocul.*, and the other by Sulzer which appeared in the *Archives d'Ophthalmologie* in the year 1890. Now Mr. Z.'s case did not contain some of the features mentioned in one or two of the patients spoken of in those communications, but both of the authors mentioned, and Poncet in particular, lay stress on the appearance of optic neuritis in malaria, and Poncet pointed out that very frequently there is disturbance in the choroid. It is also clearly stated, both by these authors and by others, that scotomata and especially colour scotomata and

disturbances of the field of vision, both for form and for colour, are quite common in malaria. Poncet also mentioned that in the optic neuritis of malaria there is very frequently much distension of the veins. In some of the cases with which these authors deal there were retinal hæmorrhages. Now there were none such in the case of Mr. Z. nor were there any vitreous opacities in his eye, but then he had not by any means attained the stage of malarial cachexia which was the condition of the patients described by Poncet. The whole picture of the case suggested malaria to my mind in the strongest manner. Optic neuritis with distension of the veins, disturbances in the fields of vision, colour scotomata, and yet even in the more seriously affected eye good visual acuteness, were to me very suggestive. Even if we admit, which personally I do not, that either tuberculosis or malaria might cause the symptoms, surely it is more reasonable to attribute the malady to a condition which the patient unquestionably had rather than to one as to the existence of which in his individual case there was no proof whatever. Poncet has particularly dwelt on the frequency of choroidal disease. One of the last paragraphs of his communication I have freely translated as follows :—“Cases of amaurosis *siné materia* connected with intermittent fevers and in which the older writers even with the ophthalmoscope have found no lesions should be classed as cases of malarial retino-choroiditis with embola of melanotic leucocytes in the capillaries.” To my mind the diagnosis became clearer the longer the case was observed. It is perhaps also of some interest to note that, as already mentioned, he had an attack of ague while in this country, and that the choroidal spots were observed for the first time after that attack. One of the writers on the subject says that there are eye lesions sooner or later in something like ten per cent. of patients who suffer from ague. It is perhaps of some importance to note that the injection of tuberculin aseptically was not followed by any local reaction.

The other case which I wish to mention differs materially from that of Mr. Z. in so far as the patient had never been in the East till the present war broke out, but while there had been tolerably severely attacked with malaria. In this case I think there is much greater doubt as to the affection of the eye having been in any way due to malaria. I think there is much more to be said for a tubercular foundation in the patient now to be discussed than there was in Mr. Z. The patient, whom we shall call Private Y, was admitted to the 4th Scottish General Hospital about the 13th of September, 1915. He stated that he had been under shell fire in Gallipoli, that since then the vision of the right eye had been defective but that at the time of his coming to the 4th Scottish General Hospital he was improving. While in the East he had an attack of malaria and then of pleurisy and was sent home from the hospital at Malta. On examination on the 13th of September the visual acuteness of the right eye was found to be 6/36 and that of the left 6/9. The right retina and optic nerve were observed to be swollen and the vessels veiled. Opacities were found in the vitreous both on the right side and on the left. He was put on tuberculin and iodide of potassium, and on the 11th of November it was noted that the left eye had much improved, the optic nerve being almost as in health. In the right eye the swelling of the nerve was observed to have somewhat decreased but there was still a considerable effusion at the back of the right lens. He was seen for the last time on the 1st of January. The left eye was practically as in health with 6/9 vision. The right eye had not improved in vision, and there was still a considerable amount of effusion at the back of the lens although the vitreous had cleared up considerably. In a case such as this the likelihood is that we were dealing with some tubercular disease. Von Pirquet's test was positive although that perhaps is not altogether very reliable, but the condition seems to have cleared up considerably on the use of

tuberculin. Still it is to be observed that the man had ague which might possibly be the determining factor in the case. So far as I have been able to study the matter fundus changes are not often noticed in the early stages of malaria, it is only in the later, but there is no reason in the nature of things why the parasite should not work havoc in the eye in the early stages, and if the man's story is trustworthy he certainly had malaria in the month of June, 1915. There could be no doubt whatever that the case was one of optic neuritis affecting the right eye. On the first occasion of my seeing him I rather put out of account any idea of cerebral neoplasm. There had been no vomiting, there had been no headache, and the nerve of the other eye was perfectly as in health. He gave no account of any injury to his head, all he said was that a shell exploded a few feet in front of him but none of the fragments had struck him. I have no great experience in such matters but it seemed to me that that was rather a far-fetched explanation of a well-marked optic neuritis in the right eye. There could be no doubt whatever as to the pathological changes. Incidentally it may be mentioned that the ophthalmometer showed about two dioptries of astigmatism in the left eye and three in the right. Von Pirquet's test, as already stated, was positive, but there was no evidence whatsoever of syphilis. On the 14th of October it was noted that there was a fair amount of effusion into the right vitreous humour in addition to the disturbances in the right optic nerve, and on the 10th day of the same month the vision was still found to be 6/36 in the right, 6/18 in the left, and distinct opacities in the vitreous.



