MALARIAL PARALYSIS.

Clinical Lecture delivered at the Pennsylvania Hospital.

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Physician to the Pennsylvania Hospital.

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Gentlemen,—I present you this morning a case of paralysis of unusual kind, one that will repay a close analysis. The patient, a man twenty-one years of age, has been in the hospital for some time, and we have had full opportunity of watching the varying features of his malady. He was admitted September 2, 1889. His illness began seven days before, while at sea and a few days after leaving Savannah, with intense occipital headache, and a violent chill followed by fever. The fever continued for three days; then another chill occurred, and he became delirious. There was a third chill the day before admission. On admission he was shaking violently, the tongue was furred, he vomited, the spleen was found to be much enlarged, the temperature was 106° F.; he was evidently suffering from a severe attack of remittent fever. Under decided doses of quinine, aided by phenacetin, the fever subsided in two days, the morning temperature being 98.6°. He sweated profusely and complained of excessive thirst. In the next few days the apparent convalescence continued, and the quinine was reduced to twelve grains daily. But this proved insufficient to overcome the strong hold the malaria had on him, for on the 8th he had a chill with a temperature of 105°; and the same happened on the 16th; from the 8th to the 12th the temperature fluctuated between normal and 101°. During the profuse sweating that followed the outbreak of the 16th he became wildly delirious, though the temperature had fallen to 99°, and he remained delirious all night, wakening quite himself in the morning.

By the 20th of the month the patient was sitting up in his clothes; he looked pale and complained of weakness in his legs and of inability to walk without support. Basham's iron mixture was added to his
On the 23d cramps were noticed about the knees, and he had vertigo. My colleague, Dr. Arthur V. Meigs, who then had the patient in charge, fearing further malarial seizures, increased the quinine to four grains every four hours during the day hours. There was no return of the chills, but by the 24th the weakness of the lower extremities had culminated in complete paralysis; motion and sensation were alike lost, the arms were not affected. Soon, however, they too showed signs of impaired power, though not to a marked degree. The quinine was stopped and iodide of potassium given, which by the 27th had been increased to thirty grains three times daily. An examination of the eyes by Dr. Harlan detected nothing but a slight degree of hypermetropia.

In the next three weeks there was not much change in his condition. It may be thus summed up: He sits up in bed; can use his arms, though the muscular action is not strong; the grip of the hand is impaired, the right more than the left. When the fingers are extended there is marked rhythmical trembling in them; cramps occasionally occur in the muscles of the neck, especially on the right side. There is absolutely no power of motion in the right leg; slight power exists in the left leg, enabling him to lift it a few inches from the bed. Both knee-jerks are exaggerated, particularly the right; there is no ankle-clonus. The nutrition of the muscles is unimpaired; they are firm. The sensation in the legs is completely abolished. There is no rectal or bladder disturbance; the temperature is normal.

The palsy now improved slightly, and he went around the ward on crutches. The iodide produced a marked rash; it was stopped October 22, and arsenic, beginning with three drops of Fowler's solution, was commenced. On the 24th he had a slight chill, followed by fever. There was no change of marked character noted by Dr. Norton Downs, the resident physician, who watched him closely, until November 5, except that the palsy had improved to the point that he could raise the right leg from the floor; he had some difficulty in emptying the bladder, and complained of a gnawing pain in the back in the middorsal region, which was, however, greatly relieved by a blister. The sensory phenomena showed no amelioration. The anesthesia, both in the legs and arms, especially in the right arm, was decided, and coexisted with marked formication in the legs; there was a zone of anesthesia encircling the chest about two inches below the nipple; he had almost complete loss of taste. The co-ordination of the muscular movements in the legs was decidedly disordered; his gait was that of an ataxic; he could not stand with his eyes closed, nor walk in the dark.
muscular response to the faradic current was good; the pupils reacted normally to light and to accommodation.

On the 5th of November a group of head symptoms was manifest. He had severe occipital headache; his hearing was found to be affected in a marked degree; he had decided bitemporal hemianopsia, and his memory was so impaired that he forgot almost instantly a question asked. The appetite was poor; the urine had a specific gravity of 1020, was acid, contained neither albumin, sugar, nor casts; he had a light chill followed by slight fever, though he had been taking off and on about six grains of quinine daily for weeks, since the larger doses given in the early part of the case were reduced. From now on until the 14th the cerebral symptoms were very marked. There was intense boring occipital headache with flushed face, complete loss of taste except for sour things, and inability to use the weakened muscles of the jaw for chewing solid food. But the tongue was protruded without difficulty and straightly, the pupils were normal, though the left was noticeably larger than the right; and nausea without vomiting, anorexia, a firm, rapid pulse, a temperature varying between 101° and 103.4°,—the latter in the evening,—urine of specific gravity of 1030 and free from albumin, sweating of the feet and legs, and greater muscular power than previously observed, made up the clinical features of his singular state. Yet more striking than these symptoms were the outbreaks of hallucinations and of maniacal delirium that necessitated his being confined to the bed with straps. They mostly came on at night, though the first one was a morning attack, were only slightly controlled by bromides, but were decidedly influenced by hypodermic injections of one-ninetieth of a grain of hydrobromate of hyoscine, which not only quieted him, but steadied his mind. Between these spells, which occurred irregularly and not frequently, he was rational.

By the 14th, although there was still some evening fever, the patient's condition had greatly improved. The headache was much less; he could walk with a cane, though the gait was almost a run; he slept well, and no vesical or rectal disturbance existed. An examination at the eye department, by Dr. Harlan, gave us the particulars of the half vision that had become a marked feature. The patient had complete inability to see on either side; could only see anything that was directly in front of him,—"like a horse with a big pair of blinders" was his own description. He complained of dimness of sight, but the ophthalmoscopic appearances were absolutely normal. Vision, however, was very much diminished \( V = \frac{1}{CC} \), and existed only in small
nasal fields, which were sharply defined and perfectly symmetrical.\(^1\) On the 18th, following a maniacal outbreak on the afternoon of the 17th of a few hours' duration, he rather suddenly became entirely blind. Prior to the loss of sight he began to see yellow, a few objects, however, appearing black or green. The temperature was normal; he was rational. The yellow vision persisted on the 19th, though he could recognize some colors and see light on the nasal fields, but could not distinguish objects; there was no perception on the temporal sides.

Let me here interrupt the narrative to remind you that at about this time he was brought before the class a paralytic, with the strange history I have given you, and that, dwelling on the irregularity of the symptoms, on the fact that they did not indicate any of the known affections of the brain or spinal cord, and on the history of the case, I pronounced it one of malarial paralysis, and suggested that a close search of the blood be made for malarial germs; a partial examination of the kind had been already attempted, but was not satisfactory. Dr. Joseph Leidy, Jr., kindly undertook the investigation, and with the most decisive results. I show you here the appearances under the microscope as he has drawn them, and you will see how conclusive they are. You will observe the hyaline bodies, pigmented vacuoles, and masses of free pigment in Figs. 1 and 2, and instances of the pigmented bodies, with one in which the haemoglobin had been entirely consumed, in Fig. 3. In Fig. 4 you will note a pigmented crescentic body, detected in the case, for the first time, in the examination made just before the clinic. Now, these appearances are all very striking, and closely correspond with what Laveran has described as the characteristic elements found in the blood of persons subject to the malarial poison,—namely, pigmented bodies in the interior of red corpuscles; a pigmented ciliated organism; pigmented crescentic bodies. In our

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\(^1\) The ophthalmoscopic details have been published in full, with charts, by Dr. Harlan in the Transactions of the American Ophthalmological Society, vol. v., 1890.
examination we did not encounter the pigmented ciliated bodies; they are, indeed, very much more common during the acute than during the protracted disease. Fig. 4, a is not apt to show itself before the later stages, and in the malarial cachexia.

To resume, now, the history of the case. Fully convinced of the malarial origin of all the symptoms, twenty-four grains of quinine were given daily, for the most part four grains at a time. He began at once to improve decidedly, and the improvement, with slight exceptions, continued without drawbacks. One of the exceptions was on the evening of the 18th,—before, therefore, he had completed the second day of the treatment,—when he had one of his attacks of delirium, promptly, however, checked by the hypodermic injection of hydrobromate of hyoscine; another was pain and stiffness at the back of the neck with slight retraction of the head, relieved by ice to the spine. Hearing and sight gradually got better; vision returned first to the nasal fields, extended rapidly to the temporal, and was normal by the 24th. The taste had become natural, and there were now many complaints of the bitter taste of the quinine, which previously was unperceived; he could chew his food well. The sensation all over the body was good, and he walked without marked difficulty. The temperature was mostly normal; though the evening temperature of the 24th is recorded as 100°. There was a great diminution in the number of the malarial corpuscles, yet the vacuole-bodies were always present, and at times the crescentic.

Influenced by the striking improvement, the quinine was reduced to sixteen grains daily; but this proved to have been premature, for on the evening of the 27th the temperature went up to 102°, declining to 100° on the morning of the 28th. Twenty-four grains of quinine daily were resumed, and there were no more interruptions to the steady
and complete convalescence, barring a very slight delirious attack on the night of December 2, yielding, as before, quickly to the hyoscine. Frequent examinations of the blood failed to discover the presence of any of the malarial elements described, with the exception of a few masses of free pigment; on one occasion a single crescentic body was detected. The red corpuscles, which had diminished to 3,390,000, increased in three weeks to 5,100,000; the haemoglobin was not tested. The quinine was lessened, and the patient left the hospital December 4, 1889, fully convalescent and rejoicing in the free use of his limbs.

[The recovery was complete and radical; for a letter to Dr. Leidy from the patient, from San Francisco, written over a year after his discharge from the hospital, speaks of his enjoying perfect health.]

Let us now look at the features of this case of malarial paralysis and notice the peculiarities that characterize the malady. First, let me point out to you the profound malarial impression, which, however, notwithstanding its obstinacy, was far less regular in its manifestations than we commonly find in malaria; the chills occurred irregularly, the fever was irregular in the heights to which it attained, and persisted in an irregular way for days; and we observed later in the case no certain periods in the outbreaks of the extraordinary maniacal attacks. These maniacal outbreaks were, indeed, most peculiar. They happened without warning, and lasted several hours. The delirium was noisy, boisterous, associated with great restlessness, with a disposition to leave the hospital so marked that the patient had to be strapped to the bed to prevent it; there was incessant singing and shouting; the temperature was slightly elevated; the face was flushed. An extraordinary fact connected with the seizures was the way in which the hypodermic injections of hyoscine controlled them. The graver attacks were all modified by them, and the patient awoke rational from his sleep; in the slighter ones the injection soon brought him to his senses.

But the features of the paralysis are, with possibly the exception of the eye-phenomena and of the state of the blood, those on which attention must centre. We find a motor paralysis of the lower limbs, at first complete, and partial paralysis of the arms; no impairment of the rectum, though some of the bladder; good electro-muscular reactions, and, further on, returning power, but gait and symptoms like those of an ataxic, except in the well-preserved knee-jerks and in the pupillary reactions. Throughout the case is seen the prominence of the altered sensation, the great amount of anaesthesia all over the body, the lost sensation being manifest to touch, to pain, and, so far as tested,
to temperature. The special senses, too, are impaired,—taste, hearing, eyesight. Indeed, the sensory phenomena are even much more striking than those of the motor palsy. It is further to be noted that they persisted while the motor palsy gradually yielded. Let me add, with reference to this, that its improvement was irregular; the paralysis returned for a time decidedly after having greatly lessened, yet with the intense development of the cerebral symptoms, it did not retrograde; indeed, it seemed to improve all the more quickly.

It was this transfer of signs of disorder, as it were, from one part of the nervous system to the other, without definite cause, that made me believe in the malarial origin of the symptoms, notwithstanding the long treatment with quinine and with arsenic. I was, too, strongly influenced in my diagnosis by what I dwelt on when I first showed the patient to you, by the great and general anaesthesia, by the motor palsy, markedly lessening while the signs of locomotor ataxia seemed to supersede it, by the recurrence of some of the symptoms after their disappearance; in one word, by the want of continuity in the symptoms. Then, they did not belong to any fixed disease of brain or spinal cord; there were features present and features lacking of more than one affection. Take those which in the latter stages were the most to be thought of, locomotor ataxia and brain tumor. We looked in vain for the violent neuralgic pains of ataxia, for the conditions of the pupils, for the absence of the knee-jerks; and the motor palsy that preceded the staggering gait and disturbance of co-ordination was much too great to belong to the earlier symptoms of ataxia. As regards brain tumor, it must be admitted that the diagnosis was at certain stages very difficult; the hemianopsia so suggestive of this made it especially so, as did the disorders of hearing and of taste and smell, and the violent headaches. But with reference to these, they were not persistent; the perversions of hearing, taste, and smell formed evidently a part of the very general sensory disturbance,—too general to be likely due to a tumor,—and the hemianopsia was unconnected with any signs of optic neuritis or of choking of the disks.

The eye-symptoms of the case were, indeed, remarkable. Dr. Harlan, our ophthalmic surgeon, who examined them minutely, has been unable to find another instance of bitemporal or binasal hemianopsia due to malaria. Instances of bilateral hemianopsia, the result of malaria, have been observed, as well as amblyopia, with or without changes in the fundus. The loss of sight is, however, not nearly so frequent in the poisoning from malaria as it is from uræmia. In the case we have been discussing, the loss of vision was on both sides and
complete, but it was transient. The marked colored vision is also a symptom worthy of note.

But perhaps the greatest interest in the case attaches to the examination of the blood; it furnishes the positive knowledge, in the light of which we read everything clearly. I shall not repeat what I have told you of the exact appearances we found; but I shall point out to you how the recent researches of Laveran and those who have followed him may be turned to useful clinical account, and may be employed to advance practical medicine. Doubtless, many a puzzling case will thus be solved, not only of malarial paralysis, but of other obscure forms of disorder of the nervous system caused by malarial poisoning. For we find persistent headaches, convulsions, mental derangement, obstinate neuralgias due to it; and ataxic symptoms may be developed by it, as we see not only from this case, but know from one recorded by M. H. Bell; and a form of epilepsy may be owing to it, as the case interestingly described by H. C. Wood teaches.

Malarial paralysis, the manifestations of which I have been endeavoring to explain to you in connection with a striking case, is not a common disease, though it is probably more common, especially in highly malarial districts, than is supposed. It may come on in the acute, well-defined malady; but what I have seen of it makes me believe that we are to look for it rather in the irregular than in the typical cases of the disease, and that it is the outcome of malarial cachexia quite as often as, or oftener than, of acute outbreaks of malaria. It is difficult to lay down for it any absolutely conclusive rules of diagnosis. But, speaking generally, I shall point, besides the history, to the general character of the paralysis, the great frequency of paraplegia, the extreme rarity of hemiplegia, the intact reflexes, the rapid change and variability in the symptoms, the marked sensory disturbances, the well-preserved faradic electro-muscular contractility, and the finding of the malarial organisms in the blood. The paralysis, too, though variable, does not come and go in paroxysms, as may be inferred from the way it is mostly mentioned. The common belief is that it is strictly periodical. "The characteristic feature of the paralysis is that it is intermittent, and that it occurs at regular intervals, just as the ordinary febrile paroxysms," is the statement made by Bramwell, a distinguished recent authority on diseases of the spinal cord. But I am certain that this is only one form of the malady, and,

I think, not the most usual, though it is necessarily the easiest to recognize.

The rarity of hemiplegia has been just alluded to. For myself, I have seen but one case, and that was of a character which separates it from the ordinary instances of malarial hemiplegia. There are, however, cases described, for instance, by Grasset, in which hemiplegia with aphasia existed and passed away under the influence of quinine; and Whittaker\(^1\) narrates the history of a partial hemiplegia in connection with trigeminal neuralgia which was distinctly periodic in its recurrence, and in which all the manifestations of the disease yielded rapidly to large doses of quinine. The case to which I alluded as having come under my own observation was one I saw some years ago with Dr. R. J. Levis. It quickly followed remittent fever, great headache and strabismus having been observed during the fever. It was at first strictly a hemiplegia with marked loss of power in the leg, with very little in the arm. There was hyperaesthesia rather than anaesthesia, and well-preserved electro-muscular contractility, sensibility, and good reflexes existed. No periodicity was noticed in the symptoms of paralysis. The boy improved slowly, until, after treatment with a "pneumatic cure" in the hands of a charlatan, the other side became paralyzed; finally convulsions and enlargement of the head supervened. It is very evident that we had here throughout an organic cause for the paralysis, most likely in the first instance a meningitis with exudation; and what I want to explain to you is, that there are cases of hemiplegia, especially, I believe, in remittent fever, which are due to a distinct organic cerebral cause, however brought about by the malarial poison, and are to be separated from the other kinds.

I have thus endeavored to make it clear to you that there are three forms of malarial paralysis to be taken into account. First, the form, which I hold to be most common, of general paralysis or paraplegia with irregular symptoms, of which the case we have been examining has given us a marked illustration. Secondly, the form in which the periodicity is striking, and which is much more apt to show itself as a hemiplegia. Thirdly, the rarest form, that in which actual organic disease is produced by the malarial poison, and in which periodicity and variability are not prominent, the case running much the course of ordinary paralysis when produced by its usual causes. This kind of palsy in malaria, commonly due to a brain-lesion, such as meningitis or apoplexy, shows itself most often in the shape of a hemiplegia.

\(^1\)Cincinnati Lancet-Clinic, April 9, 1887.
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It is true that it is not, strictly speaking, a malarial palsy, though a malarial fever has brought it about; it is rather palsy in malarial disease.

The cases of malarial paralysis that are periodical, in which the palsy comes quickly, disappears, and returns, must be distinguished from cases of intermittent paralysis that have been described by Westphal, Hartwig, and Cousot,\(^1\) which are evidently not malarial. It may be very difficult to distinguish such an affection, which in truth has been noted even in malarial subjects. Generally, however, we can obtain no history of malaria; often there is the fact of several cases having happened in the same family; the special senses and the general sensibility are not affected; very great diminution or even abolition of electric excitability without reaction of degeneration is met with; the attacks are irregular, may come on for years, and are not permanently influenced by quinine. We find thus that periodicity is not a strictly characteristic sign of malarial paralysis; since here we have a palsy which is periodical and intermittent, but not malarial. It would be interesting and, I believe, valuable to examine the blood in cases of the kind.

The prognosis of malarial palsy is favorable; it is certainly so when the disorder is treated early and decidedly. Excluding the third group I have mentioned, which, as I have already said, is not really a toxic or malarial paralysis, we may expect recovery. I have seen this take place (as in a sailor in this hospital some years ago with complete paraplegia of malarial origin) even where the loss of power existed for a considerable time. Yet, if the affection have lasted long and have had no active treatment, secondary changes may be set up leading to serious organic changes. This is especially the case in the spinal cord; for poliomyelitis and various scleroses may follow. You will find in Morton Prince's article useful information bearing on the subject.\(^2\)

As regards the cause of malarial palsies, we cannot speak with certainty. An accumulation of pigment, with the capillary embolism it may produce in brain, in spinal cord, or in organs of special sense as the cause, is a theory only qualifiedly admitted by Frerichs, and denied by Charcot, and is not tenable when we take into account the rapid change in the symptoms, as well as their recurrence, and the prompt recovery that may happen. There is, in truth, much doubt about these capillary pigmentary apoplexies. None were found in the elaborate

\(^1\) Revue de Médecine, No. 7, 1887.

\(^2\) Medical News, July, 1889.
researches in this hospital made by my late eminent colleague John F. Meigs. To me it seems very likely that the malarial germs carried about in the blood may have a direct action on special nerve-centres; not a mechanical one, but one such as several vegetable poisons possess, or as the poison of diphtheria exerts. The destruction of the malarial germs or their rapid augmentation would account for the great and sudden changes that may be seen in the cerebral or the spinal phenomena, including the outbreaks of wild delirium.

In the treatment of these malarial palsies we witness marvellous effects from large doses of quinine. I say advisedly large doses; for the malady will go on unchecked by small doses,—nay, may develop rapidly while these, or even while what are generally quite sufficient doses, are being employed. This was clearly shown in the case we have been examining. Quinine, given at first in large doses, was for a time replaced by smaller ones, when the doubtful nervous symptoms appeared. Large doses of iodide of potassium were administered; the patient grew worse. Arsenic for a time was beneficial. But it was only when quinine was again given continuously in large doses, and the small ones, which the patient had indeed rarely entirely abandoned, were wholly discontinued, that the rapid and striking change leading to recovery took place; eye-symptoms, brain-symptoms, all disorder, seemed to melt away under the potency of the drug.

In the record of the patient we have been examining, there is a further point to which I wish to call attention,—the rapid lessening and the quick disappearance from the blood of the micro-organisms, coincident with the obvious amelioration, under the decided doses of quinine. This was studied several times daily, and in a few days the change was extraordinary. We have in this observation a fact which must interest every therapeutist, and which, it is to be hoped, will prove an addition to positive knowledge.

1 Pennsylvania Hospital Reports, vol. i.