spread of nematodes. There remains a fourth factor, which is not so directly connected with, or dependent on, civilization, namely, the transmission of helminths through the active agency of insects. The outstanding instance, of course, is filariasis. This is independent of food, sanitation, and clothing—unless, indeed, the whole body, including the face, could be covered. Even here, however, a means has been found to limit the occurrence of the disease—namely, by filling up the swamps and marshes, and thus destroying the breeding grounds of the mosquito. This measure might well enough be included under sanitation. These, then, are the main prophylactic and preventive measures, and, could they be efficiently carried out in all cases, man would cease to be afflicted with helminth parasites. This, certainly, is a counsel of perfection, and it seems vain to hope for its ultimate attainment in tropical countries. So long, however, as it fails of complete realization, just as long will there be helminthiasis in these regions. Medicinal remedies in places where helminthiasis is endemic are of merely transient utility. They only touch the outcrop in various isolated individuals, all the while the root of the evil remains untouched. Here, assuredly, one effort directed towards prophylaxis is worth a hundred towards cure.

ON RECURRENT MOTOR PARALYSIS IN MIGRAINE,

WITH REPORT OF A FAMILY IN WHICH RECURRENT HEMIPLEGIA ACCOMPANIED THE ATTACKS.

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Recurrent paralyses in some of their varieties have recently attracted considerable attention.[1] In migraine an opportunity for observing such paralysis is very rare, for it is a commonplace that the symptoms in the great majority of attacks of migraine are exclusively on the sensory side. In what follows I propose to give an account of a family in which hemiplegia, with, as a rule, loss of speech, was a constant feature of attacks of migraine, and to such a degree as to be almost unique, so far as I can ascertain; and also to deal with the forms of motor paralysis which occasionally occur in this disorder.

The restriction of the attack to purely sensory phenomena is one of the most interesting features of migraine, and at the same time one of the most puzzling. In an affection like migraine, of which the exact cause is unknown, and in which there are no recognizable pathological changes, the diagnosis rests upon the symptoms and their grouping. As a rule, the peculiarity of the symptoms and the regularity of their order of occurrence make the affection as definite as any symptom-group in medicine. But in diseases where the diagnosis depends upon the symptoms it is essential that these should conform to the accepted type. This is especially the case when phenomena are present over and above those recognized as proper to the attack. In some cases of migraine which lie on the borderland between it and other neuroses the distinction is by no means easy, and sometimes must be left in doubt. Especially may such difficulty arise in deciding between a diagnosis of epilepsy and migraine.

In the family history given below the strongly hereditary character of migraine is well marked, and also the tendency to direct transmission of the disease. The characters of the attacks which mark them as belonging to migraine will, however, be better considered when the cases have been described.

Attacks of migraine may be associated with motor paralysis in several ways, excluding those cases in which it occurs in accidental association with independent organic brain disease, such as tumour, or in which it is doubtful whether atypical migraine does not belong to another affection such as epilepsy.

1. *Migraine Secondary to Structural Lesions.*

Attacks of migraine may be a symptom of onset in hemiplegia due to a vascular lesion or to an intracranial tumour. This group I do not propose to consider. In connexion with the production of an attack of migraine by occlusion of an artery it may be recalled that Leonard Hill[2] produced an attack in himself by digital compression of one carotid artery.

2. *Long Standing Migraine Complicated by Paralysis.*

Cases in which migraine of long standing has issued in permanent paralysis, generally due to a vascular lesion. In some of these one of the phenomena of the aura of the attack, such as aphasia or hemiopia, has become permanent, but in others the permanent disability in no way corresponds to the aura. Instances of this kind are fairly numerous.

In a case reported by Oppenheim,[3] in a patient who suffered from old-standing migraine, there occurred in the course of an attack stupor with persistent aphasia and right hemiplegia, found to be due to thrombosis of the internal carotid at the origin of the Sylvian artery.

In Infeld's[4] case, a woman aged 27, who suffered from hereditary migraine, in one attack felt something give way in her head, and fell but did not lose consciousness. There resulted right hemiplegia, with hemianaesthesia and blindness of the right eye. One month later there remained weakness and spasticity, with post-hemiplegic disorder of movement and slight paraesthesia.

J. J. Thomas[5] gives two cases, in one of which an attack like migraine was followed by left hemiparesis, hemianaesthesia, and hemiopia; in the other, a woman aged 27, subject to migraine, left hemiparesis, hemiparaesthesia, and hemiopia resulted. In both cases hemiopia was permanent; the other symptoms cleared up. He gives another case of migraine in which permanent hemiopia resulted.

Indeed, hemiopia as a permanent result of migraine seems to be more common than paralysis, although both are fortunately rare. Often in these cases the hemiopia forms a very marked feature of the aura preceding the attack,[6] but this, as stated above, is by no means invariable. In one case under my care a woman, aged 35, had suffered for seventeen years with attacks of migraine preceded by right hemiopia. One morning she woke up with dimness of vision for objects to the right, and this in the course of a week developed into right hemiopia, which remained permanent. The optic disc looked pale, but was otherwise normal. Her vessels were healthy.

With regard to such cases as the above, those who believe that attacks of migraine are due to vasomotor spasm of cerebral vessels have raised the point whether constantly repeated spasm of an artery may not in time lead to disease of its walls, and hence to rupture or thrombosis. It is difficult to speak with certainty on this point, but the great infrequency of permanent paralysis in a disease so common as migraine, the fact (at any rate, in my experience) that sufferers from migraine do not suffer in greater proportion from atheroma or arterio-sclerosis than other persons not so affected, and the fact also that such paralysis when it occurs often affects persons under 40—the age of the patients mentioned above is noteworthy—are all against this view. There must, in addition to migraine, be some other factor at work. Further, as Spitzer[7] points out, if repeated vasomotor spasm led finally to thrombosis it would be expected that the finest arterial twigs would be affected, whereas in some of the recorded cases large vessels must have been involved. Exception to this last statement should be made for a few cases in which there was good evidence of thrombosis of the central artery of the retina.

J. J. Thomas[8] states the case very fairly by concluding that migraine may occasionally result in permanent paralysis, aphasia, or hemiopia, and that in most instances this is due to an attack favouring a vascular lesion in persons who already have disease of the vessels, but that in others the lesion may occur in young persons whose blood vessels are in all probability in a normal condition; and that although great caution is necessary, before ascribing such paralyses to migraine, to exclude coincident and independent disease—for example, of the vessels—yet a few cases remain which justify the statements made by Charcot and others that the normally transient hemiopia or aphasia may become permanent.

3. *Migraine Attended by Temporary Paresis.*

Cases in which paresis or even paralysis, temporary and recurrent, is one of the regular phenomena of the attack. In the ordinary way this consists of slight motor weak-

ness in the limbs, generally the arm, accompanying or following the sensory disturbance—for example, pins and needles, etc.—of transient duration, from a few minutes to half an hour, not of common occurrence, and, as a rule, only present in severe attacks. For instance, a patient of mine, who suffered from severe migraine, described a pricking sensation in the right arm, which then went numb, and she could not feel if touched upon it. With the numbness there came loss of power; she could "move it but not use it." The same feelings spread to the leg, so that "she could not walk" for a few minutes. The symptoms passed off in the same order, and were most severe in the arm. According to her statement the sense of position of the limbs was retained. In Dr. Liveing's classical work on migraine, p. 14, a good case of this kind is given. His general conclusion is that "in some few cases loss of sensibility is accompanied by a certain loss of motor power in some parts—in fact, a transient hemiplegia" (p. 87). He quotes some other cases where the temporary paralysis was marked; one of those from Dr. C. H. Parry of Bath is a good example, but in some of the others the diagnosis seems to be doubtful; one of them, for instance, was a case of Adams-Stokes disease.

Spitzer [9] refers to the occurrence, as an unusual feature of migraine, of transitory paresis, of monoplegia or hemiplegia, but gives references chiefly to "ophthalmic migraine." Féré describes a case in which paralysis and loss of sensation came on with attacks of migraine shortly after the onset of the attack. The paralysis lasted for one to one and a half hours and disappeared with the scotoma. Cases of transitory aphasia are not so uncommon as part of the attack; in most of the cases the speech affection is stated to be sensory aphasia, but in some it is due to defective articulation, the patients are not able to "form their words," whilst full comprehension is retained. Otherwise, I have not been able to find in the literature of recent years any cases of transient hemiplegia occurring during attacks of migraine and complete for the time they last, which are quite free from objection as not being possibly due to other morbid conditions, for example, a previous attack of syphilis, present at the same time.

A remarkable case is reported by Professor Osler, in which attacks of recurrent hemiplegia, migraine, and angio-neurotic oedema were associated in the same patient, though not at the same time. I quote from the account given by Dr. A. E. Russell.[10]

"The patient, a medical man, aged 29, at the age of 12 years had an attack of right hemiplegia with aphasia which lasted seven or ten days. Within the year he had five or six further attacks of hemiplegia, each successive one less severe and not accompanied by aphasia, and from that date was subject to occasional attacks of numb, tingling sensation in the side. From the age of 26 he became subject to severe attacks of migraine. At 28 he had a sudden attack of pain and swelling in the feet, and at the same time began to suffer from soreness at the ends of the fingers. He had frequent attacks of angio-neurotic oedema of the upper lip and outbreaks of urticaria associated with severe darting pains in the legs. He had one attack of abdominal colic with pain in the calves of his legs, and an outbreak of purpura and urticaria; later, he suffered from haematuria and albuminuria. Professor Osler considered that the recurring attacks of hemiplegia were probably associated with changes in the brain of essentially the same nature as those which subsequently occurred in the lip and skin—in other words, that an angio-neurotic oedema occurred in the brain substance."

History of a Family in which Migraine was Attended by Recurrent Hemiplegia.

I will now give the history of the family which has recently come under my observation. They belong to the working class, and, as is well known, people of this status often lose sight of their relations, and are unable to give accurate details of their condition. The three members of the family from whom I obtained the information were above the average in intelligence, and clear in their statements. Evidence as to four generations was available. The great grandparents (H) were said to be free from the affection, and had a very large family (the exact number was not ascertained), of whom four certainly—one son and three daughters, and possibly another son—were affected. Two of the daughters were unmarried, the third married a man not liable to migraine and had a daughter, who had at least one attack of migraine with paralysis.

CASE I.

The son, H_2, suffered from attacks of headache with transien paralysis all his life; the paralysis involved one side only, and there was marked affection of vision. His last attack occurred about the age of 54; he was taken in a tram-car with loss of power in the right arm and leg and great impairment of vision followed soon by intense headache. He had to be carried home from the car, as he could not walk without support. Pleurisy or pneumonia followed shortly after this attack, of which he died three weeks later.

The history of the affection of vision, hemiplegia, and headache which occurred in the tram car in this order was very definite, and the other attacks from which he had previously suffered were stated to be similar, and equally severe as regards the loss of power.

This man had a son, H_3, a daughter (M), both affected, two other sons unaffected, and another daughter who at the age of 5 years had whooping-cough. After a violent paroxysm of cough she had right hemiplegia, which lasted three weeks, and then cleared up, together with loss of speech, from which she took a long time to recover.

CASE II.

H_3, examined, but not seen in an attack. A small, pale man, a porter, aged about 47; no evidence of organic disease. Has suffered from attacks of hemiplegia with migraine since the age of 28. For years they came on about every two to three months, but of late years have been much less frequent, and he has had freedom from them for as much as two years. If at any time he was run down in health the attacks came much more frequently. Order of phenomena in the attack: (1) Dimness of vision in both eyes, no scintillating scotoma; (2) sometimes simultaneously with this a feeling of numbness or tickling, starting in toes or feet, and spreading upwards; (3) loss of speech, consciousness being unaffected, "he can understand what is said to him, but cannot reply"; (4) hemiplegia, in which there is absolute loss of power on one side, and he cannot stand, together with slight loss of sensation on the affected side; (5) nausea, occasionally vomiting. The loss of power, of speech, and the nausea last for about an hour, and as they pass away, (6) intense and incapacitating headache comes on and lasts for one to two days. Although the hemiplegia is of short duration, he is generally laid up for two days by the attack, and often does not feel quite well for a week. The hemiplegia is nearly always right-sided; both sides of the body are never affected in the same attack; loss of speech accompanies the hemiplegia, whether the latter is on the right or left side.

This man married a healthy wife; of the four children, aged 17, 14, 12, and 9 years, two are affected.

CASE III.

H_4, daughter of above, aged 14. This patient looks healthy, and presents no signs of organic disease. The attacks began at the age of 7, and recurred every two or three months, but have ceased for the past year. They consist of (1) dimness of sight, (2) loss of speech, (3) right hemiplegia, (4) intense headache with vomiting, followed by (5) drowsiness. She may sleep or lie in a drowsy condition for two or three days after an attack. The hemiplegia is always right-sided; loss of consciousness or muscular twitchings have never occurred. The hemiplegia sometimes comes on with extraordinary suddenness, so that she has been taken with an attack when standing, and has suddenly fallen from giving way of the leg. In this case the hemiplegia lasts for a few hours, or even a day.

CASE IV.

H_5, a boy, aged 9. An intelligent child, but has always been delicate, and goes to invalid school. As a small child he suffered from severe rickets, and in consequence had difficulty in walking until the age of 7 years. He then had an operation for straightening his legs, and after that was able to walk and improved in health. He has been well lately, and on examination, except for some anaemia and traces of rickets, there was no evidence of disease. He has had two attacks in which there was a greater extent of paralysis than in any of the other patients.

On October 25th, 1909, he was taken for a midday drive in the carriage belonging to the invalid school which he attended, and the lady in charge thought that he looked ill. The child then said to her: "Miss R——, it is getting dark. I can't see you." Shortly afterwards she lifted him out of the carriage, and found that he could not stand, and had lost the use of his right leg, loss of power in the right arm quickly followed, together with loss of speech; he seemed to know what was said to him, but could not answer; the face was not affected. Twenty minutes later he lost power in his left leg, and then in his left arm, so that he was helpless and paralysed all over; moreover, he could not hold his head up; if lifted, it dropped again to one side. This attack lasted about two hours, and the paralysis began to improve towards the end of this time; he complained of headache in the frontal and occipital regions, asked to go to bed, and vomited two or three times. There were no muscular twitchings or convulsions. The paralysis passed off in the order of onset. The attack left him weak for three or four days, especially in the right arm and leg, and then he recovered completely.

On November 26th he had a second attack, without assignable cause, whilst at school. It began at noon with loss of sight, followed by loss of power, first on the right, and then on the left side, as in the first attack. Speech was also lost, but he was quite sensible. When brought home at 4.30 p.m. he had

recovered speech, but was quite helpless, the loss of power affecting both sides of the body. He complained of very severe headache, and vomited all the day. Recovery took place in about the same time.

He was admitted into the Bristol General Hospital and remained there for nine weeks. During this time he had no attack. Beyond some anaemia, which improved under treatment, he appeared healthy, active, and intelligent for his age. At Christmas time he was purposely allowed to eat indigestible and rich foods, and as he had a large appetite he took full advantage of this, but no attack resulted.

After being for a week on a diet of bread 6½ to 7 oz., butter ¾ oz., meat 3 oz., 1 egg, potatoes 2 oz., rice pudding 3 oz., milk 16 oz., with one orange or apple, the analysis of the urine made by Dr. Emrys-Roberts was as follows:

Quantity in twenty-four hours, 515 c.cm. Specific gravity 1020, acid, no albumen, no sugar, no deposit. Urea, 2.5 per cent. Uric acid (Hopkin's method, 0.3757 gram). Creatinin (twenty-four hours) 1.455 grams (Johnson's method; two estimations). Phosphates calculated as phosphoric acid 1.03 grams. Chlorides calculated as NaCl 5.66 grams.

CASE V.

M_1, sister of Case II (H_3), a healthy-looking woman, about 35 years of age. Examination detected no disease of the nervous system or of thoracic or abdominal organs. In her case the attacks began in childhood, and continued at intervals of two to three months until her last pregnancy two years ago, during which they were much more frequent, sometimes recurring two or three times in one week. Since then for the past fifteen months she has been free from them. There was never any recognizable cause, and they came on at no particular time of day.

The first symptom is visual; apparently there is hemiopia of the upper halves of the visual fields, for she sees only the lower half of objects looked at. This gives her a warning to lie down, as the next symptom is hemiplegia, which sometimes comes on suddenly, as she states that if she were standing she would fall down. The affected limbs feel heavy, "like lead." The hemiplegia is generally right sided, but occasionally left sided; it is accompanied by loss of speech, but not of comprehension; the speech affection accompanies the hemiplegia, whether the latter is on the right or left side. The face is apparently not affected. She has a peculiar feeling of swelling or thickness on the same side of the tongue as the hemiplegia. There appears to be hemianaesthesia as well as hemiplegia, at any rate in some of the attacks, for on one occasion when tested by a pin prick there was no sensation on the affected side. There is no deafness, and no affection of the sphincters. After about two hours vomiting with severe frontal headache (bilateral) comes on, and the paralysis after the first attack of vomiting begins to gradually pass off. The headache always came with the vomiting, and never preceded the other symptoms. The patient has five children; the eldest, 9 years old, is Case VI; the younger ones have so far had no attacks.

CASE VI.

M_2, a boy, aged 9, was admitted to the Bristol General Hospital on November 30th, 1909. He had had two previous attacks of migraine with transient right hemiplegia during the preceding six months, from which he had completely recovered. He had had no other illness, and was a healthy, intelligent boy. He was left-handed.

On the morning of November 30th the boy complained of not feeling well and of a headache, and stayed home from school. His mother did not see him again until the afternoon, when she found that he was paralysed in the right arm and leg, could not stand, and could not speak. He also vomited.

On admission the patient was very cold and somewhat collapsed. His temperature was 95°. There was no head retraction, no convulsions, or muscular twitchings. There was right hemiplegia, complete; the paralysis was flaccid. There was paresis of the right side of the face, affecting the lower part most, as in the ordinary hemiplegic type; the tongue was protruded to the right. He spoke very indistinctly and with difficulty, and occasionally used wrong words. He recognized his mistakes and understood what one said to him. He had some difficulty in swallowing. The right knee-jerk was said to be absent on admission, but as he was only examined lying down this is doubtful; it was certainly present next day.

On the next day, December 1st, the temperature was 97.6°; respirations 20; pulse 80, regular; tension normal. There was still well-marked right hemiplegia with flaccidity and slight hemianaesthesia—that is, sensation to touch and prick distinctly less acute than on the left side. He was conscious of the position of the paralysed limbs. He was still dull and drowsy, complained of left-sided frontal headache, had difficulty in speaking, used words wrongly, spoke slowly and indistinctly, and had slight difficulty in swallowing; he could only take liquid foods.

Reflexes.—Elbow, supinator, knee, and ankle jerks present, normal and equal on both sides; abdominal reflexes present, cremasteric absent, plantar reflexes extensor.

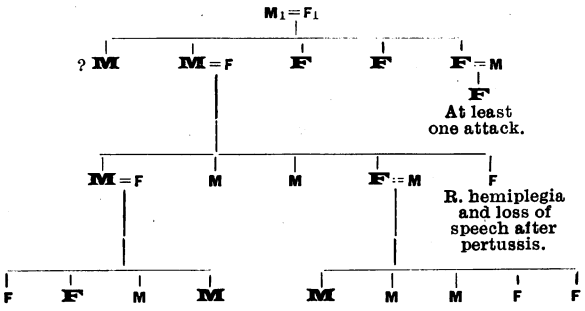
Cranial Nerves.—Well marked right hemiopia. Optic discs normal, except for some fullness of the veins. Smell normal.

No oculo-motor paralysis; no nystagmus; pupils equal, large, act to light and accommodation. Paresis of lower part of face on right side; orbicularis palpebrarum and frontalis muscles unaffected. Not deaf. Tongue protruded to right. Palate normal. No affection of sphincters.

On December 3rd there was still very slight defect of sensation to light touch, and prick on right side of face, front of chest and abdomen, and right arm and leg. No loss of sense of position of limbs. Paresis of right side of mouth and of right arm remained; the leg had recovered. There was no ataxy of movement. The reflexes as before, except that whilst the right plantar was of extensor type still, the left was flexor. He was still rather drowsy and speech was indistinct.

During the next two days the condition rapidly improved, and on December 5th he was normal, and there was no trace of paralysis left.

It may be added to the above that the motor loss was throughout much greater than the sensory, which was always slight; and that as this patient was the first member of the family to come under observation, and on admission we had no complete history with him, nor could he give any account of his two previous attacks, owing to the temporary loss of speech, the true nature of the condition was not at once recognized, and the electrical reactions were unfortunately not taken at the height of the paralysis. Later the muscles reacted well to interrupted current.



GENEALOGY OF A FAMILY WITH ATTACKS OF MIGRAINE WITH HEMIPLEGIA.

M_1 and F_1 had a numerous family (exact number uncertain), of whom four certainly, and probably five, were affected.
The heavy type indicates the affected members.

Seeing that, as I have shown, motor paralysis to such a marked degree as existed in these patients is extremely rare in migraine, it is first necessary to establish the point that the attacks are of this nature. As there is no exact clinical test or pathologico-anatomical change to which we can appeal to make the diagnosis, each case must answer to certain criteria, which will naturally be those symptoms which are generally recognized as typical of the migraine attack. The more a case departs from the well-recognized type, or presents features not hitherto recognized as component parts of it, the greater care must be taken that the typical characters of migraine are present.

Attacks of headache more or less exactly reproducing the phenomena of migraine are occasionally seen as symptomatic of organic disease, such, for instance, as a cerebral tumour. Organic disease in these cases can be positively excluded by:

1. The hereditary history.
2. Lapse of time in the older patients—the attacks have occurred for years—during which no sign of organic change has appeared.
3. The recurrent paralysis has not become permanent in any of them. In such severe attacks this of itself is remarkable, and is sufficient for the argument.

The following are the points on which I base the diagnosis of migraine for the actual attacks: (1) The marked hereditary tendency, direct transmission, and absence of other neuroses in the family; (2) the onset of the affection in most of the patients in childhood; (3) the characteristic visual phenomena preceding the headache, especially temporary hemiopia; (4) headache, generally unilateral; (5) the vomiting which generally accompanied the onset of the headache, and after which the condition of the patient began to improve; (6) return to the normal in the interval between the attacks; and (7) the temporary loss of speech and sensory disturbance which are well-known features of some severe attacks of migraine. In all these points the attacks in this family so exactly correspond and these features so regularly repeat themselves in successive attacks—this regularity of repetition of the phenomena of the attack in the same patient being another characteristic of migraine—that the diagnosis of migraine seems to me established.

The remarkable feature is the addition of hemiplegia, or in one case of paralysis of all four limbs and muscles of neck, which cannot be accounted for as a secondary result of the sensory disturbance present.

There are a few points in the attacks in this family worthy of further remark. First, the hemiplegia, loss of speech, and hemiopia were phenomena of the aura of the attack, and in all cases regularly preceded the headache. In most attacks in all the patients the hemiplegia was right sided, and much less often occurred on the left side of the body. The speech defect was on the outgoing side of the cerebral mechanism for speech, the patients either could not articulate or only imperfectly, but could always understand what was said to them. This is contrary to what is described as the usual condition when aphasia occurs in migraine, for "sensory" aphasia is stated to be more common than "motor," although the latter occurs. Some of these patients were, however, definite on the point that they could hear and understand, and knew what they wanted to say, but could not speak. I think, speaking generally, that in migraine the affection of speech is not infrequently of this type.

This speech defect occurred indifferently with either right or left hemiplegia—that is to say, it regularly accompanied the hemiplegia, and in the adult patients, as well as in the children. In the latter it is well known that aphasia may accompany either right or left hemiplegia of organic origin. This indifference to the side of the hemiplegia seems to me a point of great interest. It has been observed before that in cases of migraine with sensory disturbance speech defect might accompany sensory phenomena in the left arm, left side of tongue, or left hemiopia.

The attacks seem to be becoming more severe as they descend the family, the two children last affected have more severe attacks than their parents, so much so that in one of them the paralysis affected the muscles of the trunk and limbs on both sides.

The frequently sudden onset of hemiplegia is particularly noticeable; more than one of the patients stated that if it came on when they were standing they had fallen down, and one used to lie down on the first appearance of the visual aura to avoid a fall. This is comparable with the sudden onset of hemiopia in some recorded cases of migraine. The relation of the attacks to pregnancy in Case v is curious, and it is well to accentuate the points that in none of the patients, even in case of a fall from sudden hemiplegia, was there ever a momentary loss of consciousness, or muscular twitchings, or convulsions, or affection of sphincters, or spasm of the muscles; the paralysis being of flaccid type.

Lastly, the recovery is complete between the attacks, and in no case have they left so far any permanent paralysis or disability.

In relation to the diagnosis of these cases reference must be made to the form of recurrent paralysis known as "family periodic paralysis." There can, I think, be no question as to the marked differences which distinguish the attacks of the latter disease from those of my patients. I have already given the points which identify them with an unusual and severe form of migraine, and need not recapitulate these further than to say that severe headache, hemiopia, and sensory disturbances—other than occasionally tingling and numbness—are not present in "family periodic paralysis," which consists of a recurrent and transient flaccid motor paralysis, not of cerebral type—for example, there is loss of electrical irritability in the affected muscles—affecting usually the trunk, all four limbs (proximal parts first), and muscles of the neck.

Whilst the attacks are thus distinct, there is another question as to a possible relation between the two affections. As a rule, migraine does not appear in the family history of the victims of family periodic paralysis, but in one remarkable family described by Holtzapple,[11] the disease was closely associated with migraine. In four generations of this family, eighteen persons suffered from severe attacks of migraine, and seventeen from periodic paralysis. Of the latter, five were subject to both affections, twelve to periodic paralysis only, and thirteen to headache only. All the patients were descended from an ancestress who suffered from sick headache only, and in the branch of the family most severely affected, and in which three deaths occurred, the mother had migraine but no paralysis.

In some respects the family I have described above affords features which carry whatever relation there may be, if any, between the two diseases a stage further, for in it there is the very unusual addition to typical migraine of an extensive motor paralysis, with a closer hereditary transmission than is often seen in ordinary migraine, and in one of the patients last affected in the third generation the paralysis, in the attack, beginning as a hemiplegia rapidly spread to the opposite side and affected the neck muscles, so as to become general.

The character of the paralysis in the two affections is, however, so essentially different that any apparent connexion may be no more than the common tendency for one neurosis to be associated with another in the same or different members of a family.

In family periodic paralysis the seat of the lesion is in the muscles or in the junctions of the lowest motor neurones with the muscle fibres, whilst in migraine the paralysis is of cerebral type. It is impossible not to be struck with the similarity of the hemiplegia, accompanied by more or less degree of anaesthesia, in the cases described above, to the hemiplegia of functional disease, especially hysteria. There are, however, differences between them which probably indicate in this case also a difference in the anatomical seat of the lesion. For instance, in hysteria the alteration of the visual field is not a hemiopia, but a concentric contraction; the face altogether escapes, the paralysis is "ideational," and due to the dissociation of the highest psychical centres from those next below. According to Campbell, associated with each of the known cortical centres there is a corresponding higher or psychical centre. He describes a psycho-motor, psycho-sensory, psycho-visual, and psycho-auditory centre in close relation to the motor, sensory, visual, and auditory centres seated in the praecentral, occipital (calcarine), and superior temporal gyri. Dr. McDougall,[12] in his paper on the mode of action of fatigue in the nervous system, incidentally suggests that in hysteria the supply of energy is insufficient to overcome the resistances of the highest levels of the brain and to keep open the connecting channels.

In the recurrent hemiopia, disorders of sensation, and occasional paralysis of migraine the anatomical position of the lesion must be below these levels. It is important to note that these disorders occur early in the attack, precede the severe pain, and therefore they cannot be explained on any theory of inhibition due to the intensity of the latter. Moreover, abortive attacks are known in which transient hemiopia, aphasia, etc., are the sole features.

In Dr. McDougall's paper, referred to above, he attributes the phenomena of fatigue or exhaustion to such an increased ratio of the resistance to the supply of nervous energy at command at the synapses or junctions of the neurones that nervous impulses can no longer pass through, and the connexion between the neurones at the points of junction or synapses affected is interrupted. This increased resistance at the synapses may be induced by exhaustion or by accumulation of the waste products of activity.

It is reasonable to suppose that some endogenous or exogenous poisons may act in a similar way on the nervous system and produce paralysis by greatly increasing the resistance at certain synapses.

Without entering into a full discussion of the various theories of migraine, it seems to me that the disease may be best accounted for by the accumulation within the body of some self-manufactured poison, gradually accumulating until a periodical attack results, and showing a selective action on certain neurones, or rather upon their synapses, and possibly by becoming attached to their receptors preventing them from carrying out their functions. In view of the known selective action of various poisons upon special sets of neurones, there is nothing improbable in such a view of the localization of symptoms which characterize most attacks of migraine.

Such a view has, to my mind, more in its favour than the theory which is perhaps most generally accepted at the present time—namely, that vasomotor disturbance or spasm of cerebral vessels is the cause of the attacks of migraine. It must be admitted, however, that the pathology of migraine remains obscure in spite of the many explanations that have been offered, and, indeed, to suppose that in ordinary attacks the action of the poison remains localized to cortical sensory structures, whilst in cases such as the family above described there is in

addition a toxin able to act upon the kinaesthetic (motor) centres is but to state in other words a clinical observation and not to explain its essential nature.

4. There is still another form of motor paralysis associated with migraine—the so-called ophthalmic migraine (Charcot's "migraine ophthalmique"). I have left this to the last, as it is impossible to consider it fully in this paper, and its connexion with migraine is denied by good observers. Thus, it has been called hemicrania with third nerve paralysis.[13] Undoubtedly cases grouped together under this head own different pathological causes. Most commonly the paralysis is confined to the third nerve on one side, but in other cases of a similar kind the fourth, fifth, and sixth (and occasionally the seventh) nerves may be also affected. The reasons why some authors have separated these cases from true migraine are that in many cases there is no aura, no heredity, the pains may last for weeks, and some degree of paralysis persists in the intervals. There are, however, other cases which satisfy all the above criteria for ordinary migraine, and in which there is a return to normal between the attacks.

Probably the accounts have been written from two distinct groups of cases: (1) Cases in which intermitting attacks of third nerve paralysis are preceded by attacks of headache corresponding in clinical aspect (including aura and heredity) to typical migraine, and do not end in permanent paralysis; (2) cases which show periodic exacerbations, but in which from the first, or early in the course of the disease, there is a certain amount of persistent weakness which ends in permanent paralysis.[14]

In the first set of cases we may probably go further and say with Senator and Bernhardt that there is no recognizable lesion, whilst in the second group the lesions that have been found in the few cases that have undergone pathological investigation are (1) tumours (Karplus and Thomsen) at the base of the brain involving the third nerve, (2) a mass of granulation tissue, and (3) syphilitic lesions in the same situation.

Cases of this nature, however, form a clinical group so distinct from ordinary migraine that they are better considered apart from it until more is known about them.

REFERENCES.

[1] William Russell, On Intermittent Closing of Cerebral Arteries, BRITISH MEDICAL JOURNAL, 1909, vol. ii, p. 1109, and correspondence, ibid., pp. 1313, 1380, 1499, 1580, and 1715. [2] *Cerebral Circulation*, 1898, p. 124. [3] Casuistische Beiträge z. Prognose d. Hemikranie, *Charité Annalen*, xv, 1890, p. 298. [4] Zur kenntniss der bleibenden Folgen des Migränes Anfalles, *Wien. klin. Woch.*, 1901, Nr. 28, p. 673. [5] J. J. Thomas, *Journ. Nerv. and Mental Dis.*, 1907, vol. xxxiv, p. 153. [6] See also W. Harris, *Lancet*, 1907, vol. i, p. 276. [7] *Ueber Migräne*, Jena, 1901. [8] Loc. cit. [9] Loc. cit. [10] *Some Disorders of Cerebral Circulation*, Goulstonian Lecture, 1909. London: Medical Publishing Co, 1909. [11] *Journ. of Amer. Med. Assoc.*, 1905, xlv, p. 1224. [12] McDougall, *Brain*, 1909, vol. xxxii, p. 256. [13] *Nervous Diseases in Childhood and Early Life*, J. Taylor, London, 1905, p. 344. [14] See Spitzer, loc. cit., in which numerous references are given.

ON THE VALUE OF SERUMS AND VACCINES IN THE TREATMENT OF DISEASE.

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IN the hospital to which I am attached are admitted almost every variety of acute disease, some in a favourable condition for treatment, but a great many others in a very unfavourable condition, but I have included in my results all the most unfavourable cases, so that a fair and accurate conclusion as to the value of these remedies should be reached.

Acquired Immunity.

In the case of certain diseases such as small-pox, scarlet fever, typhoid, and measles, one attack protects against another for many years or even a lifetime. In other diseases such as erysipelas, influenza, and pneumonia, a person may suffer from several attacks, and in the case of erysipelas and influenza may even be more disposed to other attacks. I think it will be granted, however, that every disease produced by an organism does confer a certain immunity for a longer or shorter period. We do not know precisely how the human body recovers from an acute infection by dangerous organisms. It is presumed that the virus becomes exhausted in a varying time, and so dies out, but it has been found that in the case of such diseases as acute pneumonia, diphtheria, typhoid, and cholera, certain antibodies antagonistic either to the organisms or their toxins are formed in the blood. It would appear that a process of immunization is going on during the course of an acute disease, and when this immunization is complete the disease comes to an end. Now we want to encourage and promote this good effect, and if by the administration of serums and vaccines we can assist the blood to produce immunity, we are going a long way towards promoting the recovery of our patient.

Antistreptococcic Serums.

I have during the last twelve years treated 210 patients suffering from acute streptococcic infections with injections of antistreptococcic serum—an antibacterial serum prepared by inoculating a horse with increasing doses of streptococci until immunity is complete, and then using the serum of the horse as a remedy. Some authorities hold that all the various streptococci are in reality the same organism modified by circumstances. Marmorek holds this view and Aronson finds that an antitoxin produced from any single strain will produce an immunity against them all. My first 28 cases were treated with a dried serum manufactured from a single strain of streptococcus which was I believe isolated from a case of erysipelas; 17 of these cases were puerperal septicaemia, all of a severe type and generally sent into hospital when the disease was far advanced. In spite of this we observed in a fair proportion of cases distinct benefit followed the injections, which were then given under the skin, and a few patients recovered whom we expected to die. I noticed that the reaction from a single strain serum was always more severe than from a serum made from many strains. Eight cases of acute erysipelas were treated with this serum and in all cases recovery followed its use without the formation of pus. The remaining 4 cases suffered from cellulitis of a streptococcal origin and in 3 cases the result was good, but in 1 it had no effect and the patient died.

In my opinion we have made a distinct advance in preparing a polyvalent serum prepared from 20 to 26 distinct strains of streptococci. We have treated 182 patients with polyvalent serum, and I can unhesitatingly say that the results are most gratifying. The more local infections appear to do better than the general systemic infections such as puerperal septicaemia, but even in this formidable disease we have obtained excellent results. It is our general practice now to inject the serum into the rectum instead of under the skin; 20 or 30 c.cm. of serum are mixed with 40 c.cm. of normal saline solution and gently poured into the rectum, which has been previously washed out with a little water. The serum is rapidly absorbed, and seems to act quickly and efficaciously without any toxic effects such as urticaria, erythema, or headache, which sometimes follow injections under the skin.

Puerperal Septicaemia.

The cases vary enormously in intensity, but must be carefully distinguished from sapraemia, the result of absorption from retained débris within the uterus, in which emptying the uterus generally ends in recovery. In puerperal septicaemia we have to deal with a systemic blood infection with streptococci, and we must direct our efforts to assist the blood in producing an immunity. In many cases the violence of the infection is too acute and the woman is destroyed, but in a great many instances much can be done; and, combined with general and restorative treatment, injections of 20 or 30 c.cm. of serum twice daily seem to have a good effect. Every case of streptococcal infection, whether mild or severe, is invariably treated with rectal injections of polyvalent serum. Sometimes it is only necessary to give one or two injections before general improvement commences.

Erysipelas.

In acute erysipelas we get the very best results from serums; in fact, I look on all cases as favourable if there is no formation of pus or extensive subcutaneous cellulitis. In these cases extensive incision and drainage must be combined with large doses of serum two or three times daily.