THE PAIN PATHWAYS IN MIGRAINE

BY

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The term "migraine," the derivation of which has been stated by Kinnier Wilson (1940),* is probably best used in a clinical sense to denote a particular variety of headache and not with a pathological implication suggesting that the physio-pathological processes which cause the head pains are known. The characteristic features of migrainous headaches are unilaterality and periodicity, the pain starting slowly, reaching a peak of severity, continuing at this degree of severity for a varying period of time, and then slowly receding. Most typically, the headache is associated with black spots in front of the eyes, with flashes of light, or with formed and coloured visual hallucinations. There are, of course, many variations. In particular, the pains may be mild or severe: they may or may not be accompanied by visual phenomena: they are often bilateral, and they may radiate into the face or neck.

Headaches of a migrainous type may be divided into two distinct groups: (i) those associated with a demonstrable pathological lesion, such as a cerebral aneurysm; (ii) those which cannot be accounted for by local cerebral change or by gross metabolic disturbance. It is with the latter group only that this communication is concerned.

In migraine, as in other painful conditions, before treatment can be instituted the clinician must have some conception of the nature of the disturbance which initiates the pain cycle, of the site at which the painful impulses arise, and of the anatomical pathways by which painful impulses are conveyed to the brain.

First let us consider the site at which the painful impulse arises. This may be in the brain tissue itself or in one of those structures of the head—the scalp, periosteum, meningeal vessels, the large arteries at the base of the brain, and the dural sinuses—which are known to be capable of reacting in a painful way to an adequate stimulus (Penfield, 1940). From all these possibilities—and, of course, there may be others unknown—the pain of migraine is believed to arise in the arteries of the scalp and dura mater. The reasons for this belief are as follows:

(1) The walls of large blood vessels have been proved to be painful, and some to possess local sign. When operating under local anaesthesia, crushing of the trunk or of the large branches of the meningeal artery will cause extreme discomfort, and the patient will be able at least to "lateralize" the pain.

(2) Spasm of a large artery will lead to pain. Once when dissecting in the neck under local anaesthesia, in order to carry out cerebral angiography, the internal and external carotid arteries went into extreme spasm. Immediately severe pains were complained of in the same side of the head and face, and the patient slowly developed a contralateral hemiplegia, which equally slowly receded.

(3) Extreme dilatation of an artery will lead to pain. This can be proved by isolating a segment of a large artery in the scalp and by injecting saline forcibly into its lumen.

* "Migraine is derived from Galen's *ἡμικρανία* through L. hemigranium and L.L. hemigranea, later migranea. In England hemigranea became mygrame, myegrym, migrim, and megrim. Migraine itself is French."

(4) The vascular changes which accompany migraine. The skin of the forehead in an attack is often deadly pale, the temporal arteries are distended, and there may be associated neurological signs which can only be accounted for by cerebral ischaemia. Occasionally a retinal vessel can be seen to be in spasm.

(5) The experiments on headaches produced by histamine (Clark, Hough, and Wolff, 1936).

(6) The relief of migraine by injections of ergotamine tartrate.

If the vascular origin of migrainous pains is accepted, then it is easy to conjecture on the essential disturbance which starts the pain cycle.

A popular theory is "neurosis of the cerebral autonomic nervous system." This postulates that there is an unstable equilibrium (Hughlings Jackson, 1931) in one or other of the central mechanisms of the autonomic nervous system, such as the hypothalamus, which reacts abnormally to some of the many stimuli that reach it from other parts of the nervous system or blood stream, thereby discharging abnormal impulses to the more peripheral parts of the sympathetic and parasympathetic nervous system (Fig. 1). This theory may

FIG. 1.—The sympathetic innervation of the blood vessels of the brain, dura, and scalp.

explain why the so-called causes of migraine already described are legion. It will be seen, however, that the nature of the original disturbance which causes migraine and the site at which the painful impulse arises are essentially matters of speculation.

The last point to be considered is the pathway by which the painful impulses are conveyed to the brain. Do these impulses pass to the brain stem by way of the known or rather by way of the described autonomic pathways or otherwise? An attempt to answer this question will be found in the following series of cases.

Case I

Mrs. J. S. reported to me at the Salford Royal Hospital on July 12, 1940, complaining of migraine which she had had for many years and for which she had received treatment by Dr. Don and Prof. Jefferson. Her pain was chiefly right-sided, but occasionally the left side was affected. Typically, it would come on suddenly in the region of the forehead, rapidly spreading to the eye and to the back of the head. Often it would travel down into the cheek but never as far as the lip. In severe attacks she would vomit and the sight in the right eye would become dim. The pain often lasted for a week or more, when she might be incapacitated for several days and be confined to bed.

On examination she proved to be a well-built little woman, aged 40, with no emotional complexes and of good average intelligence. There were no abnormal neurological signs, and special investigations failed to reveal any pathological change to account for her pain. The diagnosis of migraine, made by other competent observers, was confirmed, and later I saw her in a typical attack. She insisted that something surgical must be done to give her relief, as all kinds of medical therapy had failed. Therefore I discussed with her the possibilities of thoraco-cervical sympathectomy and trigeminal root section, but before deciding to operate persuaded her to submit to a further course of medical therapy, including injections of ergotamine tartrate. Again the recognized forms of treatment, adequately administered, failed to satisfy her.

On the afternoon of Sept. 3, 1940, I operated on her under general anaesthesia in the sitting position, and divided the upper and inner third of the right trigeminal root, through the lateral extradural approach of Frazier. At the end of the operation she was conscious, and the next morning was perfectly well and fully co-operative. The denervation was satisfactory, the anterior two-thirds of the scalp on the operated side being numb, as well as the upper part of the cheek. A Buller's shield was fixed in position to protect the insensitive cornea. The immediate result was excellent; she felt easy and confident. From the time of the operation she has not had another attack of migraine, although she does complain of tingling pains at the junction of the numb and sensitive areas in the cheek. The following is an extract of a report from Mr. Wyse, resident surgical officer of the Salford Royal Hospital, dated June 18, 1942:

"I saw Mrs. S. yesterday. She has had a very worrying time recently, having lost her mother, and she states that she would never have been able to carry on had she not had her operation. She has never had migraine since, she states; and says that the operation has been a wonderful success. She gets occasional pains in the right side of the forehead in the form of hot stabs, but these do not worry her. She has practically no pain on the left side. She feels her face a bit numb and stiff, of course, and says the cheeks swell badly at times, but she has had no trouble with the right eye."

Case II

Miss D. R., aged 25, first came to see me on Nov. 23, 1935, at my out-patient department of the Christie Hospital at the request of her general practitioner, Dr. Friedlander. She was complaining of pains in her head, which were so severe that she had been completely disabled and off work for several weeks. The pain was so bad that her doctor thought in the early stages that she might have a cerebral tumour, or an obstructive hydrocephalus due to meningeal adhesions. Typically, the pain started low in the right temple as an indefinite ache, then travelled across the eyebrow to the middle line, at which time it became exceedingly severe. She likened the pain to the sensation that might be felt if something were being driven hard into the frontal bone. At no time did she have visual hallucinations, but in some attacks felt so ill and nauseated that she would lose several pounds in weight. Occasionally she had pains on the left side of the head, but these were much less severe than those on the right and certainly were much less frequent.

Examination showed her to be a thin little woman who looked about 18 rather than her 25 years, and weighed only 6 stone. Intellectually she was well above the average. She was rather highly strung, but enjoyed life and had no psychoneurotic tendencies. Apart from a moderate degree of hyperreflexia, there were no abnormal neurological signs to point to any focus of organic disease in her brain; also special investiga-

tions revealed no abnormality. A diagnosis was made of migraine, and she was put on a further course of medical therapy, including injections of ergotamine tartrate. In May, 1939, she declared that medical treatment, which I believe was correctly administered, had not given her satisfactory relief, and she asked for something further to be done. I therefore discussed with her the possibilities of fractional trigeminal root section, alcohol injection into the Gasserian ganglion, and thoraco-cervical sympathectomy. It was decided to divide the upper fibres of the posterior trigeminal root.

On May 11, 1939, under general anaesthesia, I divided the ophthalmic fibres in the right trigeminal root and also the second division of the trigeminal at the foramen rotundum by the lateral extradural approach of Frazier (Fig. 2). A rapid

FIG. 2.—The trigeminal in the middle fossa. For the treatment of migraine usually the ophthalmic fibres only in the posterior root are divided. In some cases, however, it is also necessary to divide the second division at the foramen rotundum.

and uninterrupted recovery was made from the operation. The trigeminal denervation was satisfactory. Anaesthesia was present in the first and second divisions of the trigeminal field, the third division being spared.

Since the operation, in spite of loss of sensation in the cornea, there has never been any suggestion of keratitis (ulceration of the cornea), and this is due to the eye remaining moist, the nerve of tear secretion—the great superficial petrosal nerve—having been spared at the time of the operation (Rowbotham, 1939).

There was complete relief of pain until Sept. 20, 1939, when at the end of a period of menstruation a pain was experienced on the right side of the head (that is, the side operated on). The pain was much less severe than before the operation, and lasted for a shorter time. Moreover, it was changed in character, being now described as a hot rather than as a deep pressing sensation. In spite of this recurrence of pain Miss R. stated that she "was a different girl" and quite able to do her work, whereas before the operation she had been seriously incapacitated. In Oct., 1940, she was still very satisfied with the results of the operation. The following is the latest report from her, dated Aug. 1, 1942:

"You will, I know, be just as pleased to hear, as I am to write, that I am quite a different and happier person from what I was a little over three years ago, thanks to the complete relief from pain effected by the operation which you performed."

Case III

Miss M. U., aged 48, reported to me at the Christie Hospital in April, 1939, complaining of severe pains in the right side of the head, from which she had suffered periodically for three years. In character the pain was a severe ache, and at its peak would affect the whole of the right side of the head, radiating into the eye and upper part of the cheek. The headaches were accompanied by nausea, although she never vomited; sometimes she noticed black spots in front of her eyes. On rare occasions she had attacks of pain on the left side of the head.

On examination she was seen to be a thin miserable-looking woman of an obviously neurotic disposition. Moreover, she was a spinster, and it was suspected that the pain might be psychogenic in origin. Clinically, there were no abnormal neurological signs to point to any cerebral change to account for her pain, and special investigations were negative.

A provisional diagnosis was made of migraine, and this was confirmed by keeping her under observation in hospital. Medical therapy failed to give her any lasting relief. With some hesitancy I decided to sever the upper fibres of the right trigeminal root. On April 27, 1939, under general anaesthesia, I divided the ophthalmic fibres in the trigeminal root and also the second division of the trigeminal at the foramen rotundum, via the lateral extradural approach of Frazier. After the operation she was anaesthetic in the first and second divisions of the trigeminal, the third division being spared.

The right cornea remained healthy until investigations into the problems of tear secretion were carried out. After this a keratitis developed which necessitated closure of the lids by tarsorrhaphy. For many months this woman was completely relieved of the pain in the right side of the head, but later began to complain of pains elsewhere in the body and, according to her doctor, was beginning to show distinct mental changes.

On Jan. 24, 1942, Prof. Jefferson wrote to me to say that he had seen the patient again. He told me that my operation had completely relieved the pain on the right side of the head but that obvious migrainous pains were starting on the left side. Moreover, she complained of pains elsewhere in the body.

Discussion

The possible criticism that, in my posterior root section cases, the relief of pain might be due to division of the auriculo-temporal and meningeal arteries is vitiated by the fact that injection of the Gasserian ganglion (Harris, 1936) will give relief, and this does not interfere with the blood vessels concerned. Also, division of the meningeal artery, and presumably also of the auriculo-temporal artery, in some cases of migraine has proved not to give relief (Craig, 1935). Moreover, the auriculo-temporal artery is not necessarily divided in posterior trigeminal root section, and certainly in two of my cases the large trunk of this vessel was not ligatured or diathermized. In any case, the ophthalmic artery is not involved in the lateral approach to the posterior trigeminal root, and it is along this vessel that many migrainous pains presumably arise. Finally, it is unlikely that local interference with a distal mechanism will ease pain of an extensive distribution.

If it is correct that the painful impulses in migraine do, in fact, enter the brain stem along the posterior trigeminal root, then it is still necessary to discuss how they reach the ganglion from the periphery. There are two possibilities—either they enter the ganglion from the autonomic plexus in the region of the foramen lacerum medium or they course along the ophthalmic and maxillary trunks of the trigeminal (first and second divisions). Probably the trigeminal trunks are the anatomical pathways concerned. This opinion is difficult to prove because the critical operation of section of the first and second divisions themselves in a suitable case has never been carried out, for the reason that section of the ophthalmic division (not the ophthalmic fibres in the posterior root) is a very difficult manoeuvre, although it can be done (Rowbotham, 1939). In two of my cases, when the pain extended into the face, I sectioned the ophthalmic fibres only in the posterior nerve root, and the second division at the foramen rotundum, with the relief of pain. It must, however, be realized that it is impossible to know precisely how many fibres are being divided when fractional section of the posterior trigeminal root is being performed.

In one case, when a migrainous pain was confined to one side of the forehead, I divided the supra-orbital and supra-trochlear nerves without dividing the supra-orbital vessels, with relief of pain. This is a very simple operation, and is worthy of trial when severe pains are localized to the forehead.

At this point it would be profitable to inquire into the results of thoraco-cervical sympathectomy in the relief of migrainous pains. Unfortunately very few such operations have been carried out for the deliberate relief of headaches, but in cases done chiefly for vasospastic states in the arm, Love and Adson (1936) found that of 16 cases of concomitant headache the headaches were relieved in 12. The efficiency of this method in relieving pain, I find, has been questioned by White (1942) and Telford (personal communication). Whether or not relief is obtained by sympathectomy does not help in settling the route of conduction of the painful impulse, because relief when it is obtained by this operation can easily be explained by destruction of those pathways along which the original disturbance that initiates the painful impulse is conveyed. In other terms, sympathectomy destroys the motor and not the sensory arc of the mechanism of migraine.

My series of cases at least suggest that the painful impulse in migraine passes through the posterior trigeminal root, but they do not prove by any means that this is the main sensory pathway of the autonomic system of the head. Possibly the trigeminal pathway acts purely as a special defence mechanism. The main problem of the sensory pathways of the autonomic

system still remains an enigma, and will possibly remain so until better methods of staining autonomic fibres have been discovered.

I have published these cases at this time because they throw light on the state of post-concussional headache, which is one of the main problems in His Majesty's Forces to-day. In many cases of post-concussional headaches no organic cause is demonstrable, either clinically or by encephalography, and many are labelled psychoneurotic or nervous. Possibly in many so-called nervous headaches the pain is not purely one of perception but is due to an unstable mechanism resulting from the injury, leading to atypical migrainous pains. This type of headache in Service cases is, I believe, much more common than the headache due to dural traction the result of adhesions.

REFERENCES

- Clark, D., Hough, H., and Wolff, H. G. (1936). *Arch. Neurol. Psychiat.*, Chicago, **35**, 1054.
 Craig, W. McK. (1935). *Proc. Mayo Clin.*, **10**, 362.
 Harris, W. (1936). *British Medical Journal*, **2**, 112.
 Jackson, J. Hughlings (1931). *Selected Writings*, vol. 1, Hodder and Stoughton, London.
 Love, J. G., and Adson, A. W. (1936). *Arch. Neurol. Psychiat.*, Chicago, **35**, 1203.
 Penfield, W., and McNaughton, F. (1940). *Ibid.*, **45**, 43.
 Rowbotham, G. F. (1939). *Brain*, **62**, 364.
 White, Jas. C., and Smithwick, R. H. (1942). *Autonomic Nervous System*, 2nd ed., Kimpton, London.
 Wilson, S. A. Kinnier (1940). *Neurology*, **2**, 1570, Arnold, London.

THE SYNDROME OF HAEMORRHAGIC SUPRARENAL INFARCTION

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The syndrome of primary infarction of the suprarenals is very rare, and unilateral infarction has not been described at all. There are only some 14 cases of haemorrhage into the suprarenals in adults recorded in the literature in which any description is made of the clinical picture. None of them were diagnosed in life, even at laparotomy, and all were fatal. The syndrome described in this paper is that produced by thrombosis of the suprarenal vein with resulting haemorrhagic infarction of the suprarenal gland, in an adult. Other causes of haemorrhage into the suprarenal are: (a) in the newborn; (b) in meningococcal and other acute infections, in which the picture clinically is that of the acute infection: the Friderichsen-Waterhouse syndrome is discussed in differential diagnosis here, and another case added to the 60 already described; (c) as a part of a general haemorrhagic state. The thesis put forward is that the suprarenal infarction syndrome is recognizable in life, and possibly treatable.

Case History

The patient (D. V. K.), an intelligent woman aged 32, was 8 months pregnant. The pregnancy had been normal except for occasional morning vomits, in some of which there had been streaks of blood. Two days previous to the illness the urine was albumin-free and the blood pressure 120/80. On March 28, 1941, at 12.30 p.m., she complained of feeling cold, after which she walked half a mile with no further complaint. Half an hour later pain appeared in the right side below the ribs—persistent, "like a stitch"—which made her put her right hand to the side and bend over to the right. This pain was exacerbated by the movement of the car and by walking. The pain below the right costal margin steadily increased in severity. There was no nausea, and the appetite was good. Pallor and sweating now became evident in spite of a strong pulse of 70 a minute.

2 p.m.—Patient restless in bed, in severe pain, which remained the whole time localized to a spot over the fundus of the uterus to the right of the umbilicus about 2 in. below the costal margin in front. There was no pain in the loin. Vomiting began at this time—copious, free, and sudden. This continued repeatedly until the end. Micturition was natural, and urine showed no haematuria. On examination there was some cold-