PAIN AND ITS UNDERLYING PATHOLOGY.*

By G. F. ROWBOTHAM, B.Sc., F.R.C.S.,
Neurosurgical Unit, Newcastle-upon-Tyne.

INNUMERABLE attempts have been made to define pain by physiologists, by pathologists, by clinicians and by philosophers, who all see the problem from a different angle, and who discuss it each according to his own particular mode of expression and training. The distinguished writers of the past centuries devoted much attention to the subject of pain, but wrote largely on its origin and on the various types rather than on its actual nature.

This communication, I believe, would serve a useful purpose if its sole achievement were to persuade readers to write down their own definitions in clear, unambiguous language. My own opinion is that pain is the sensation of disagreeableness; of disagreeableness in its own right, as distinct from that type of disagreeableness which exists as a quality of other modalities of sensation such as smell and from misinterpretations at the neural level of consciousness. The first type of pain will, in future, be referred to as true pain.

It is very illuminating to listen to a patient's description of his symptoms unaided by suggestions or by leading questions. Usually the investigator receives a very blurred picture of the discomforts from which the narrator is suffering. On prompting, a pain may be described as "sharp and shooting," "deep and boring," "bursting," "pressing," "dragging," "burning or cold." Severity of pain is also variable and one commonly hears the terms "unbearable, awful, terrible, just annoying or irritating." Allusions are occasionally made to colour and, of course, description depends on temperament, education and nationality, etc.

In the attempt to solve any scientific problem the first thing to do is to formulate the questions that are going to be asked and on which the research must be based. In the case of pain the questions to which an answer must be attempted are five-fold, and they are, I believe, as follows:

1. What is the essential disturbance that causes the pain cycle?
2. At what region does the pain impulse arise?
3. How is the pain initiated or—in other words—what is the adequate stimulus?
4. What are the pathways by which the pain impulses are conveyed to the brain?
5. Where does the impulse reach consciousness?

1. Disturbances causing a pain cycle fall easily into three distinct categories:

(*a*) When the lesion is obvious.

(*b*) When the lesion is not obvious, but can be demonstrated by special investigations.

(*c*) When the lesion cannot be demonstrated by any known means.

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2. A painful impulse can arise in any region from the terminal nerve fibrils to the sensory cortex; moreover, with the exception of the cerebral cortex, any quality and any severity of pain can be aroused in any region and by all sorts of pathological lesions. On the other hand, sensations other than those of pain seem to be appreciated only when they are initiated at their specialized end-organs, and I can recollect no case where stretch or any other kind of interference with the trunk or root of a mixed sensory nerve has led to an unpainful sense of touch, or of heat or of cold. From the cortex of the brain itself it is exceedingly difficult to arouse by artificial stimulation any sensation other than that of pins and needles, and this probably by means of initiating an epileptic disturbance.

How is a Painful Impulse Initiated?

In the large majority of cases, whether the pathological lesion be a carcinoma, an abscess or a spasm of the bowel resulting from an ulcer, the painful impulse is probably initiated by distortion. More rarely the impulse is aroused by the direct action of noxious chemical substances or by physio-chemical phenomena, such as osmosis.

Pathways by which Pain Impulses are Conveyed to the Brain.

Can a true pain, which arises peripherally, be transmitted to the brain by any sensory nerve fibre and tract, or is it conducted along pathways restricted to painful impulses only? The problem is not yet resolved, but there is a good deal of evidence that there are specific pathways for pain. For example, there are special nerve-endings for every modality of sensation, and in the antero-lateral or spino-thalamic tracts of the spinal cord there is a discrete tract for the conduction of painful impulses. Also, in peripheral nerve, histology has shown that there are fibres of differing diameters and myelinizations suggesting that each is concerned with conduction of a different type of message. By means of the oscillograph, electrical disturbances of differing patterns and speeds can be registered when differing sensations are passing along the sensory nerves and, in particular, a pain sensation arouses a relatively constant type of electrical disturbance.

It must be realized, however, that our knowledge of the sensory pathways is still very imperfect. Little or nothing is known of the sensory autonomic pathways, and I believe that pain impulses not only travel up the spino-thalamic tracts, but also up the posterior columns of the spinal cord.

Sensations, other than those of the special senses, enter the brain stem from the face and head, not only through the trigeminal nerve but through the 7th, 9th and 10th cranial nerves and probably through the others also.

With these few introductory remarks let us venture into the realms of clinical medicine, and in particular let us consider the very difficult problem of pains in the head and face. A pictorial representation of the various painful syndromes will save time, and this can be done most easily in the form of graphs (see Fig. 1). Let us consider the problem of migraine. This is a well-known disease. It is common amongst university staffs and, like epilepsy, it remains

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one of the enigmas of clinical medicine. Typically, a patient gets up in the morning feeling a little off colour, with a sense of discomfort in the head. He may feel sick and refuse breakfast. Soon his head begins to ache, the pain slowly increasing in severity until a plateau is reached, as shown in the diagram. Classically, the pain is unilateral, though often it is bilateral, severe pains

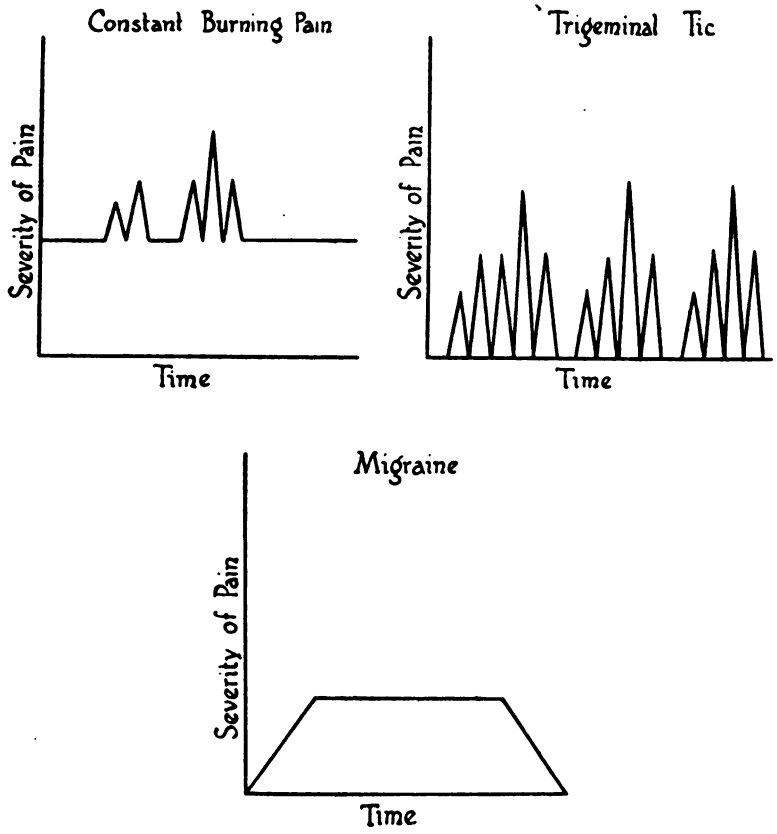


FIG. 1.—Diagrams.

behind the eyes or in the forehead being common. Occasionally the pain radiates into the ears and down into the neck, and more rarely into the face. There may or may not be visual hallucinations, such as spots, lights, scotomas or blackouts. In severe cases transient palsies, particularly of the extra-ocular muscles, may result. Relief most easily comes with sleep. The variants of migraine are, of course, legion. I take it that most of you are clinically acquainted with the picture and, no doubt, some of you have had first-hand experience.

According to medical writings the causes of an attack of migraine are innumerable: a stuffy atmosphere or too much fresh air; too little or too much sleep; too little or too much food; boredom or mental exhilaration. Often the attacks come on for no known reason, and many sufferers will tell you that their malady is controlled or conditioned by the phases of the moon.

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First of all, let us ask in what structure does the painful impulse arise and what is the adequate stimulus? We know from operative experiences that:

1. The scalp with all its five layers is painful.
2. The periosteum is extremely painful.
3. The bone itself is insensitive and can be cut without causing the slightest discomfort other than that of noise.
4. The dura is painless save for three distinct regions—
   (*a*) Near the meningeal vessels.
   (*b*) Around the margins of the bony foramina at the base of the skull.
   (*c*) Near the large dural sinuses, and particularly at the points where the cerebral veins drain into them.
5. The large vessels at the base of the brain before they enter the brain tissue itself are sensitive.
6. The brain tissue is completely insensitive. It can be cut, diathermized, squashed, torn, etc., without causing the slightest sensation, given that an epileptic disturbance is not started up in the sensory cortex.

Now of all these possibilities, which of the tissues are affected in migraine? Most of the evidence, I believe, points to the blood vessels of the scalp and dura and to the large arteries at the base of the brain, the adequate stimulus for pain being excessive spasm or dilatation. The reasons for this belief are as follows:

(*a*) The walls of large blood vessels have been proved to be painful and to possess local sign.

(*b*) Spasm of a large artery will lead to pain.

(*c*) Extreme dilatation will lead to pain, and this fact I have proved by forcing saline under pressure into a segment of the auricular temporal artery.

(*d*) Vascular changes which accompany migraine: for example, the skin of the forehead in an attack is often deadly pale and the temporal arteries sometimes can be seen throbbing wildly. Also associated neurological signs can only be accounted for easily by cerebral ischaemia. Occasionally a retinal vessel can be seen to be in spasm.

If we believe that the painful impulse in migraine does, in fact, arise in the surface arteries of the head and that excessive spasm or dilatation is the adequate stimulus, then we may continue our inquiry and ask by what pathways the painful impulses are conveyed to the brain. The answer to this question is exceedingly difficult, because few anatomical facts are known about the sensory side of the autonomic nervous system of the head.

It has been one of my interests to try to solve this part of the problem. In a small series of cases of migraine I have divided the upper third of the posterior trigeminal nerve root on the affected side with satisfactory relief from pain. Thus, it is reasonable to say that at least in some cases of migraine, the painful pathways pass through the upper third of the trigeminal root.

It is known that no sensory fibres enter the Gasserian ganglion other than through its trunks or divisions. Since the ophthalmic division is represented in the upper part of the trigeminal root, the pain pathways in migraine

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must traverse the ophthalmic trunk for, at least, some part of its distance. Exactly where the nerve fibres do enter the ophthalmic trunk is not known. At the periphery, it is not known with certainty whether nerve fibres subserving pain actually end in the arterial coats themselves. What is certain, however, is that most of the large vessels of the head are accompanied by branches of the trigeminal nerve which could be easily effected by movement

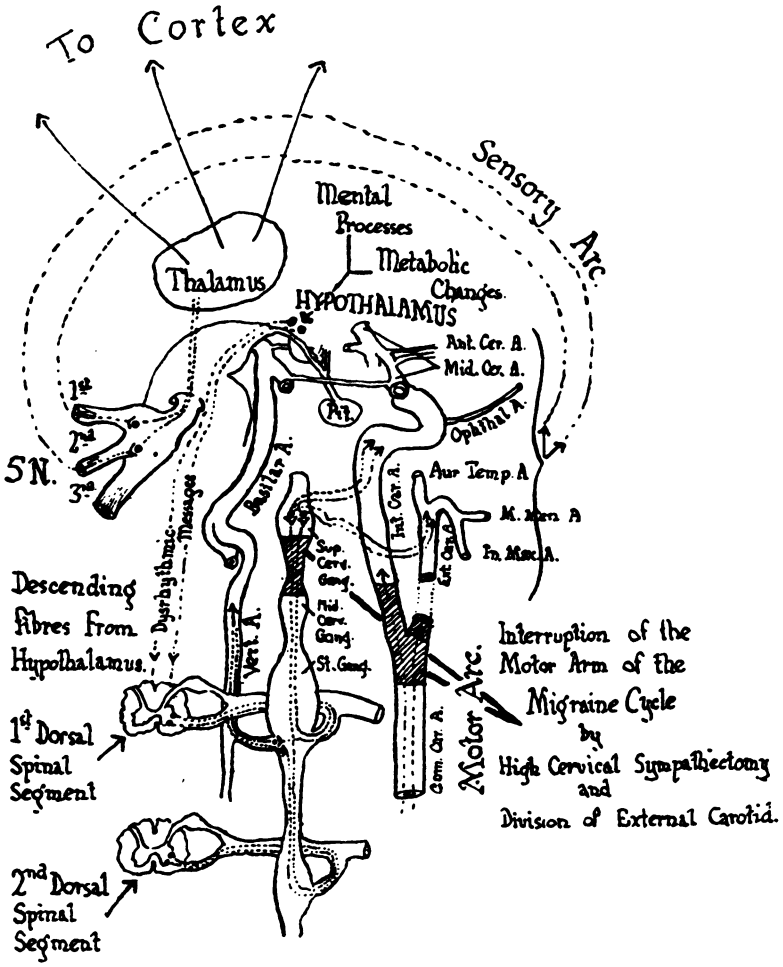


FIG. 2.—The Migraine Cycle.

of the adjacent blood vessels. To summarize, the only fact of which we are absolutely certain is that in some cases of migraine the pathways of pain traverse the upper third of the sensory root of the trigeminus.

The Motor Arm of the Reflex Arc.

Let us now consider the efferent autonomic nerve supply to the blood vessels concerned. The efferent or vaso-motor pathways are fairly well known to neuro-anatomists and the diagram summarizes present-day knowledge (Fig. 2). In a series of cases I have divided the cervical sympathetic

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pathways high up in the neck, have stripped the external, internal and common carotid arteries for a distance of one inch each way from the bifurcation of the common carotid, and at the same time have ligatured and divided the external carotid artery. In other words, I have made radical attempts to prevent motor impulses from the brain reaching the arteries concerned. The results have been as follows:

CASE 1 concerns a young medical practitioner, born of migrainous parents, who suffered from such severe and oft-repeated headaches that he had become completely incapacitated. After a bilateral high cervical sympathectomy he was relieved of his pains and has now been free from headaches for over a year; he is back at work.

CASE 2.—The second patient was a young man whom I saw at the request of Dr. Pool. He had been admitted to The Retreat as a result of intractable headaches, and Dr. Pool believed that this young man was not a psychoneurotic and that he showed no psychotic tendencies; in fact, it was suspected he might be suffering from a cerebral tumour or some other equally serious intracranial lesion. I was fortunate to see him in a severe attack of pain and diagnosed a cerebral aneurysm. Neither diagnosis was confirmed by special investigations, and later it was obvious that the man was suffering from severe migraine. A high cervical sympathectomy completely relieved him of his pain, and he is now fully occupied on the land and can carry out a heavy day's work without inconvenience.

CASE 3 concerns an Assistant Matron who was in danger of losing her position because of intractable and incapacitating migraine. Satisfactory relief was obtained in this case, again by cervical sympathectomy, and she has been back at work for many months without a break.

CASE 4 was a young lieutenant in the Army who suffered from severe and oft-repeated unilateral headaches, to account for which no organic lesion or metabolic disturbance could be demonstrated. In this case a sympathectomy gave him no relief.

The Migraine Cycle. (Fig. 2.)

With the foregoing experimental information allied with neuro-anatomical and neuro-physiological facts, we can build-up a system that will help us in the better understanding of the mechanism of migrainous pains. It is justifiable to suggest that there is but one cause of migraine—an inheritance of an unstable mechanism, usually in the hypothalamus. This unstable mechanism reacts excessively, on occasions, to some of the multitudinous stimuli that normally reach it, either from the higher centres or from the blood-stream, and consequently sends explosive or dysrhythmic messages to the blood vessels concerned, setting them into spasm and dilatation, too much of this or too little of that being merely precipitants or activators of the migraine cycle.

From the spinal cord dysrhythmic messages are conveyed to the cerebral vessels via the known motor pathways of the cervical sympathetic nerves. The painful messages are conveyed to the brain via the upper part of the posterior trigeminal root. Thus, relief from pain in certain cases of migraine can be obtained by interruption either of the sensory or motor arm of the migraine cycle, by fractional trigeminal root section or by high cervical sympathectomy.

I could take up many similar problems—for example, the problem of pain in the pelvis—but time makes it necessary to ascend to higher neurological levels. My experience of trigeminal tractotomy has been that it relieves

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pains that are relieved by posterior root section, but does not relieve pains that are unrelieved by trigeminal root section.

The Higher Neural Levels.

I have had no operative experience with the optic thalamus, but I have had some with the cerebral hemispheres. In three cases of intractable facial pain I have resected the facial area of the sensory cortex, the delineation being accomplished, first of all, by mapping out the corresponding motor area with a faradic battery. In the first case there was no relief from pain, and no material difference in the mental attitude of the patient towards his pain. The same result was obtained in the second case. In the third, though there was no relief of pain, the patient's attitude changed. Instead of being completely morose, he became a little more social and genial; in particular, whereas before the operation he would sit brooding by the kitchen fire, he would now go out and meet his friends and drink a glass of beer. In a few weeks' time he had put on 1½ stones in weight.

Again, in three cases of intractable facial pain I have performed a bilateral frontal leucotomy with the following results:

(*a*) In one case there was no relief from pain and no apparent difference in the patient's reaction towards it.

(*b*) In Case 2 there was no relief from pain and the patient showed a tendency to exhibitionism.

(*c*) In the third case, following operation, the patient remained mentally confused, and probably he should be regarded as a high-grade mental defective. He was incontinent of urine and of faeces, and his condition was suggestive of akinetic mutism. When spoken to he would answer after a long latent interval, often relevantly, usually facetiously, and occasionally impertinently. When chided about his incontinence he would go off to the lavatory and remain there for hours until somebody went to bring him back. On the other hand, he voluntarily declared that he was free from pain, and when questioned would never admit that he was suffering any facial pain.

If this experiment can be repeated I believe it is an observation of fundamental neurological importance, because it shows that interruptions of the sensory arm of the nervous system can be made at levels higher than that of the well-known cortical reception areas. Surgical interruptions, of course, cannot be made at the thought level; they must be neuronal disturbances, and thus leucotomy raises the question whether physical sensory impulses do, in actual fact, reach consciousness in the post-rolandic sensory cortex. We are led to the conclusion by the foregoing experiments that some forms of consciousness are reached only at the highest neural or neuronal levels. Possibly, when in other surgeons' experiences resections of the sensory cortex have given rise to relief from pain, the relief may have been due to subtle changes in personality and in ways of thinking. There may be more than one way of performing a leucotomy, since the operation is merely a surgical interference with a neural integration, and would have been classified by the old physicians as an alterative. For the appreciation of pain there must be a certain type of neural "set-up," and certain alterations of this "set-up," whatever agencies are sought to bring them about, may so alter the mechanism that it is no longer receptive to pain. Leucotomy, as we all know, is a crude alterative.

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It has, however, directed our thoughts to the highest neural levels for the relief of intractable pain and, no doubt, other and better methods of interfering with the highest neural integrations will be found, the best of which would be of a psychiatric nature.

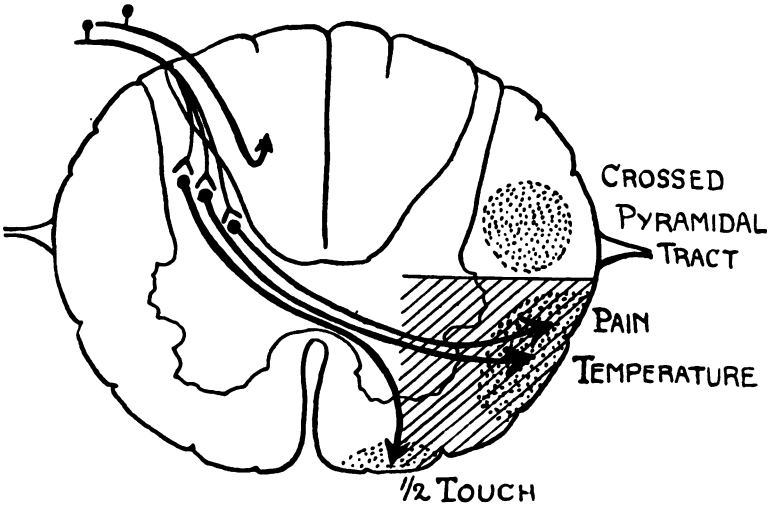


FIG. 4.

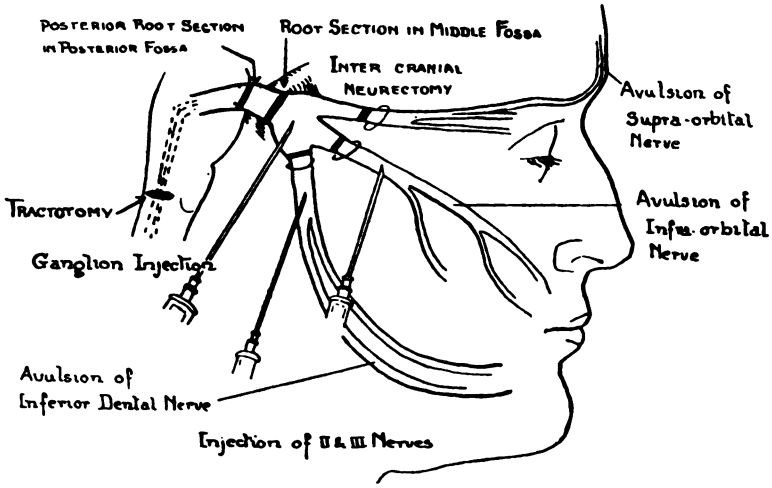


FIG. 5.—Injections of the Trigeminus.

Pathological and Clinical Groupings.

From the study of 1,000 cases of intractable pain and from my surgical experiments of cordotomy, injection of the trigeminal nerve, trigeminal root section, tractotomy, corticectomy and leucotomy (Figs. 3, 4, 5, 6 and 7), I believe that pain rests on four broad pathological bases and consequently there emerge four distinct clinical groupings:

Group 1 consists of those cases where the essential cause of pain is a physical agent, such as a pin-prick, and where a physical message is aroused thereby

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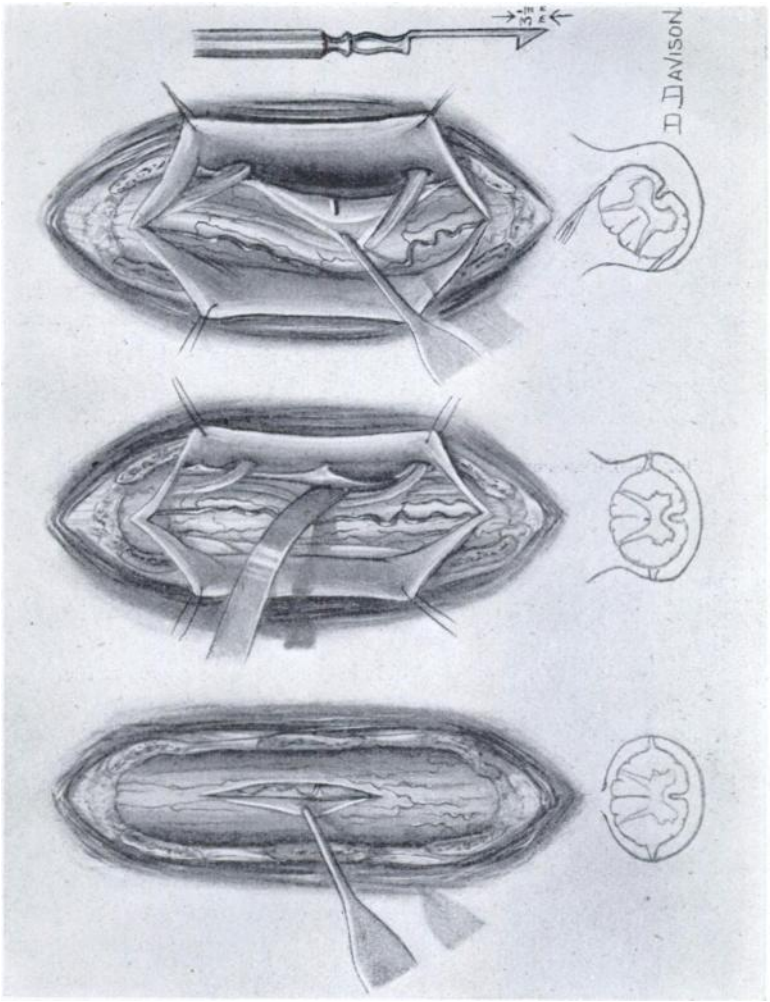


FIG. 3.—Operation of Cordotomy.

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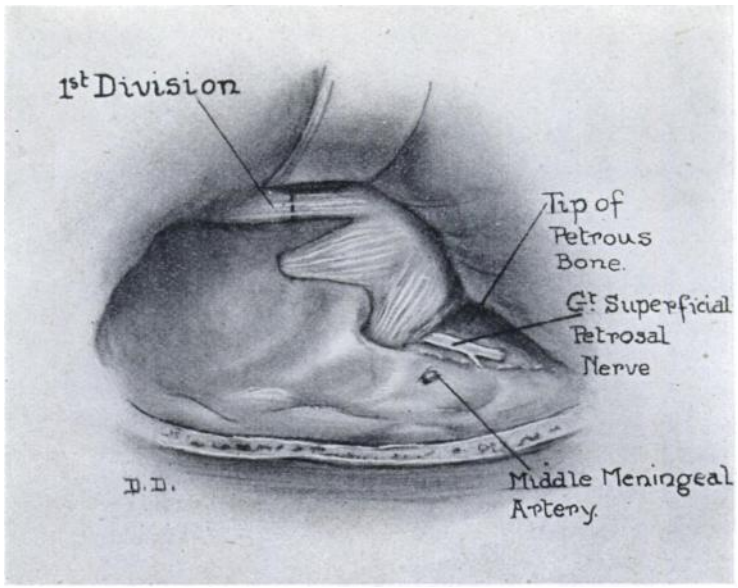


FIG. 6.—Exposure of the Gasserian Ganglion via the temporal route.

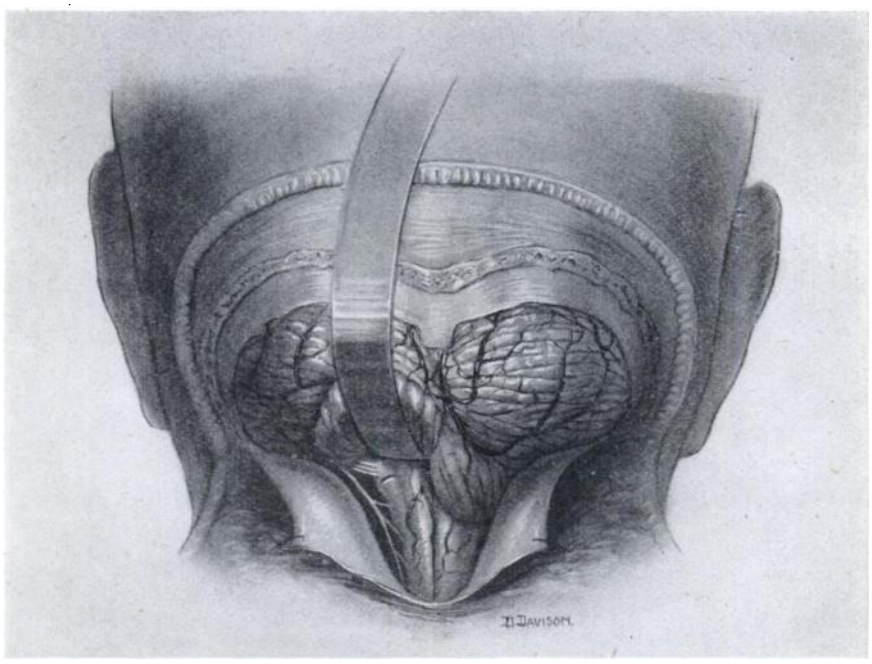


FIG. 7.—Tractotomy.

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and conveyed along physical pathways to arouse a physical activity in the neurones of the brain. From the brain a non-physical translation occurs into the mind.

Group 2 contains those cases where the abstract or thought process or worry, anxiety or ambition arouses a physical message in the periphery of the body followed by a physical neuronal disturbance in the brain. This type of case we find in migraine and in some instances of duodenal ulcer. This is a most important group from the psychological point of view, and merits a further study by this society.

In Group 3 we have those cases where sensations of the autonomic activities, which normally are quiescent, reach consciousness; we see this possibly in psychosis where patients complain of " feeling like a block of ice from the neck downwards " or a feeling of board-like rigidity in the stomach or perineum, or who say that when food reaches their throats it becomes completely lost and does them no good. I would like here to suggest that this be a subject for discussion at a future meeting.

Group 4 concerns psychogenic pain. By this we mean pain which is indistinguishable from physical pain but which arises in the mind and has no known accompanying physical process.

Conclusions.

In some conditions, of which migraine is an example, the start of a pain cycle is in the abstract—a thought process. The thought process initiates a physical disturbance in the periphery of the body, a physical message in the nerves and, finally, a physical metabolic disturbance in the neurones of the brain. From the neurones the physical phenomena go back to the abstract —to consciousness. This complex abstract-physical-abstract mechanism must engage the interests both of the psychiatrist and of the organic neurologist. The thought process is essentially in the province of the psychiatrist; the physical disturbance is the concern of the organic neurologist. The link between the abstract and the physical processes is a metaphysicalo ne, and it is on this metaphysical no-man's land that the psychiatrist and the organic neurologist are now meeting. Moreover, this metaphysical link occurs at the beginning as well as the end of the pain cycle, and up to now it has been at the early link where the neurosurgeon's interest has been primarily engaged.

The nature of the metaphysical link is one of conjecture, and as far as I can understand from the writings of Locke, Hume and Berkeley, the answer is not known, and cannot be until the stature of man's mind increases and a better conception of the universe is formulated.

Discussion.

The President said that the paper would arouse much thought and was open to a variety of comment. As a neurologist he would be interested to know whether patients after the operations suffered corneal lack of sensitiveness, and whether they had to use a Buller's shield. At the end Mr. Rowbotham had raised the question of the physiogenic and psychogenic basis of pain. One could not afford to ignore either aspect. Different schools of thought had been fashionable from time to time. Whereas twenty years ago the psychogenic approach was the more

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popular, recently there had been, as it were, a reaction in favour of the physiogenic, with leucotomies and insulin shock treatment. They had all seen the vast number of " causes " to which Mr. Rowbotham had referred, but in some cases symptoms suggested a definite toxic basis, although others seemed to show a psychogenic origin. Perhaps further developments with electro-encephalography would vouchsafe an answer in the future. He was interested, too, in the comments on hypothyroidism.

He would like to hear the comments of a gynaecologist. Those psychiatrists who worked in out-patients' departments often had referred to them women who had lost a considerable portion of their internal genitalia before it occurred to someone that the trouble might be psychogenic in origin. Often it was largely a defence reaction against advances on the part of the other partner which were not desired. He had had one such woman who had one ovary removed as well as the whole of her uterus and half of the other ovary; it was only after the pain had spread up her side that she was referred to the psychiatrist.

If they had a discussion on the paper from the psychogenic and neurological points of view, it might last until many of them were in London!

Dr. Pool described a case whose history showed two epileptic fits at five-year intervals up to 1939. The subject was then called up, and although he reported the epileptic fits and a typical migraine, he was accepted for the Army. He was promoted to be an officer and was sent out East, where his migraine became worse and worse, and he was finally sent home and discharged on medical grounds. The Army psychiatrists considered him to be a psychoneurotic, but Dr. Pool said he considered their statements much too dogmatic, particularly in view of the past history of epilepsy. The Ministry of Pensions rejected the man's claim for compensation, but Dr. Pool advised him to appeal, and told him to write out in support of his appeal extracts from all the standard text-books, which showed that all neurologists classed migraine with epilepsy, whereas Ross did not mention it among the neuroses.

He felt that tribute must be paid to the organic and autonomic basis of migraine, and one must not neglect the borderland between the two. He was interested in Mr. Rowbotham's diagram of the cycle of migraine, and his query as to whether it might be completed through the meninges. He had had a case in which the cause ultimately turned out to be a parietal tumour.

Mr. Rowbotham, in reply, told how he, as a young man, had been in a company of neurologists when another young doctor who was with him, said, " Look here, it is no good being a neurologist; one must either be a neuro-surgeon or a psychiatrist. What are you going to be? " Mr. Rowbotham replied that his course was already mapped out for him; his companion was, of course, going to be a psychologist. Another of those present overheard this conversation and said: " I suppose you two think you are taking divergent routes and will never meet again, but I tell you that before long you will both meet—somewhere in the frontal lobe! "

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