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MIGRAINE AND THE SYMPATHETIC NERVOUS PATHWAYS

BY

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The pain of migraine is probably due either to excessive spasm or to dilatation of the arteries of the scalp and dura mater. It has been shown that the painful impulses are, in some cases, conveyed to the brain through the upper half of the posterior root of the trigeminal nerve on the same side, and so the trigeminal pathways may be regarded as a sensory arm of the "migraine cycle" (Rowbotham, 1942).

What is not known is why the arteries concerned occasionally contract or dilate excessively. One theory is that a migrainous person is born with an unstable mechanism in the hypothalamus which reacts excessively to the multitudinous stimuli that reach it, either from the higher centres or through the blood stream, and causes explosive or dysrhythmic messages to be sent to the large blood vessels of the head. It is an anatomical fact that these large blood vessels are supplied with motor fibres from the efferent side of the autonomic nervous system. Therefore, if disordered messages from the hypothalamus are in fact transmitted by the motor autonomic pathways to the vessels concerned, then section of those pathways should give relief in cases of migraine.

Experiments to Test Hypothesis

The following series of experiments was designed and carried out to test the verity of this supposition.

Case 1

This concerns a young doctor aged 30 years. The history is that from the age of 8 he had suffered from periodic headaches. At the age of 14 he began to study for matriculation and higher school certificate, and from then onward the headaches became increasingly severe and more frequent. He obtained a scholarship into a medical school and finally qualified M.R.C.S., L.R.C.P., intending later to sit for a university degree. In the postgraduate period his headaches became so severe that he became virtually incapacitated, and on occasion suffered pains in the head which lasted for five days or more. His condition apparently was hereditary, as his mother, grandmother, and great-grandmother had all suffered from migraine.

Typically, an attack of headache would be preceded by hallucinations of light in the right homonymous field which ended in a complete right homonymous hemianopia. The hallucinations of light would, on the average, last for twenty minutes, and the homonymous hemianopia for about an hour. Occasionally tingling feelings would also be felt in the right hand and the right leg. Sometimes, during an attack, the right pupil would be contracted and the right side of the face flushed. One hour or so after the onset of the visual hallucinations a pain would start as a burrowing sensation in the region of the left temple, and as the pain became more severe it would radiate backwards and forwards until the whole of the left side of the head was affected. Only rarely did the headache extend to the right side of the head. Sometimes the pain on the left side radiated into the upper part of the face. A feeling of nausea was usual during an attack, but actual vomiting was only occasional. After the attack was over the left side of the scalp was sore and accommodation of the eyes was difficult. The attacks of headache might occur without being preceded by visual hallucinations.

On examination the patient was found to be a man of good intelligence; mentally alert in every way, quick to answer questions, and quick to appreciate the logic of an argument. He showed no sign of nervousness when being closely cross-questioned. All his movements were smoothly co-ordinated, and the pulse was normal in rate and rhythm. No abnormal neurological signs were found, and later special investigations and tests failed to reveal any abnormality in the head or in the general metabolic processes. Though it was realized we might be dealing with a cerebral vascular anomaly of the arteriovenous type, we felt that angiography was not called for.

Diagnosis.—From the periodicity of the head pains and the premonitory visual hallucinations there was little doubt that we were dealing with a case of migraine. Moreover, in view of the long-standing history and the absence of abnormal physical findings, it was justifiable to regard the migraine as being of the idiopathic or primary type.

At a neurological clinic elsewhere, full investigations had been made and a diagnosis arrived at of a psychoneurosis of the anxiety type. Moreover, in the near past my patient had been taking excessive quantities of analgesic and soporific drugs, and had on this account been in trouble with higher governmental authorities. The doctor admitted that he was highly strung, and agreed that his headaches were almost invariably precipitated by some psychological activity. What he was adamant about was that it was mental excitement or exhilaration which led to trouble, and not a sense of depression. When fully enjoying himself, making investigations into a problem which particularly interested him, he would be struck down by a violent headache and left incapacitated for a week or more. He had no objection whatever to the periods of mental exhilaration: it was the pain, and only the pain, which incapacitated him. His father was also of the same opinion, and thought that his son could become satisfactorily readjusted and resocialized if he could be relieved of what he considered to be physical pain.

After having made careful observation, I came to the conclusion that, whatever this man's psychological state, he was suffering from the condition which we know as migraine. In view of this decision and the fact that all kinds of drugs, including ergotamine tartrate, had been given an extensive trial, I decided that some kind of operation was necessary.

Operation, Feb. 14, 1945.—Under general anaesthesia, the patient lying on his back with the head turned to the right, an incision was made along the anterior margin of the left sternomastoid muscle, starting at the tip of the mastoid process and extending downwards as far as the thyroid cartilage. The carotid sheath with its enclosed vessels and the vagus nerve were isolated and retracted backwards, the sympathetic chain between the middle and upper cervical ganglia was exposed and divided, and the lower half of the upper cervical ganglion was removed. The outer coats of the common internal and external carotid arteries were stripped and removed in the manner of Leriche's periarterial sympathectomy. Finally the external carotid artery was clamped and divided between two ligatures (Fig. 1). The wound was re-formed in layers without drainage, and the patient made an uninterrupted recovery from the operation.

The following is a series of statements taken from the progress reports. Feb. 28, 1945: "Since my operation 14 days ago I have been perfectly free from symptoms of headaches and visual hallucinations." May 13: "The operation on the left side has so far

proved an unqualified success. In these last three months I have not had the slightest trouble in any way with the left side." May 31: "I have had five right-sided headaches since I last wrote you, but no trouble at all with the left; otherwise I am keeping pretty fit."

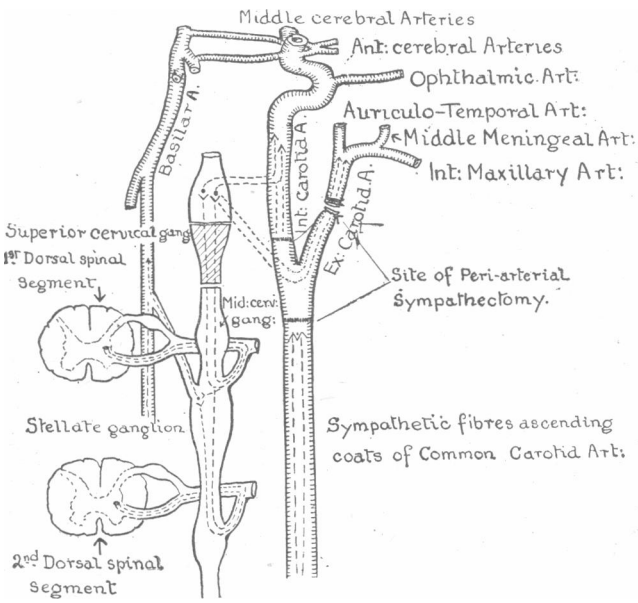

FIG. 1.—The operation of high cervical ganglionectomy and periarterial sympathectomy. (The part of the ganglion and sympathetic chain removed is shown by shading.)

Operation, June 20, 1945.—On account of the fact that the right-sided headaches were increasing in frequency and severity, and because of the apparent success of the left-sided sympathectomy, it was decided to carry out a similar operation on the right side of the neck. The details and technique were the same as those of the previous operation.

The following are extracted from the progress reports. Sept. 12, 1945: "I must tell you that the effect of the second operation, and therefore of the two combined, has been truly dramatic: it gives me very great pleasure to be able to tell you that every symptom of the migraine has completely vanished. There has been no further trace of pain on either side; the visual fields have cleared completely; there are no longer any hallucinatory or defectual faults of vision. All throbbing and tenderness along vessels and in the scalp have vanished. I can now go to the cinema, indulge in hot and cold baths, etc., with impunity." Nov. 18: "I am happy to be able to tell you that I am still completely free from all migrainous symptoms: especially so now that I am doing a full-time job." Feb. 18, 1946: "I am happy to be able to tell you that I am still absolutely without symptoms and signs of migraine in any form. I have put on 18 lb. [8.16 kg.] in weight, I sleep like a log, and I am generally more placid and far less excitable than I used to be." May 8: "I have great pleasure in informing you that I am still quite free from any sign or symptom of migraine."

Case II

A young man aged 21 years, whose illness commenced in 1942 while he was in Gibraltar serving with the Navy in a non-commissioned rank. For many months he had been on convoy duty between Gibraltar and Malta. One night, for no special reason, he developed a very severe headache, but after a time was able to get off to sleep; that same night he woke up and vomited. The next night he had another severe headache, which was also associated with vomiting, and this was followed by a period of lassitude which lasted for about two days. On account of the frequent recurrence of the headaches he was returned to the British Isles and finally had to be discharged from the Services.

I first saw him on Jan. 18, 1945, at the Retreat Hospital, York, at the request of my friend Dr. Pool. It was Dr. Pool's opinion that this man was suffering from neither a psychosis nor a psychoneurosis; in fact, he had come to the conclusion that his patient was suffering from a serious organic lesion and possibly from a cerebral tumour.

On my first examination I found the man to be fully and easily co-operative, to be quick and alert in every way, and that he revealed no obvious signs of psychoneurosis. Neurologically there were no abnormal signs. He was admitted to the Neurosurgical Unit on Feb. 1, 1945, for observation. After a day he began with very severe left-sided headache which made him vomit, and during the height of the painful attack he developed a left external rectus palsy which persisted for 36 hours.

Full investigations were carried out, and these failed to reveal any organic abnormality in the head or in the general metabolic processes. Although the probable existence of a vascular anomaly of the aneurysmal type was borne in mind, an angiogram was not made. In spite of adequate medical treatment, including injections of ergotamine tartrate, the headaches came on at intervals of about two days, and the pain was so exceedingly severe as to be completely incapacitating. On one occasion it was necessary to inject morphine to give him relief. Later he was transferred to the rehabilitation centre in the hope that a change of air would relieve his symptoms, but within two weeks he was returned to my care still complaining of severe pain.

Diagnosis.—In view of the unilateral character of the pain, its periodicity, and the temporary ocular paralysis, there could be little doubt that this was a case of migraine. Moreover, as no physical abnormalities could be demonstrated, it could be classed as idiopathic or primary migraine. Because of the severity of the pain, and the fact that it had been causing the man to take large quantities of analgesic drugs, I decided to operate.

Operation, March 14, 1945.—The following procedure was carried out: (*a*) Removal of the lower half of the upper cervical sympathetic ganglion and the chain below it; (*b*) stripping of the outer coats of the external and internal common carotid arteries; (*c*) ligation and division of the external carotid artery.

After the operation wound had healed the patient was transferred to the rehabilitation centre, where he remained for two months. During this period he had no recurrence of the headaches, and the medical report from the matron was satisfactory in every way. After a short stay at home he volunteered to the Society of Friends to go to Burma as an ambulance driver. However, on advice he found work on the land, and has been in full-time agricultural employment ever since. He occasionally gets a sense of discomfort on the left side of the head, but he has had no more severe head pains; moreover, he has no need to take analgesic drugs and finds that he has no desire to indulge in them.

Case III

A woman aged 38 years, an assistant matron in a general hospital. The history was that at least six years ago she started to suffer from attacks of right-sided headache and had, in fact, been off duty for long periods because of the pains. The headache would start slowly in the right temple or in the right forehead, and gradually increase in severity and spread until the whole of the right side of the head was affected. It was preceded or accompanied by spots in front of the eyes and by photophobia. Often she felt sick, but only occasionally did she vomit. In the early years of her illness the pain would disappear after a quiet rest, but in later years the headache had lasted for several days. Attacks were particularly liable to occur about the time of menstruation.

On examination she was found to be an intelligent woman and in every way satisfactorily co-operative. Though anxious about her present state of ill-health she showed no signs of a formal psychoneurosis. Neurologically no abnormal signs were found, and full investigation failed to reveal any abnormality in the head or the general metabolic system.

Diagnosis.—There was little doubt that here we were dealing with a case of migraine of the idiopathic or primary type. In view of the severity and frequency of the headaches I decided that operation was justifiable.

Operation, July 11, 1945.—This consisted in (*a*) removal of the lower half of the upper cervical sympathetic ganglion and the chain below it; (*b*) stripping of the outer coats of the external and internal common carotid arteries; (*c*) ligation and division of the external carotid artery.

Shortly after operation she was able to return to work, and the following is a statement from her on Oct. 18, 1945: "I am very pleased to say I have been free from attacks since the operation. I shall never be able to thank you for all you did for me; words cannot express my appreciation." I saw her again on April 3, 1946, and she said that the operation had been a great success. She had been able to stay on duty continuously. On one occasion she developed a pain in the head similar in character to the ones she had before the operation, but it was very much lighter and within an hour or so it passed off. She has had a lot of what she describes as "little headaches," which begin as though major attacks would follow, but these soon disappear and do not develop into actual pain.

Case IV

This was a young man aged 29, a lieutenant in the Army. The history is that, as far back as he can remember, he has suffered from headaches of varying degrees of severity. Until 1935 the pain had never been so severe as to incapacitate him completely or to

compel him to go to bed. In 1940 the headaches became more frequent and increasingly severe, and it was noticed that they were particularly liable to occur on Sundays. He entered the Services in August, 1941, and was put into Grade A1. From then until 1943, though he had attacks of headache, he did not have any serious incapacitating head pains. The first really bad attack occurred in the early summer of 1943, and because of a repetition of the severe headaches he was sent to a military hospital for further investigations and for treatment. There a diagnosis of migraine was made by the attending neurologist, and he was put on a course of analgesic drugs. During the winter of 1944 he had a series of extremely bad headaches, and these he attributed to excessive work and the fact that he had to deal with a difficult commandant.

In the past year the headaches have been coming on at intervals of from three to six weeks. He has never been able to discover any definite cause, but he has noticed that there is a tendency for them to occur whenever he has been mentally excited—for example, after an enjoyable evening spent with friends. He is a teetotaller and smokes fewer than 20 cigarettes a day. It was discovered that the only two drugs which gave him any real relief were ergotamine tartrate injected intramuscularly early in an attack, or enough morphine to put him to sleep.

In a typical attack he gets a feeling of discomfort in the head the night before the onset; he wakes up the next morning with a general kind of headache which later becomes intense, and a pain develops in the right temple, gradually spreading all over the right side of the head. The pain is stabbing in nature, and when at its height is almost unbearable; it is also of a throbbing character and occasionally spreads into the right side of the face. Any kind of head movement aggravates the pain; during an attack he finds it difficult to focus his eyes, but he has never been troubled with double vision, spots, or light; he has vomited not more than three times, and then only after the giving of morphine or of femergin.

On examination he proved to be above average intelligence, and in no way unduly emotional. He was obviously highly strung, but there were no frank psychoneurotic tendencies; certainly there was no desire to escape from his duties, and the one thing he wanted was to remain in the Services. The headaches troubled him chiefly because they interfered with his capacity to carry out his duties efficiently. Neurologically I could find no evidence of any organic intracranial lesion. Special investigations and tests failed to demonstrate any abnormality in the head or in the general metabolic processes.

Diagnosis.—In view of the periodicity and the long history of the head pains there could be little doubt that we were dealing with a case of migraine; moreover, it was probably of the idiopathic type, because no underlying pathological lesion could be demonstrated.

Operation, Aug. 10, 1945.—In this case removal of the whole of the upper cervical ganglion, stripping of the outer coats of the common internal and external carotid arteries, and ligation and division of the external carotid artery were carried out. Appended are copies of the follow-up reports.

Sept. 16, 1945: "I had an attack of right-sided headache to-day, which was similar in every way, neither more nor less severe, to those I experienced prior to the operation." Oct. 24: "The operation has afforded me no relief from my headaches." Dec. 12: "I am still having occasional right-sided headaches of the type similar to those I had before I was operated on." Dec. 31: "I am convinced that the attacks are now less frequent and, if anything, a trifle less severe than at one time. I find that I am able to go about without the fear of an attack materializing. I have occasional stabs of pain, or a dull ache for some while in either left or right temple, but I am now disregarding these, as they have not led to further trouble."

Feb. 3, 1946: "As mentioned to you when I was in Newcastle last, I am of the opinion that the operation has been of some help. Whether it is that I am now taking the precaution of having something done before the attack becomes too serious for the femergin to take effect I cannot say, but certainly no attack, since the one on Sept. 16 last, has been so severe as those experienced before. On this occasion, however, you will see from the report that I was unable to obtain femergin, and morphine was administered only at night. There would not appear to be much difference in the frequency, except that at times, of course, in the past there have been periods when I would have attacks two or three times during the month. This, however, has only been exceptional." Feb. 23: "There have been no other attacks, severe or mild, during the month, so there is little to report. One thing does amaze me, however, and that is that the attacks in over 75% of cases occur on a Sunday. It does not seem to matter where I am or where I have been. You will recollect that the last attack prior to the operation was on a Sunday, whilst in hospital. It does not seem material, therefore, that any particular place, work, or happenings have any bearing upon this aspect, which always has appeared to me to be very mysterious."

Comment on the Operations

In all four cases the nervous tissue removed was proved by histological section to be sympathetic ganglia and lengths of the sympathetic chain. In all cases the patient was left with Horner's syndrome, and dryness of the face and of the nasal air passages on the operated side. In no case was the carotid body itself removed, though, of course, its connexions must have been extensively severed. The identity of the external carotid artery was established, both by its position and by demonstration of its lower branches. In Case IV the patient complained of a persistent and unpleasant sense of stuffiness in the dried nostril, and this complication is a serious disadvantage of the operation. In Case I, following the second operation, the patient developed paralysis of the vocal cord due to retraction of the vagus nerve. Recovery is now taking place.

Assessment of the Pain

The Amount of Pain.—Though electrical disturbances can be measured in peripheral nerves when pain is being conducted

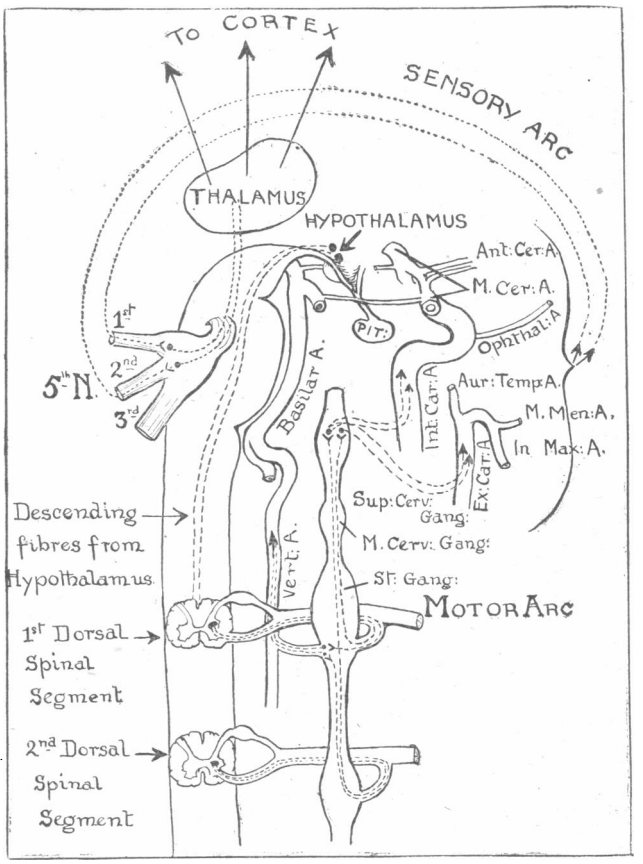

FIG. 2.—The "migraine cycle."

along their pathways, the amount or severity of pain cannot be precisely measured in scientific units. We depend for our assessment on how much a patient complains, on how the pain affects his happiness and human relationships, and how it affects his ability to work.

Its Relief.—Assessment of the result of the relief of pain depends partly on the patient's own statement, on his ability to enjoy himself, on the way he is socialized, and on how he can carry out his work. The possible objection that at least two of the patients in the above series were suffering from a psychoneurosis rather than migraine is not a strong one, because psychoneurotics are rarely cured, or relieved for any length of time, by a simple incision in the neck. Moreover, a disordered mental state can precipitate the "migraine cycle."

If it is true that (1) the pain of migraine arises in the arteries of the head from excessive spasm or dilatation, that (2) the pain in some cases is transmitted to the brain through the upper part of the posterior root of the trigeminus, and that (3) the arterial spasm is aroused by dysrhythmic messages passing along the

motor sympathetic pathways, then a neural mechanism can be constructed which will account for many of the phenomena in migraine. Fig. 2 illustrates this possible mechanism.

That the hypothalamus exists is an anatomical fact; that certain of its cell clusters can, with suitable stimulation, affect the calibre of the peripheral arteries is also a fact. The hypothalamus can be stimulated by chemical changes in the blood stream which reflect changes in general metabolism, and by messages of the intellect and emotions from the higher centres. If the hypothalamic mechanism happens to be in unstable equilibrium it can react abnormally to all kinds of stimuli and transmit dysrhythmic messages to the peripheral blood vessels, and particularly to those of the head. Possibly, therefore, a central unstable mechanism is the essential cause of migraine; all other stimuli, too much or too little of this and that, being merely precipitants or initiators of the "migraine cycle." The connexions of the hypothalamus with the peripheral anterior pathways are not known. They are, however, believed to lie deeply within the brain stem and spinal cord. The peripheral motor sympathetic pathways are known, and the main neuro-anatomical details are depicted in Fig. 1.

By my own previous experiments it has been shown that in some cases the pain pathways are transmitted through the upper part of the trigeminal root on the same side. It is known that no nerve fibres enter the posterior root other than through the ganglion, and no fibres enter the ganglion other than through the divisions of the nerve. Therefore, since the fibres of the ophthalmic division are represented in the upper part of the root, the pain pathways in migraine must traverse the ophthalmic division of the trigeminal nerve. Where precisely the pain pathways enter the ophthalmic nerve is not known. Moreover, it is not known whether the blood vessels themselves are supplied with pain fibres. This, however, is merely a point of academic importance, because radicles of the trigeminal nerve so closely follow the vessels that, even if they do not supply them, they could easily be stimulated by changes in their calibre.

In Case IV the fact that peripheral sympathectomy failed to cure possibly means that the unstable mechanism in this case lay in the vessels themselves and not in the hypothalamus. Another possible reason for failure is that the whole, and not the lower half only, of the upper cervical ganglion was removed.

REFERENCE
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CRASH HELMETS*

BY

Sir HUGH CAIRNS, K.B.E., D.M., F.R.C.S.

My interest in crash helmets arises solely from the fact that during the war I spent a considerable part of my time treating injured motor-cyclists at the Military Hospital for Head Injuries at Oxford. In other words, it was the segregation of the Army's head-injury patients in special centres which made possible the prompt recognition of the importance of crash helmets. In subsequent work on the subject I was fortunate in having as collaborator my colleague at Oxford, Dr. Holbourn, who was a motor-cyclist as well as a physicist.

In 1940 we observed that a large proportion of our head-injury patients were motor-cyclists: of the first 290 patients with blunt head injury 70 were motor-cyclists. Of these 1 died, 10 were invalided from the Service, and the remainder were absent from duty for an average period of four months. There were at that time no medical statistics relating to motor-cycle accidents, but the records of the Claims Commission showed that about 600 motor-cycle accidents occurred in the Army at home each month. The total death rate in the country was mounting: in the first 21 months of the war 2,279 motor-cyclists and pillion passengers were killed on the road—over 3 a day—and calculations showed that to this death roll the Army was contributing about two-thirds. With the help of the Royal Society for the Prevention of Accidents, and the Registrar-General, we found that head injury was present in 92% of a series of 111 fatal cases, and, though not the sole cause of death, was clearly a major factor in the majority.

* Read at the Royal Society of Medicine, March 20, 1946.

In 1940 the Army already had some crash helmets. These were issued only to certain types of motor-cyclist, and some were of canvas and others were meant for use in armoured vehicles. Some motor-cyclists wore the ordinary steel helmet. In 1940–1 only 1 in 20 of our motor-cyclist patients at Oxford had been wearing crash helmets at the time of the accident, but in these the relative mildness of symptoms was impressive enough to justify a report to the Director-General of the Army Medical Services, and to the Military Personnel Research Committee of the Medical Research Council, who were at that time considering helmets (Cairns, 1941).

In November, 1941, the Army Council made the use of crash helmets compulsory for all motor-cyclists. The R.A.F. followed suit in 1942. Whether the Royal Navy took any action I do not know—which is perhaps a humble argument in favour of a combined medical service. *After* recommendations had been made and action taken, by the end of 1942, we had accumulated enough evidence to prove that crash helmets were really very effective, and also to show how they might be still further improved (Cairns and Holbourn, 1943). This is an example of the impelling need for hasty decision in wartime on questions which really should have been worked at thoroughly between the wars.

The medical interest in crash helmets would have had no immediate effect if the Army, by the end of 1941, had not had crash helmets ready to supply all its 100,000 and more motor-cyclists in this country. The fact that it had got them may have been influenced to some extent by the early medical reports, but was, I suspect, mainly due to the example, before the war, of the racing motor-cyclists and men like A. B. Bourne and Graham Walker, who helped the Army to build up its motor-cyclist training. From about 1921 the Auto Cycle Union had made the wearing of crash helmets compulsory at speed trials, and their standard laminated fabric helmet is still one of the best available. When we began to treat Army motor-cyclists at Oxford we naturally got to know their comrades—keen motor-cyclists in the Army Training Schools, Royal Corps of Signals, and other units, who were very much alive to the wastage of their man-power from accidents, and they needed little encouragement to become enthusiastic advocates of compulsory use of crash helmets.

Structure and Mode of Action of the Crash Helmet

The components of a crash helmet are a firm outer shell, and an inner sling and hat-band which act as buffers. To understand the action of crash helmets it is necessary to consider what happens in a blunt head injury. There are two important effects of the blow: (1) the local injury beneath the site of the blow; (2) distortions in parts of the brain remote from the blow which depend on sudden change of velocity of the head.

At the site of the blow the scalp may be torn, the skull bends and may break, and fragments of it may penetrate the brain; and the brain may be bruised as well as torn. According to Holbourn (1943, 1944, 1945), when the head is made to rotate suddenly by a blow from a moving object, or against a stationary one, the brain, not being a rigid structure, lags behind. The brain makes the only kind of movement possible to a highly incompressible substance in an enclosed space—namely, a swirling movement—and the surface of the brain slides along inside the cranial cavity. These sliding movements of the surface of the brain have been observed with a high-speed camera and a perspex window in the skull, using the technique of Shelden *et al.* (1944). The movements set up shearing stresses in various parts of the brain; they are most severe where the lesser wing of the sphenoid juts into the cranial cavity, and it is in this region that bruising and laceration of the brain are so often seen, no matter where the blow has been struck. The clinical state of concussion is clearly due to remote effects, since it does not arise from the local brain injury of many gunshot wounds or of surgical operations.

The crash helmet modifies both the local and the remote effects. Locally the shell of the helmet spreads the blow over a wide area and protects the scalp and skull from the pointed pieces of road metal or whatever object is struck. In some cases it prevents fracture of the skull; in others, where a fracture is produced, it prevents the fracture from becoming