THE ROLE OF SYMPATHECTOMY IN THE TREATMENT OF CAUSALGIA

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Although the holocaust of two world wars has provided ample opportunity for further study, causalgia remains an enigma, for its pathogenesis is still obscure and the treatment by sympathectomy largely empirical. In this paper some of the current theories of the pathogenesis of causalgia will be reviewed and an attempt made to explain the role of sympathectomy in the relief of pain. These observations are based on a study of forty-eight patients treated in various peripheral nerve injury centres in Great Britain, and the author is indebted to the surgeons working in these centres for the use of their detailed case reports.

CLINICAL FEATURES

In all the patients causalgia resulted from an incomplete lesion of one or more nerve trunks. The pain usually had a burning quality, was situated in the hand or foot and was aggravated by physical and emotional stimuli. In the latter respect causalgia differs from all other painful states arising from a nerve injury. Noise, high notes, low-flying aeroplanes, or a child's cry often provoked a severe spasm of pain. Excitement and worry were badly tolerated and many of the patients complained that they did not enjoy a sensational film or an exciting novel. Some of the patients acquired reclusive habits and spent the greater part of the day sitting or lying in a corner of the ward.

TABLE I
TIME OF ONSET OF PAIN AFTER WOUNDING
(Forty-one cases in which a clear record was made)

Within twenty-four hours	26
Second to seventh day	9
Second to fourth week	5
Over one month	1

The pain usually commenced within a few hours of wounding (Table I) and often increased slowly in severity over the first few days. Sometimes, after a period varying from a few months to a year or more, there was a slow but steady improvement in the pain, though for several years after wounding many patients still complained of twinges of pain when they were excited or during hot weather.

The trophic and vascular changes were a striking feature but were very variable. In some patients the skin of the hand or foot was warm and glossy, in others it was cold and clammy.

THE NERVE LESION

There was a striking similarity in the pattern of the nerve injury in the arm and leg. The main features were as follows (Tables II and III):

1) There was always an incomplete lesion of the brachial plexus, or median nerve in the arm, and of the sciatic, medial popliteal or posterior tibial nerves in the leg. In some of the cases there was only a transient motor paralysis, and by the time the patient arrived at the

nerve injury centre the only evidence of neural injury was pain and hyperalgesia in the sensory distribution of the nerve. Even in the few cases in which, at the time of operation, all muscles were paralysed distal to the injury there was always a lesion in continuity of the nerve with varying degrees of intraneural scarring, and in every case there was some subsequent motor recovery. These findings conform with those of Shumacker, Speigel and Upjohn (1948), and many other authors. Causalgia must be a rare complication after complete division of a peripheral nerve and reports of its occurrence require critical examination, as in the following case: A patient was referred for examination with a diagnosis of ulnar nerve causalgia.

TABLE II
ANALYSIS OF NERVE INJURY IN UPPER LIMB
(Twenty-seven cases)

Type of lesion	Number of cases	Level of lesion	
		Above elbow joint	Forearm
Median	4	4	—
Median Ulnar*	12	11	1
Median Ulnar Radial†	9	9	—
Brachial plexus	2	2	—

* In three of the twelve patients the ulnar nerve was completely divided.

† In one patient the radial nerve was completely divided. None of the remaining nerves was severed.

TABLE III
ANALYSIS OF NERVE INJURY IN LOWER LIMB
(Twenty-one cases)

Type of nerve lesion	Number of cases	Level of lesion	No.
Medial } popliteal	18	Buttock	3
Lateral }		Thigh	11
		Popliteal fossa	4
Medial popliteal	2	Popliteal fossa	2
Posterior tibial	1	Middle third of leg	1

None of the above nerves was severed.

Clinically there was complete ulnar palsy and at operation the nerve was seen to be severed. The only evidence of a median nerve lesion was pain and hyperalgesia in the median area of the hand, yet the pain was abolished for four hours by blocking the median nerve at the wrist with 2 per cent procaine.

2) Multiple nerve lesions were common and the pain was often associated with more than one nerve. In the upper limb this was verified by blocking consecutively the ulnar nerve at the elbow and the median nerve at the wrist. Three patients with an incomplete lesion of the median and ulnar nerves were investigated in this manner. In two patients blocking the ulnar and median nerves in succession caused relief of pain in their respective areas in the hand, but in the third patient the nerve blocks did not relieve the pain, though they did in some way alter its character.

3) All the nerve injuries were caused by bomb or shell splinters or high velocity missiles, and with two exceptions all the lesions were at or above the level of the knee and elbow.

Ulmer and Mayfield (1946), Sunderland and Kelly (1948), and many other writers have drawn attention to the rarity of causalgia after a nerve lesion in the distal part of a limb. It is unlikely that the greater incidence of causalgia in high lesions is connected with any particular relationship between the numbers and arrangement of sympathetic and sensory fibres, for most of the sympathetic and almost all the sensory fibres leave the nerve trunks distal to the wrist and ankle. In most of the cases there was a dual nerve injury, and this probably explains the preponderance of high lesions. In the lower limb the medial and lateral popliteal nerves are usually joined to form the sciatic nerve down to the level of the lower third of the thigh, and they are closely related in the popliteal fossa. Below this point they diverge and therefore there is less risk of an injury to both nerves. The same considerations apply in the upper limb. Here the median and ulnar nerves are closely related in the upper two-thirds of the arm; below this level they diverge, again reducing the chances of a dual injury.

It is generally agreed that causalgia is a rare complication of an incised wound of a nerve. Puckett, Grundfest, McElroy and McMillen (1946) have demonstrated that when a high velocity missile passes close to a nerve the latter is subjected to a considerable degree of stretch, which cannot occur when a nerve is cleanly divided. A stretch injury of this type may cause various degrees of damage to the neuraxons and degeneration of their myelin sheaths. Granit, Leksell and Skoglund (1944) have demonstrated that in these circumstances an artificial synapse may be formed, which allows impulses to pass between the various nerve fibres at the level of injury. This has an important bearing on the pathogenesis of causalgia and is discussed later.

TREATMENT

Of all the maladies that may afflict man causalgia is one of the most painful, and effective treatment should be instituted at the earliest opportunity, not only to allay intolerable suffering but also to prevent the crippling deformities of the joints which follow long-continued voluntary immobilisation of the painful limb.

TABLE IV
EFFECT ON PAIN OF GANGLION BLOCK
(Thirty-six cases)

	Relief	Incomplete relief	No relief
Complete block	27	4	1
Incomplete block	—	—	4

A review of the literature which has appeared during and since the last war, and the experience of surgeons working in the nerve injury centres in Great Britain, leave one in no doubt that sympathectomy is the only form of effective therapy in a severe case of causalgia. Many other methods of treatment were employed in the centres. They included freeing of the nerve from scar tissue (neurolysis), resection of the damaged segment, periarterial sympathectomy, and radiotherapy; and although each of these appeared to relieve pain in isolated cases the effect was never dramatic, and might well have been unrelated to the treatment.

Before considering sympathetic denervation of the upper or lower limb it is wise to ascertain the response to procaine or other block of the appropriate sympathetic ganglia (Table IV). In the upper limb it is necessary to infiltrate only the second thoracic ganglion, but it is usual to include the stellate because the appearance of Horner's syndrome is additional confirmation of a successful injection. In the lower limb it is usual to infiltrate the second,

third and fourth lumbar ganglia. With practice these procedures are not difficult but the results must be interpreted with caution. A complete block of the sympathetic ganglia cannot be assumed unless there is complete anhidrosis of the limb and an appreciable increase in the warmth of the hand or foot. These effects should appear within five to ten minutes of the injection. It is also important to ascertain that the block is confined to the sympathetic ganglia, for, if the somatic nerves are infiltrated inadvertently, it is impossible to say whether the relief of pain can be ascribed to the block of the sympathetic ganglia or the nerve trunks. A successful block of the sympathetic outflow to a limb often gave relief of pain for from one to three hours: failure to secure any relief after two successful blocks was regarded as a contra-indication to sympathectomy.

The potentialities of blocking the sympathetic ganglia by tetraethyl ammonium bromide were not fully investigated as the drug only became available after the war. It was used on three occasions, in doses of 300–400 milligrams. All the patients were relieved of pain and in one patient the pain did not return until two to three hours after the injection. It is possible that the longer-acting methonium compounds now available may be even more valuable in the pre-operative investigation.

With three exceptions every patient benefited from a sympathectomy. The failures were caused by technical difficulties during the operation and subsequent examination revealed that the sympathectomy was incomplete. The interval between wounding and the sympathectomy varied from five weeks to almost seven years. The long delay in securing treatment was due to the patients being held as prisoners of war but it did not prejudice the efficacy of sympathectomy.

In some patients the hyperalgesia persisted although there was complete relief of spontaneous pain. The persistent hyperalgesia was presumably caused by an "irritative" lesion of the somatic sensory fibres at the site of the nerve injury rather than an inadequate sympathectomy.

Results in upper extremity—Two types of sympathectomy were performed—cervico-thoracic ganglionectomy and preganglionic sympathectomy. In cervico-thoracic ganglionectomy the lowest cervical and first, or first and second, thoracic ganglia, and intervening trunk were removed. This operation, a post-ganglionic sympathectomy, does not produce as effective vasodilation of the limb as the preganglionic operation, and gives the patient a Horner's syndrome. In preganglionic sympathectomy (Smithwick 1940) the second and third thoracic ganglia were decentralised by dividing the white rami communicantes to each ganglion and the sympathetic trunk below the third ganglion.

On theoretical grounds these two procedures should be equally effective in the relief of pain but in practice this was not the case. A number of completely satisfactory results were obtained with both operations but there were more failures with the postganglionic operation (Fig. 1).

Of the eighteen operations performed three were failures, and in each of them it was known that the sympathectomy was inadequate because of technical difficulties at the time of operation. Six patients had a preganglionic sympathectomy, and were completely free of pain after the operation; four of them were also relieved of hyperaesthesia and hyperalgesia. In one patient the pain returned with warmth and excitement, one year after operation, and

FIG. 1

Analysis of results of cervical sympathectomy for causalgia. Follow-up periods were: preganglionic section ten to forty-six months (average thirty-two months); postganglionic section two to forty-two months (average twenty-four months).

FIG. 2

Analysis of results of lumbar ganglionectomy for causalgia. Follow-up periods were up to eighty-four months (average twenty-three months).

Fifteen operations were performed: all patients were relieved of pain initially, but in four of them some pain returned during the first year after operation, and six still had some hyperaesthesia and hyperalgesia in the sole of the foot, which persisted for many months after the operation.

PATHOGENESIS

In spite of many investigations into the nature of causalgia no satisfactory explanation has been found, for none of the theories at present in vogue will explain all the observed facts.

Most workers agree that sympathectomy will relieve the pain in most cases and it is tempting to attribute this to the abolition of afferent pain impulses transmitted by the sympathetic nervous system (Bingham 1948). There are, however, serious objections to this hypothesis. It is impossible to demonstrate any change in the sensitivity of a limb which has been sympathectomised for peripheral vascular disease. Furthermore, lesions of the cauda equina are encountered from time to time in which the spinal nerves are damaged below the level of the sympathetic outflow; yet in spite of the normal sympathetic innervation there is complete loss of sensation in the lower limbs (Fig. 3).

In two patients a low spinal anaesthetic was administered with the intention of blocking the pain fibres from the lower limb and at the same time preserving the sympathetic innervation of the leg. This is possible because the lowest white ramus for the sympathetic chain is given off by the second lumbar nerve root (Figs. 4 and 5). One of the patients had severe causalgia after a sciatic nerve lesion at the level of the buttock. With the patient sitting, 3.5 cubic centimetres of 5 per cent procaine was

appeared to be due to regeneration of the sympathetic fibres. Eight patients had a postganglionic sympathectomy. Three were completely relieved of spontaneous pain and hyperalgesia after the operation, and remained so during the follow-up period. In the remaining five patients there was considerable but not complete relief of pain and in three of them the hyperalgesia persisted with its original intensity. In one case no record was made of the type of sympathectomy.

Results in lower extremity—The results of sympathectomy were better in the lower limb than in the upper limb (Fig. 2). The operation consisted in the removal of the first, second and third, or second, third and fourth lumbar ganglia, and the intervening chain. Both are predominantly preganglionic sympathectomies, for the cell stations for the sympathetic fibres to the lower limb are situated in the third lumbar to third sacral ganglia.

FIG. 3

Lesion of cauda equina distal to L.3 root. Although there is normal sympathetic innervation of the leg and foot there is complete analgesia in these areas.

injected into the spinal theca. There was *immediate* relief of pain long before the preganglionic sympathetic fibres were paralysed, for there was no rise in the skin temperature of the big toe as measured by a thermocouple until eight minutes after the administration of the anaesthetic. The other patient had severe causalgia following a lesion of the medial and lateral popliteal nerves in the popliteal fossa. One cubic centimetre of procaine was injected into the spinal theca and complete anaesthesia was obtained up to the level of the third lumbar dermatome. The pain in the foot was abolished but the sympathetic outflow to the lower limb was unaffected as there was no rise in the skin temperature of the first and fifth toes.

From these observations it is reasonable to assume that the pain impulses are conveyed centrally by the normal sensory pathway and not by the sympathetic nervous system. These

FIG. 4

The lowest white ramus to the sympathetic chain is given off by the second lumbar nerve root. Spinal anaesthesia to the level of the third lumbar root will abolish pain impulses from the lower three lumbar and sacral dermatomes without interfering with the sympathetic innervation of the lower limbs (see Fig. 5).

FIG. 5

Effect of a low spinal anaesthetic. The pain in the foot is abolished although there is normal sympathetic innervation, indicating that pain impulses are conveyed centrally by the normal sensory pathway and not by the sympathetic nervous system.

impulses cannot, however, originate in the afferent sensory fibres for the pain is relieved by blocking the sympathetic ganglia, which can have no direct effect on the sensory pathway (Table IV). We must assume, therefore, that sympathectomy acts by blocking efferent impulses in the sympathetic fibres, which in some way stimulate sensory afferent fibres at the site of the nerve lesion or at the periphery (Doupe, Cullen and Chance 1944).

We have now to consider how this occurs. Granit *et al.* (1944) have shown that an artificial synapse between motor and sensory fibres can occur at the cut end of a nerve, or even after a nerve injury which does not prevent normal distal conduction. Although these workers did not demonstrate a synapse between the sympathetic and sensory fibres there is no reason to suppose that it does not occur.

Causalgia cannot, however, be explained solely on the basis of an artificial synapse between sympathetic and sensory fibres at the site of the nerve lesion because the pain is sometimes relieved by blocking the nerve with procaine *distal* to the lesion (Table V). This observation led Doupe and his co-workers to postulate a distal causalgic syndrome in which the synapse between the sympathetic and sensory fibres was supposed to occur at the periphery of the limb when the nutrition of the nerves was impaired by oedema or ischaemia.

FIG. 6
Diagram of suggested pain pathway in causalgia.

A criticism of this supposition is that pain often commences within a few hours of wounding, before nutritional changes could have occurred (Table I).

Since causalgia seldom occurs when a nerve is completely divided, it seems probable that in most cases the preservation of distal conduction is essential to the development of the syndrome. If the artificial synapse between the sympathetic and sensory fibres occurs at the site of the nerve lesion, which is the only reasonable possibility, we must assume that impulses having "short-circuited" from a sympathetic to a sensory fibre can now pass up or down the sensory fibre (Fig. 6). The impulses travelling distally may cause the release of

a pain-producing substance at the periphery of the limb, or in some way lower the threshold of stimulation of the sensory nerve endings.

Lewis (1937) has shown that when the distal end of a divided sensory nerve is stimulated the skin it supplies becomes flushed and warm and that this may be accompanied by burning pain. This response to antidromic stimulation is very similar to the phenomena of causalgia. A criticism of the analogy is that all cases of causalgia do not show vasodilation, but we have no knowledge that "antidromic" vasodilation can be maintained indefinitely without compensating factors intervening: disuse will cause a large measure of cooling, and pain is known to cause vasoconstriction.

The clinical features of causalgia and the satisfactory response to sympathectomy can be explained on the basis of the following hypothesis. The nerve lesion is usually caused by the passage of a missile in its vicinity which results in a stretch injury without solution of continuity of the nerve or permanent loss of conductivity. The injury breaks down the insulation of the nerve fibres and an artificial synapse is established between the efferent sympathetic and afferent sensory fibres. Impulses passing down the sympathetic fibres are "short-circuited" to the sensory somatic fibres where they can travel both centrally and distally (antidromic) (Fig. 6). The antidromic impulses cause a substance to be released at the periphery, which either reduces the threshold of sensory stimulation, or *per se* sets up centripetal impulses in the sensory fibres which summate with those arising directly at the artificial synapse.

If this view is correct the onset of pain will usually be dependent on the return of normal conduction distal to the nerve lesion. Once the pathway is established pain will persist until effective insulation of the nerve fibres is restored which will prevent passage of impulses across the artificial synapse; or until such time as the efferent impulses in the sympathetic fibres are abolished by sympathectomy.

TABLE V
EFFECT ON PAIN OF NERVE BLOCK DISTAL TO LESION
(Fourteen cases)

Complete relief	.	.	.	.	.	8
Incomplete relief	.	.	.	.	.	2
No relief	.	.	.	.	.	4

The hypothesis explains the variable response to a nerve block distal to the lesion (Table V). A successful nerve block will abolish the centripetal pain impulses arising at the periphery of the limb. If these impulses are responsible for most of the pain considerable relief may be expected. On the other hand the nerve block will have little or no effect if the pain is caused chiefly by centripetal impulses arising at the site of the nerve lesion.

At first sight a serious criticism of this hypothesis is that resection of the damaged part of the nerve, which must interrupt both the efferent and afferent pathways, often fails to give complete relief of pain. The probable explanation is that there is usually a lesion of two or more nerves (Tables II and III). In these circumstances resection of one nerve will only relieve pain in the area of skin supplied by it alone, and pain will persist in the part of the hand or foot supplied by the other injured nerves. This undoubtedly accounted for the partial failure of resection on the three occasions it was employed in this series and the following case is typical of all three (Fig. 7): A man of thirty-one was wounded in the right upper arm by a mortar bomb splinter and sustained a lesion of the median and ulnar nerves. On the day after the injury he complained of pain "like severe toothache" in the right hand and less severe in the index finger and thumb. The pain was aggravated by coughing, sneezing,

FIG. 7

Resection of the damaged portion of one nerve often gives only partial relief of pain, for if there is a lesion of two nerves pain will persist in the area of the hand or foot supplied by the remaining nerve or nerves.

deep breathing and emotional stimuli. When he was examined seven weeks after injury there was marked weakness of all muscles supplied by the ulnar nerve and slight weakness of the median intrinsic muscles. Sensory testing was difficult but there appeared to be loss of sensation to light touch in the median and ulnar nerve areas, and pinprick caused diffuse burning pain. At operation three months after injury the median nerve was freed from scar tissue and a small lateral neuroma was excised. There was a large neuroma on the ulnar nerve; this was resected and a suture performed after anterior transposition. The day after operation pain returned to the median area of the hand but it was abolished in the ulnar area. Two months later the pain was completely relieved by a preganglionic sympathectomy.

SUMMARY

1. Forty-eight cases of causalgia are reviewed and the clinical features are briefly described.
2. Multiple nerve injuries are common and the pain is often associated with all the injured nerves. In the upper limb there was always an incomplete lesion of the lower trunk or medial cord of the brachial plexus, or of the median nerve. In the lower limb there was always an incomplete lesion of the medial popliteal division of the sciatic, the medial popliteal, or the posterior tibial nerve. These nerves carry most of the sympathetic fibres to the hand and foot. With two exceptions all the nerve lesions were at or above the level of the knee or elbow.
3. Sympathectomy gives marked relief of pain in most cases of causalgia. Prompt treatment is essential to prevent the crippling deformities which follow prolonged voluntary immobilisation of the painful limb. The results of preganglionic are superior to those of postganglionic sympathectomy.
4. The possible pain pathways are discussed, and an explanation is offered for the successful results of sympathectomy in the treatment of causalgia.

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