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CRYOSURGERY IN THE MANAGEMENT OF INTRACTABLE FACIAL PAIN

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Summary. The biological sequelae to the experimental freezing of peripheral nerves have been shown to differ in several respects from those following other types of nerve injury.

A clinical application of these effects utilising the extreme low temperature produced by modern cryosurgical equipment is proposed and a preliminary evaluation is made.

Introduction

Understanding of the effects of extreme cold on peripheral nerve tissue has developed over many centuries. The analgesic effect was recorded by Hippocrates (Davison, 1959) and in the 11th century an Anglo-Saxon monk suggested the use of cold to reduce sensation before surgery (Grattan & Singer, 1952). In 1832, Napoleon's Surgeon General, Baron Larré, reported that the limbs of soldiers which had been frozen in the snows of Russia could be amputated relatively painlessly. Arnott (1851) emphasised the anaesthetic effect of an ice and salt mixture at $-20°C$ applied to body surfaces. In 1866, Richardson introduced the ether spray to obtain local analgesia by refrigeration, this being superseded in 1890 by the ethyl chloride spray apparatus similar to the type in use today. Thus 'to freeze' became synonymous with 'to numb' or 'to deaden'. Denny Brown *et al.* (1945) showed that the myelin and axis cylinders of mammalian peripheral nerves are selectively damaged by exposure to cold, the larger myelinated fibres being more susceptible than smaller unmyelinated fibres. Severe freezing was followed by pan-necrosis of the whole nerve bundle. In conduction studies, Douglas and Malcolm (1955) observed a similar differential blockade on cooling nerves in the cat.

Interest in the effect of cold on living tissue has considerably increased over the last 15 years as a result of the development of apparatus for the controlled maintenance of extreme low temperature. In experiments on animals, it has been shown that there is a complete functional loss in nerves following freezing with a cryoprobe, but that good recovery can be expected over a few weeks. This functional loss has been shown to be associated with a second-degree type of nerve injury, according to Sunderland's (1968) classification, that is, there is Wallerian degeneration with axonal disintegration and break-up of the myelin sheaths, but with minimal disruption of the endoneurium and other connective tissue elements.

It is important to distinguish the functional loss associated with cellular degeneration from the transient functional block associated with merely cooling the nerve. Whittaker (1973) and Wener *et al.* (1973) reported early degenerative changes in nerves following freezing with a cryoprobe. Carter *et al.* (1972) subjected motor nerves

in the rat to a cryolesion of −100°C and found that there was subsequently complete loss of function. Degeneration, confirmed electromyographically, began at 14 days and was complete by 25 days. Cellular damage became apparent at 24 hours, although there was a noticeable lack of inflammation and connective tissue sheaths remained intact. In 12 days axonal growth was apparent. Chronaxia and rheobase measurements in the sciatic nerve of the rat returned to normal in 20 to 50 days following a cryolesion of −196°C (Lenz, 1974). Beazley *et al.* (1974) subjected the VIIth nerve of the Rhesus monkey and the recurrent laryngeal nerve of the dog to −40°C and −60°C respectively. Recovery began at 5 weeks and was complete by 9 weeks, assessed by muscle contraction. McMasters (1962) found that ACTH accelerated nerve regeneration in rats and postulated that this was due to the suppression of the inflammatory response and reduction in scar formation, while Poswillo (1971) reported similar features in the cryolesion.

It is likely that the combination of second degree nerve injury with continuity of neural connective tissue sheaths and minimal inflammation and fibrosis in the cryolesion, would provide an ideal environment for regeneration, which is consistent with the functional recovery following cryosurgery.

These experimental findings are supported by the clinical findings that postoperative pain is minimal following cryosurgery. Perhaps more significant is the return of normal sensation in the distribution of peripheral nerves which have become incidentally incorporated in the cryolesion. For example, Bradley and Fisher (1975) advocating the use of cryosurgery in the management of mandibular keratocysts, reported the return of sensory function of the inferior alveolar nerve in all of three cases over 3 to 6 months. The analgesic effect of cryosurgery has been used palliatively in the management of inoperable cancers, by directly freezing the tumour. Cahan (1965) and Frazer (1972) reported this principle in the management of rectal cancer and more recently Leopard (1975) and Poswillo (1975) have reaffirmed the usefulness of the technique in the palliation of oral malignancy.

These experimental and clinical findings suggest that this application of a cryoprobe to a peripheral nerve could be used therapeutically to produce an extended, but reversible, nerve block. Although cryosurgery has been used to achieve local destruction of brain tissue, its use to block peripheral nerves has not been developed. Nerve blockade has an important rôle in the management of intractable pain where even powerful analgesics may be ineffective, or incompatible with a normal way of life in ambulant patients. In the past, the reversible blocking of peripheral nerves has been achieved by the use of local anaesthetic solutions, but even so-called long-acting preparations, such as bupivicaine (Marcaine) are generally not effective for more than 12 hours (Watt *et al.*, 1970). For more prolonged analgesia, neurolytic agents such as alcohol or phenol are used. The use of these agents on peripheral nerves is disappointing as only partial destruction of the nerve may result (Nathan *et al.*, 1965), which may only serve to aggravate symptoms. Later intra-neural scarring may be responsible for secondary neuralgia (Harris, 1926; Matchabelli, 1945; Feldman, 1974). Following surgical section or electro-coagulation, recovery cannot be predicted and subsequent neuroma formation and scarring may be responsible for recurrence of pain (Wall & Gutnick, 1974). Cryogenic blockade of peripheral nerves would therefore appear to offer advantages over existing techniques, and this clinical application of cryosurgery has been termed Cryoanalgesia (Lloyd *et al.*, 1976).

Patients and method

The management of 21 patients with intractable facial pain over a 12-month period

is described. It is emphasised that all these patients had failed to respond to previous medical or surgical treatment for their pain. The nerves involved were:

V_1	Supraorbital and Supratrochlear	10 patients
V_2	Infraorbital	8 patients
V_3	Mental	2 patients
	Lingual	1 patient
	Total	21 patients

The patients had the following diagnoses:

Post-herpetic neuralgia	9 patients
Neuralgia of unknown aetiology (atypical facial neuralgia; tic douloureux)	8 patients
Post-traumatic neuralgia	3 patients
Malignant disease	1 patient
Total	21 patients

In all the patients a preliminary diagnostic injection of local anaesthetic solution was given, so that the pain relief and sensory loss produced by the nerve block could be assessed by the patient and the operator.

Nerves were frozen with a cryoprobe operating on the Joule Thompson principle with nitrous oxide as the refrigerant gas. With the small dimension of tissue being frozen and the minimal heat sink around the exposed nerve, the greater cooling power of a liquid nitrogen system was not required. The use of a fine cryoprobe was found to offer advantages by minimising the freezing of adjacent tissue and skin edges and allowing good visibility and access. In this series a fine needle-shaped probe, developed for percutaneous nerve blockade, was used (Spembly Neurostat) but a conventional oral surgery probe with a fine tip could have been employed.

First group (post-herpetic)

This most distressing condition has been shown to be extremely refractory to the many forms of treatment which had been advocated over the years, including drug therapy, central and peripheral surgery to nerve pathways and, more recently, peripheral nerve stimulation (Nathan & Wall, 1974). However, White (1974) suggested that where pain relief followed peripheral nerve block, subsequent neurectomy was likely to give prolonged relief in a few patients, even though the site of neural damage is thought to be more proximal on the afferent pathway. All nine patients had temporary pain relief following blockade of the affected nerve with local anaesthesia and in view of the debilitating and persistent nature of the pain, it was decided to treat this group by nerve section. The nerves were exposed by dissection under local anaesthesia and then frozen with a cryoprobe (Fig. 1) before dividing with a scalpel. The nerves were frozen before section as it was found that this allowed painless manipulation of nerves which were often hypersensitive in spite of the infiltration of local anaesthetic solutions.

Second group (atypical facial neuralgia; tic douloureux; malignant neuralgia)

The 12 patients in this group were treated by cryoanalgesia alone and the nerves were not sectioned. Two freeze/thaw cycles were carried out. Each freeze was timed for 2 minutes from the establishment of equilibrium in the iceball. This was assessed visually when the iceball was maximal, or by the recording of a steady low temperature

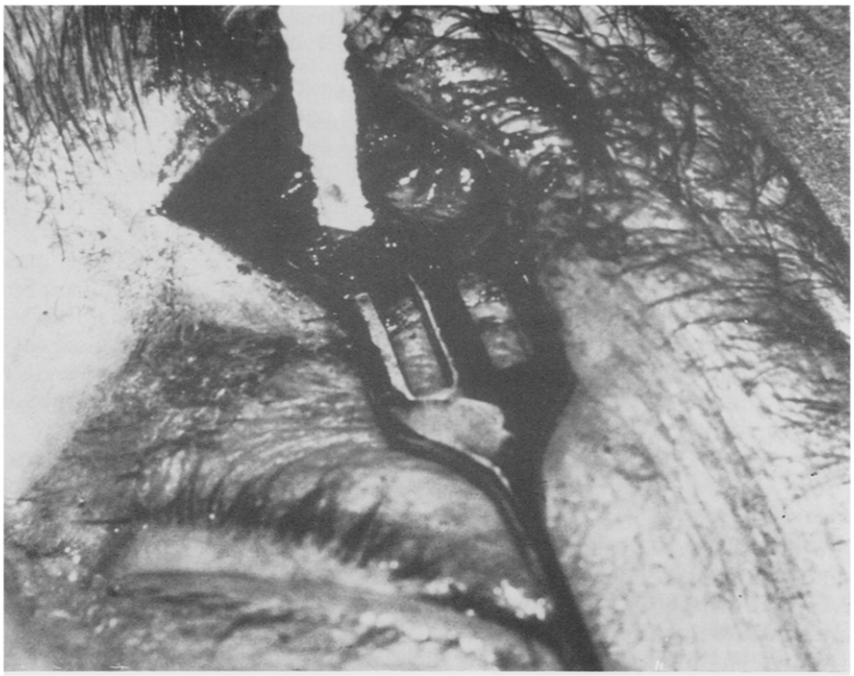

FIG. 1. Application of a fine cryoprobe (Spembly Ltd.) to the left supraorbital nerve exposed through a supraorbital incision under local anaesthesia.

as measured by the thermocouple, in the order of −60°C. The wound was then sutured and there have been no problems of wound breakdown over the frozen area.

Results

Figure 2 shows the duration of pain relief and sensory loss in the first group of nine patients treated by freezing and nerve section. The duration of pain relief was taken as the number of days from treatment that the patient stated he was free of pain. Sensory loss was assessed by the inability of the patient to feel light touch or pinprick.

The median duration of pain relief in this group was 38 days, with a range from 0 to 84 days. At the time of final review no patients had a return of sensory function, though it should be stressed that in the post-herpetic group all the patients had normal sensation pre-operatively.

For example, Patient 1 had only 5 days relief from pain, but still had sensory loss at the time of review 339 days post-operatively. Patient 2 had no pain relief in spite of total anaesthesia over the distribution of the involved nerves. Patient 8 was free of pain and anaesthetic 82 days post-operatively.

Figure 3 shows the results in the second group treated by cryoanalgesia alone. The results in the patient with pain from malignant disease (advanced carcinoma of the tongue) are not shown as no assessment of sensory function had been made. Of the remaining 11 patients, three had repeat treatments – Patients 2, 5 and 9. Of the 14 treatments there was return of sensory function before pain in eight. Seven patients were still pain-free at the time of final review. The median duration of pain relief was 116 days and the median duration of sensory loss was 49 days.

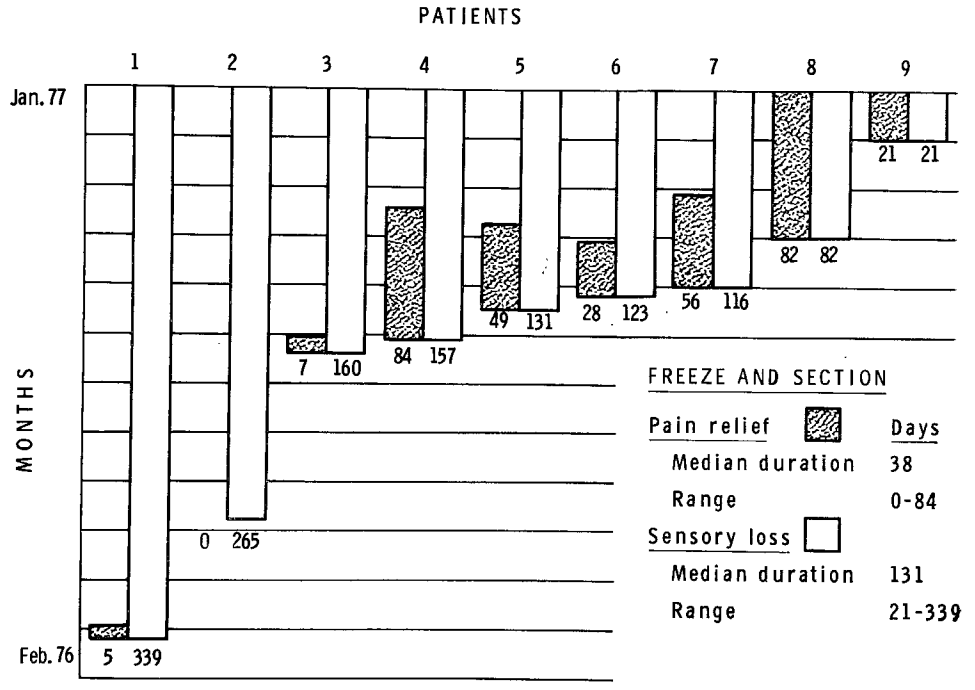

FIG. 2. Histogram showing duration of pain relief and sensory loss in the first group of patients treated by freezing and section.

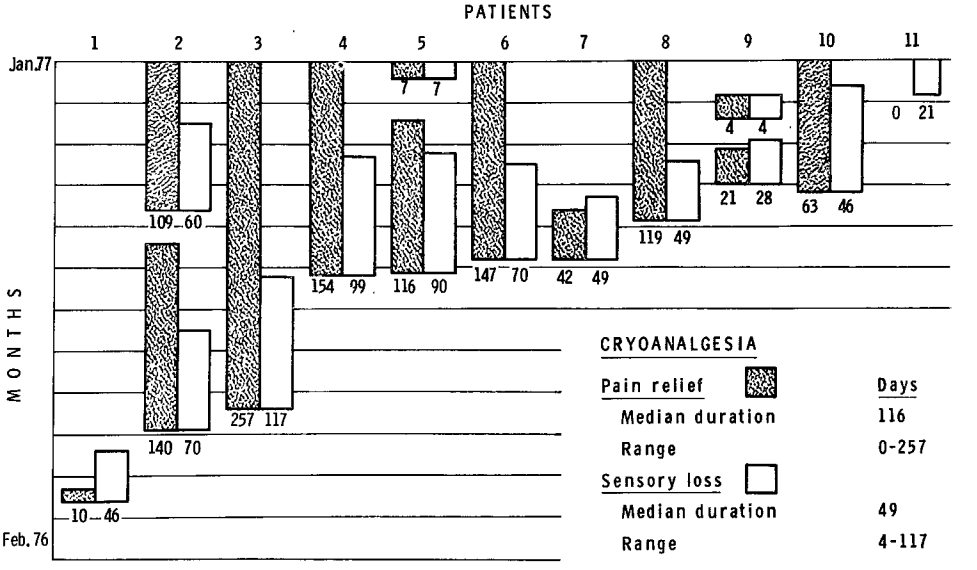

FIG. 3. Histogram showing the duration of pain relief and sensory loss in the second group of patients treated by cryoanalgesia alone.

For example, Patient 2 had atypical facial neuralgia. Following freezing of the left infraorbital nerve she had relief of pain for 140 days and return of sensation after 70 days. At the patient's request the treatment was repeated under local anaesthesia. Sensation returned after 60 days and she was still pain free 109 days post-operatively.

Patient 4 had trigeminal neuralgia diagnosed in 1963 and subsequently had only limited relief from Tegretol. The dose which he could tolerate was limited by unpleasant side effects. Following freezing of his right infra-orbital nerve in August 1976 he has had no pain, taken no drugs and had a return of sensation 99 days post-operatively.

Discussion

The interruption of peripheral nerve pathways in the management of intractable pain has a well established rôle and the technique employed should ideally satisfy the following criteria:

1. It should be a simple technical procedure, readily acceptable to the patient on an out-patient basis.
2. It should be reliable in interrupting conduction in nerve pathways.
3. It should not precipitate secondary neuritis or neuralgia.
4. Pain pathways only should be blocked, or if this is not possible sensory function should return rapidly.

The results of treatment of the patients in the two groups will be considered in relation to these ideal features. The time scales in the two groups are comparable, but there are too many other variables to make a statistically valid comparison although consideration of the results together highlights some special features of the two groups. The wide range of results (Table I) emphasises the difficulties encountered in the assessment and management of patients with intractable facial pain.

In both groups the technique is simple and relatively painless. This contrasts with the acute pain which may accompany the injection of neurolytic agents (White & Sweet, 1969; Mehta, 1973).

Nerve section reliably interrupts peripheral nerve pathways and where the cryolesion is accurately applied to the nerve a predictable and complete nerve block results. The short period of pain relief in the post-herpetic group reflects the disappointing results often achieved in treating this condition and emphasises the complexity of the pain mechanism. In several of the cases, even where a good technical

Table I

Table comparing the duration of pain relief and sensory loss in the two groups

	Cryoanalgesia	Freeze and section
	Days	
Pain relief		
Median duration	116	38
Range	0–257	0–84
Sensory loss		
Median duration	49	131
Range	4–117	21–339

block had been achieved, pain was only relieved for a very short period and there were isolated areas of hyperaesthetic skin within the area of distribution of the anaesthetised nerve. This confirms the experience of Harris (1926) and the situation is not unlike the 'anaesthesia dolorosa' which sometimes follows herpetic infection. Apart from the practical benefit of freezing the nerve before section to reduce operative pain, the minimal inflammatory response and resulting fibrosis at the amputated nerve stump may have a beneficial effect in reducing causalgic pain. However, in the group of patients with post-herpetic neuralgia, assessment of this effect is not possible and further investigation is required.

In the second group, treated by freezing alone, none of the cases had their pain made worse by treatment and it is suggested that this absence of pain from neuritis often seen following neurolytic injections, is attributable to the lack of inflammatory response and scarring and consistent structural degeneration across the nerve. Sunderland (1968) stated that where the endoneurium remains intact, as in the case of a second-degree nerve injury, neuroma formation does not occur. This may partly account for the lack of causalgic pains following cryoanalgesia.

In the group where the nerves were frozen and sectioned no patient had a return of normal sensory function during the time of review. Experimental evidence suggests that the low temperature produced by a cryoprobe destroys all fibres and that anything less than severe freezing will produce a differential blockade with pain fibres the least affected. If this were so, considering the gate control theory (Melzack & Wall, 1965) cold blockade might be expected to intensify pain by reducing large fibre activity and 'opening the gate'. However, in the group treated by cryoanalgesia the median duration of pain relief (116 days) was much longer than the median duration of sensory loss (49 days). This may be due to structural or functional changes in the nerve centrally or peripherally which are not yet understood, or to breakdown of a pain cycle. Ashby (1977) showed how prolonged relief may follow the brief interruption of a pain cycle by lignocaine block and it may be that the extended block produced by cryosurgery is an extension of this principle. In cases where pain relief is limited, the reversibility is useful as it enables patients to assess their tolerance to loss of facial sensation before more radical central procedures are undertaken.

Conclusion

Cryoanalgesia has been shown to be a useful therapeutic tool in the management of intractable facial pain. Although the number of patients reviewed is small, this technique does appear to offer distinct advantages over other methods of nerve block. A reliable, prolonged, reversible nerve block is achieved by a simple technique which does not appear to aggravate symptoms.

Experimental work is in progress to study further the biological sequelae to freezing peripheral nerves with a cryoprobe and it is hoped to correlate these findings to the therapeutic application of cryoanalgesia in pain relief.

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