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Pain Suppression by Peripheral Nerve Stimulation

Chronic Effects of Implanted Devices[1]

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Abstract. This is a study of the long range effects of pain suppression obtained by electrical stimulation of peripheral nerves. These cases were followed during 12–46 months and evaluated personally and by questionnaires. Selection for surgery was done exclusively on the basis of the results of a preoperative peripheral nerve stimulation test. Of 37 case observations, 18 were considered significantly relieved; that is, more than 50% of the intensity and/or duration of pain was consistently admitted. The results obtained in the acute preoperative trial could be reproduced indefinitely in some cases for as long as 46 months. Correlation of the results with the disease producing the pain revealed as benefitting for painful syndromes associated with peripheral nerve disorders, amputation, soft tissue injuries (nerves?), and some recurrent lumbar disc surgeries. Sciatic, ulnar and occipital nerve implantations were particularly rewarding. The best and worse results were analyzed. The complications appear to be largely preventable and of no serious consequences. Our analysis suggests that most failures take place within 2 years from implantation. Experience seems to be accumulating showing that a number of patients may receive sustained relief beyond this period.

Introduction

In a previous paper, the phenomenon of 'pain suppression' was described [9]. It consisted in the alleviation or full disappearance of pain in persons affected by certain types of painful disorders under the effect of electrical nerve stimulation. Some cases were implanted with stimula-

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tors by SWEET and WEPSIC [11], MEYER and FIELDS [8], or LONG [7]. Follow-up of up to 20 months by us [10] revealed the relatively acceptable tolerance of these implants and the possibility that a substantial number of patients could obtain worthwhile benefit. In this paper, we reconsider our observations after a period of more than 1 year and less than 4 have elapsed.

Material and Method

69 consecutive cases were implanted with peripheral nerve stimulators during the period of October 5, 1971, through March 18, 1974. Their ages ranged from 23 to 84 years. Well over one-half of these cases (41) were clustered in their fourth and fifth decade of life. About an equal number of males (37) and females (32) are represented. All were affected by intractable pain syndromes of different etiologies and had at least a 1-year trial of standard forms of pain control, medical and sometimes surgical. They consented to be implanted with full knowledge of the uncertainties of a new procedure. All patients had been previously tested for at least 1 month with transcutaneous nerve stimulation (TNS) [10]. Most had extensive neurological and psychological workups; however, implantation was suggested primarily based on the results of the TNS.

The surgical procedure consisted of the implantation of a device (Medtronic, Inc., Minneapolis, Minn.) made of a radio receiver, interconnecting cord and wrap-around electrode encased in silicon rubber (fig. 1). This device could be activated by an external radio transmitter through a coupling antenna. The device and the basic technique of implantation have been described [10]. The nerves implanted included median, ulnar, brachial plexus, cervical plexus occipitals, femoral, sciatic and peroneal. On three occasions, more than one nerve were subsequently implanted.

The patients in this study have been periodically followed, either by personal interview or by mailed questionnaire. Of the original 69 patients, no recent information has been received from 10, leaving only 59 for analysis. Of the overall total, 30 claimed significant benefit, and 29 were considered to have insignificant benefit or to have failed. An overall success/failure rate of 30/29 = 50%.

Pain Evaluation Criteria

Pain evaluation was based on the subjective estimate of pain status by the patient himself. In order to decrease uncertainty, indirect estimate was done by the observer on the objective status level from the social and medical standpoints. The estimate was intended to be quantitative, but only gross changes were considered, as previously described [10]. The current four categories of change used in clinical practice and pharmacology were used, corresponding to levels of improvement: 0 = none;

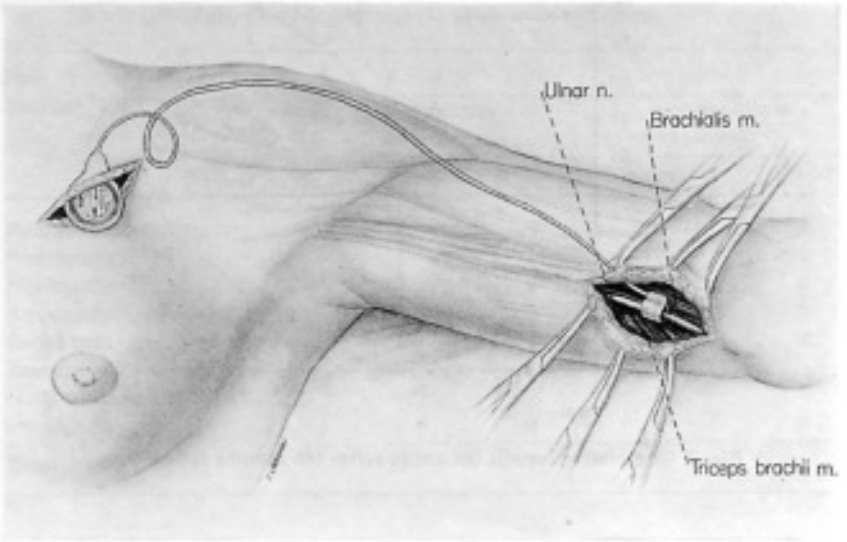

Fig. 1. Illustration of implanted device in position. Note wrap-around electrode at ulnar nerve, subcutaneous interconnecting cord placed away from the axilla, and receiver in subcutaneous subclavicular pocket.

1 = minimal (1–25%); 2 = moderate (26–50%); 3 = severe (51–75%); 4 = maximal (76–100%).

Following the criteria frequently used to estimate the effect of analgesic drugs by pharmacologists [4, 5], we adopted as *significant* relief, 'pain gone more than 50% during and/or following treatment'. Only patients claiming alleviation from 51 to 100% were considered benefitted by the procedure. This was usually supported by a corresponding drop in the use of drugs and change of life style.

Results

Of the general series of 59 cases, 37 were followed longer than a year. This group probably better represents the chronic effect of the devices. 50% of this group (19 cases) consistently admitted significant relief for as long as 4 years (table I; fig. 2).

Some patients obtaining maximum benefit (excellent) were analyzed. Without exception, those 11 cases received the same amount of benefit

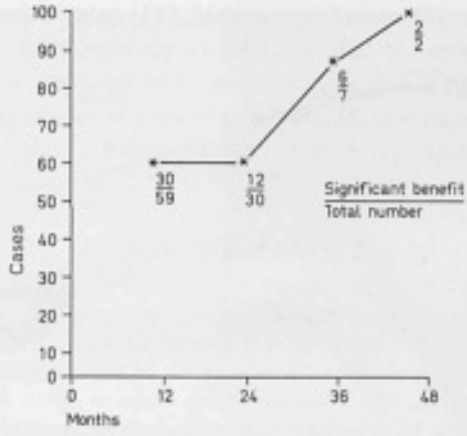

Fig. 2. Cumulative benefit for entire series (46 months follow-up).

Table I. PNS implants (results in 37 patients followed 12 to 46 months)

Qualification	Percent shift	Number of cases	Total
Significant relief (success)			
Excellent	76–100	11	
Good	51–75	7	18
Insignificant relief (unsuccessful)			
Poor	26–50	8	
Failure	0–25	11	19
			37

from the moment of the operation and throughout the period of observation; they showed neither gains nor loses in effect. When the group revealing worse results (failures) was considered, it was noticed that dramatic improvements had taken place to start with in only 2 of the 11 patients. Invariably, all relapses had taken place within a 24-month period of time.

Pain disorder was correlated to results and the findings shown in table II. As in the past, it was in disorders where nervous system damage occurred where more frequent significant benefit was achieved [8]. The ex-

Table II. PNS implants (12–46 months follow-up)

Pain disorder	Result			
	significantly improved		not significantly improved	
	excellent	good	poor	failure
Postoperative disc surgery	4	4	5	5
Posttraumatic	1	2	0	1
Myelopathy	2	0	0	0
Amputation	3	0	1	0
Facial pain	1	1	1	0
Zoster, scoliosis, underterm. occipital neuralgia, LBA, arthropathy	0	0	1	5
Total	11	7	8	11

Table III. Nerve implanted/results

Nerve implanted	Results			
	excellent	good	poor	failure
Sciatic	5	3	3	2
Ulnar	4	1	1	1
Occipitals	2	1	2	1
Femoral	0	1	0	3
Cervical plexus	0	0	1	1
Ulnar and sciatic	0	0	1	1
Ulnar and brachial plexus	0	0	0	1
Peroneal and sciatic	0	1	0	1
Total	11	7	8	11

ceptional case of a cervical herpes zoster neuralgia benefitted much from a cervical plexus implant until development of a neuroma made it necessary to remove the device. A word of caution is in order in the cases of postoperative intractable lumbar disc pain where failures have been more frequent than success.

Correlation of nerve implants to results, revealed only clear evidence of success in sciatic, ulnar and occipital implants. Evidence from other

Table IV. PNS implants (37 patients 12–46 months follow-up)

Preoperative test			Postoperative result	
30 patients	+	=	16 patients	+
			14 patients	−
7 patients	−	=	3 patients	+
			4 patients	−

nerves yielded insufficient or poor results, including more than one nerve trunk implantation (table III).

The results of preoperative TNS testing were compared with the long-term results of the implants and are shown in (table IV).

Complications (table V)

Tenderness at the *receiver* site alone was frequently due to local factors and usually reversible. Tenderness at the *electrode* site alone has been found to be due to electrode tightness or dislocation. This led to neuroma formation in 1 case and eventually to removal of the device. In the second one, tenderness gradually subsided. The 2 cases in which the whole site of implantation was tender (receiver, cord and electrode) it was due to sepsis. In 1 of these, tenderness appeared 6 months after implantation. After relapsing several times despite antibiotics, the device was finally removed 1 year after implantation, showing in cultures the presence of coagulase negative staphlococci. The second, in spite of negative cultures, finally had the device removed after several relapses despite antibiotics.

All 4 cases previously mentioned showing tenderness at the electrode site also showed sensory-motor deficit gradually developing following surgery. Neuroma formation may have accounted for the deficit in all of them.

Defective Stimulation

2 cases failed to receive subjective or objective evidence of nerve stimulation. Surgical revision in one, demonstrated a misplaced electrode (inverted). The second had the electrode wrapped around neurofibrous

Table V. PNS implants, complications (37 patients followed 12–46 months)

	Number of cases
Tenderness	
At receiver: trauma	3
kink	1
allergy	2
unknown	2
At electrode: tightness (neuroma)	2
At receiver and electrode: sepsis (neuroma)	2
Total	12
Defective stimulation	
No stimulation: misplacement	1
nerve damaged	1
Sensory-motor response decay:	
neuroma	2
Inadequate stimulation:	
dislocation	1
defective device	1
defective implantation	1
Total	7
General total	19

strands, remnants from a previously avulsed occipital nerve. The failure was assumed to be due to previously damaged neural tissue.

Gradual drop of sensory-motor response in time should be differentiated from the drop in 'pain suppression' effect. The second one takes place, in spite of the strong sensory-motor responses still available. The 2 cases where decay of sensory-motor response was observed proved to be due to development of a neuroma; one of them took place 40 months after implantation. Failure to provide steady stimulation (changes with posture) has been proved to be due either to a loose electrode or a defective device.

The ultimate results in the handling of these complications during our period of observation, revealed the following: (1) tenderness: 6 cases fully subsided, 2 partially and 4 not improved; (2) defective stimulation: 1 recovered 2 not better; (3) nerve disfunction: 2 partial recovery, 2 not improved.

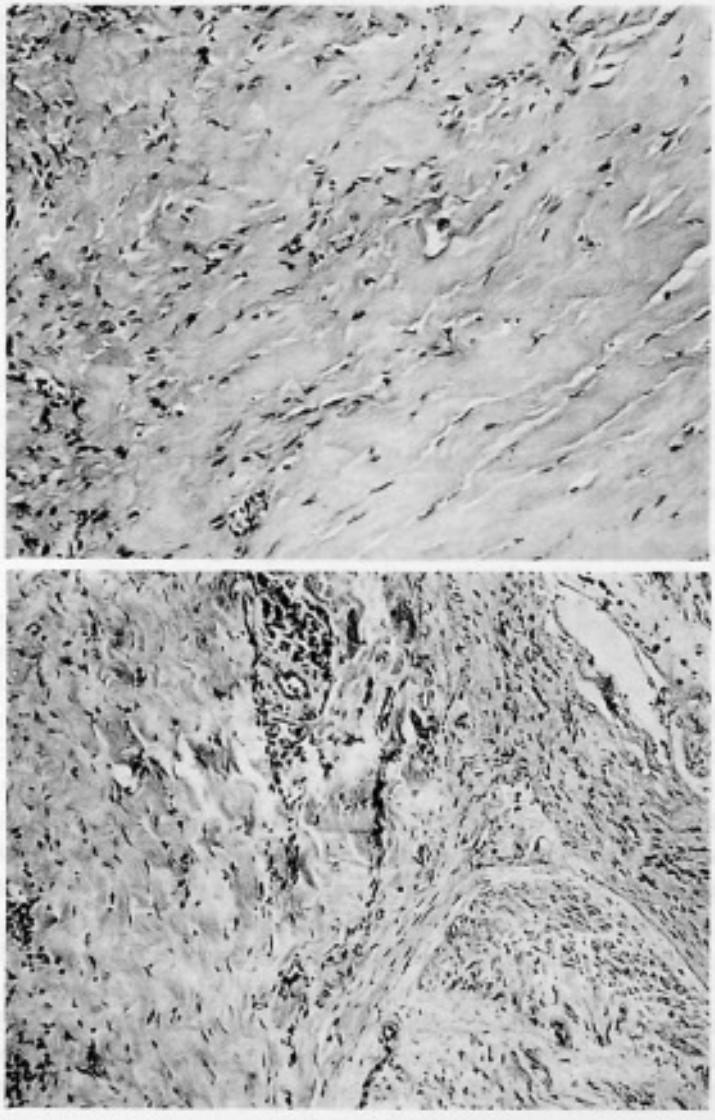

Fig. 3. a Normal fibrosis implant envelope. *b* Note thickened fibrous capsule and round cell perineural infiltration.

In conclusion, about one-half of the complications remained unsolved, although of no serious significance.

We have specially studied the tissue response to implants. Histological material was obtained from 20 cases reoperated for various reasons. The following clinicopathological groupings were noted:

(a) *Asymptomatic* (5 cases) (fig. 3a): A compact fibrous bursa surrounded the complete implant. The side in contact with the instrument showed a mesothelial layer without any adhesion to the device. The outer side of the bursa of myxoid appearance occasionally showed some round cell infiltration.

(b) *Tender implants* (6 cases): 5 of these cases were associated with gross mechanical abnormalities (kink, dislocation, pinching). These cases revealed more round cell infiltration on the outside of the capsule, at times infiltrating the fat, fibroblastic hyperplasia, fibrinoid and myxoid degeneration, and on one occasion fat necrosis.

(c) *Stimulation failure* (6 cases) (fig. 3b): 2 cases had mechanical failures and showed abundant inflammatory reaction around the bursa. The remaining 4 cases that showed gradual decrease of stimulus intensity revealed a very thick capsule between the nerve and the electrode. This could be designated as a 'fibroneuroma'. No acute inflammation was present.

(d) *Sepsis* (2 cases): 1 began at 6 months postoperative where a nonhemolytic staph coagulase-negative was isolated. The device was removed, showing granulomatous tissue around the capsule. The second one, 1 month after surgery, revealed hemolytic staph coagulase positive and purulent inflammation of the capsule.

Comments

Our information supports the hypothesis that the benefit observed in these patients was not related to placebo. The overall results show a frequency of benefit well above the 35% upper limit recognized for a placebo effect [1, 2], and the duration of benefit extends well over the 3-month period recognized for this effect fading away.

The beneficial result does not appear as clear, however, as when the type of pain disorder is considered. Disorders related to various injuries of peripheral nerves or cord appear to be favorable. We found that 75% benefitted (10 of 13 cases) when only the results on phantom pain, anal-

gesia dolorosa, soft injury traumatic neuralgia and myelopathies were considered. Most of them, clinically, fall into the group of the causalgic, dysesthetic pain syndromes or neuralgias. We have wondered if they do not represent some forms of central pain. The group of intractable post-lumbar disc syndromes, with the many factors playing in it, should deserve separate analysis in the future.

At this moment, only implants of the sciatic, ulnar or occipital nerves seem to result in benefit frequently enough to justify further trials as a way of treatment. Other implants may be regarded strictly investigational.

All cases included in this study were selected, primarily based on their response to the preoperative stimulation of their nerves. The correlation of this testing with the results obtained with long-range implants shows only 53% prediction of success and 42% prediction of failure. As a predictive tool, the procedure should be considered rather poor. The testing technique will have to be improved. Otherwise the incorporation of clinical correlates for the selection of possible candidates for implants must be developed. Indeed, the diagnosis [3] or the presence of some objective evidence of nervous system damage increases the chances that PNS could be of help.

Complication seems to be no deterrent. With the exception of the electrode site, tissue response to the implant seems similar to the heart pacemaker. Mortality is nil, morbidity of little consequence and complications largely preventable or correctable. Still there remains the same 'terra incognita' of the future: Are the results going to hold? How is the nervous system going to tolerate the devices and the inputs? The selection of cases for implantation should be carefully done considering not only the novelty of the procedure, but also exhausting the use of external devices until the patient not only convinces himself of the usefulness of the technique, but also proves to his physician that it is so by dropping the use of medication and by increasing his activities.

Moreover, the surgeon should also keep in mind that the only clear gains from the implant, as compared to the use of an external device, are efficiency and convenience, rather than any important increase in pain suppression effect. To the surgeon's dismay, most of the candidates can be helped satisfactorily by external devices, and only cases where almost continuous stimulation for a long period of time (months) is anticipated, may come to justify the implant.

We have found only three reports in the literature of follow-up observations from 3 to 5 years that may be considered to some degree long

Table VI. Long-range effects of PNS implants

Author	Number of cases	Sustained benefit	Follow-up period
SWEET [12]	31	19 (61%)	few to 68 months
KIRSH *et al.* [6]	32	17 (53%)	up to 36 months
CAMPBELL and LONG [3]	33	15 (45%)	few to 68 months
PICAZA *et al.* [9, 10]	37	18 (50%)	12–46 months

range (table VI). KIRSH *et al.* [6] reported 32 cases followed for 1–3 years. 17 cases obtained 'long-term effective result' (53%), particularly implants in the upper extremities. CAMPBELL and LONG [3] reviewed 33 implants including short and long range follow-up to 68 months. Sustained benefit was claimed in 15 patients (45%), and they remarked about the frequent failure in leg implants and frequent success in nerve injury related pains. SWEET [12] reviewed 69 cases including short as well as long follow-up for as much as 10 years. 17 cases obtained 'sustained relief'. The majority were posttraumatic pains, including peripheral nerves. He found that the results of nerve blocks could not anticipate the surgical results. He also noted 8 cases of postoperatory late infections.

These observations should be cautiously considered because they differ in the selection of cases as well as the method of pain appraisal. It is remarkable, however, that all of them claimed benefit in approximately one-half of their patients. These authors, as in our observations, are in agreement that it is in the upper extremity implants and in cases of posttraumatic or peripheral nerve injury where benefit is more likely. A superficial look to these studies, as in ours, may suggest that some patients may be obtaining relatively extended benefit (longer than 1 year). Our analysis of failures, however, points out that the critical minimum time for observing these results may be 2 years, as it was during this period of time that most relapses were taking place. Only 10 of our 18 cases reported as 'significantly improved' would fulfill this standard, including 8 of the 11 excellent results.

SWEET's [12] observations revealed that 12 of his 'sustained relief' patients, were followed more than 2 years and 1 of them for as long as 68 months. The review by CAMPBELL and LONG [3] of LONG's [7] original series has shown that of 10 patients, 4 still enjoy 'excellent' results after 44–68 months. This limited accumulating experience permits one to as-

sertain that a number of patients may obtain long-term benefit from PNS implantation. This may be of practical importance considering that this pertains to a group of pain disorders that have proven to be most difficult to control in the past.

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