THE THERAPY OF CHRONIC NON-MALIGNANT PAIN
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INTRODUCTION

The treatment of chronic pain is a difficult and vexing problem that covers the spectrum of modern medical practice combined with aspects of complementary medicine. Chronic pain is an important health issue in this country because it affects thousands of people, causes great suffering and relief is often inadequate. The financial cost to the nation resulting from work-days lost is astronomical.

It was in the 1950’s that chronic pain management became a specialty when Dr John J. Bonica, an anaesthesiologist from Seattle, established the first pain clinic. His textbook “The Management of Pain” is a major reference tome on this complex topic.

Patients with chronic pain do not show the autonomic signs associated with acute pain and hence the pathophysiology and behavioural responses are different. In recent years it has become fashionable to place several chronic pain conditions under one umbrella and call it the Chronic Pain Syndrome. This term used by Black in 1975 identified patients whose pain was inappropriate to existing physical problems or illness and formed the foundation for the psychological approach to the management of their problems.

The Nature of Chronic Pain

The definition of pain by the International Association for the Study of Pain is accepted worldwide:

“Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”.

Chronic pain is defined as pain outlasting the natural course of the disease or injury thus losing its biological significance and serving no useful purpose. Bonica suggested a period of one month beyond the usual course of the disease or a “reasonable time for healing”.

Abnormal afferent nociceptive activity occurring in the absence of a stimulus or in the presence of a weak non-noxious stimulus is thought to be the potential source of chronic pain. Sensitisation of peripheral afferent receptors may occur at the time of the original injury or disease process. In experimental neurona formation spontaneous neuronal activity can be demonstrated. Similarly axonal demyelination can produce random activity from the neurone producing pain perception.

Normal pain perception has two components:

a) The sensory component
b) The affective component.

In the thalamus the sensory component relays in the lateral part and the affective component in the medial part. Damage to the former by a stroke produces continuous burning pain in the opposite side of the body due to the unrestricted flow of activity from the medial part of the thalamus to the higher centres. The brainstem reticular formation can also inhibit pain transmission but a normal sensory input is necessary. Loss of this input by nerve injuries or viral destruction of the dorsal root ganglia can give rise to persistent pain.

Normal large A-fibre activity also has an inhibitory action on C-fibre and A-Delta fibre transmission. Peripheral neuropathies causing loss of large fibre transmission may cause uninhibited C-fibre activity and hence pain.

EFFECTS OF CHRONIC PAIN

1) Physiological

The physiological changes occurring during acute pain are only seen in chronic pain patients when recurrent severe lancinating pain occurs in trigeminal or other cranial neuralgias. Chronic pain sufferers develop habituation of the sympathetic responses during the early stages and progress to vegetative signs which have been described by Sternbach. These signs comprise sleep disturbance, constipation, lowered pain tolerance, psychomotor inactivity, loss of libido, irritability and changes in appetite. There may be a withdrawal from normal social activity and patients become preoccupied with their pain.

2) Behavioural

Patients with chronic pain whose behaviour is altered by environmental and emotional factors may manipulate their families and their workmates in an unacceptable and self-indulgent way. Similarly they may persuade their doctors to prescribe unnecessary and expensive drugs or their surgeons to perform ineffective operations.

3) Psychological

The mental effects of unremitting pain depend on the duration and the intensity of pain combined with the psychological makeup of the person. There is good evidence that personality influences the experience of pain and the magnitude of complaint that the patient makes. The degree of anxiety occurring varies enormously but clearly heightened anxiety increases the pain experience. Prolonged intense pain interferes with thought processes and will change the liveliest individual into a hopeless dejected wreck. Some studies have suggested that patients can develop the characteristics that are similar to the responses to dying. Depression, anxiety and hypochondriasis are common findings.
4) Sociological
Chronic pain sufferers can develop difficulties in relating to their families and friends. They are unable to work and may become financially embarrassed. In others, injuries at work may involve litigation and disability payments which can reinforce the maintenance of the "sick-role" attitude. Role reversal within the home may cause stress as a result of decrease in perceived status and respect.

THE PAIN CLINIC

Most district general hospitals in the UK will have a pain clinic and this may vary from a single-handed doctor seeing patients on an ad-hoc basis to a large multi-disciplinary approach in purpose-built premises with in-patient facilities. Today, the treatment of chronic pain involves many types of drugs, various techniques (e.g. nerve blocks), psychological evaluation and counselling, pain management programmes and complementary medical practices. Most pain clinics do not offer all of these services and in fact many may offer only one or two specific modalities (e.g., acupuncture and hypnosis).

Pharmacological therapy is the backbone of chronic pain therapy but nerve blocks make a significant contribution as well as stimulation techniques, psychological approaches, acupuncture and others.

TECHNIQUES FOR PAIN MANAGEMENT

A) INVASIVE TECHNIQUES

1. Sympathectomy
Most invasive procedures are performed on a day-case basis although in the elderly or when deep sedation or anaesthesia is required it is preferable to admit the patient for an overnight stay. Invasive techniques can have complications that manifest several hours after the procedure and thus careful postoperative supervision is required. Blocking the function of the peripheral sympathetic nerves can often relieve pain from a variety of conditions, particularly when the pain is accompanied by hyperpathia (e.g. post-herpetic neuralgia). The most important indications are reflex sympathetic dystrophy, ischaemic limb pain, and neuropathic pains.

(i) Stellate Ganglion
It is unusual for pain relief to be permanent after a single injection with local anaesthetic agent but repeated blocks on alternate days up to a maximum of eight often produces prolonged relief. This technique is mainly applicable to the stellate ganglion where the use of neurolytic solutions involve a high risk of complication due to spread affecting neighbouring structures. It is often better to perform a surgical sympathectomy in certain selected cases where proven improvement in pain has been achieved with local anaesthetic but prolonged relief has been difficult.

(ii) Lumbar Sympathectomy
In the lumbar region the ganglia are easily accessible to a needle as they lie on the antero-lateral surfaces of the lumbar vertebrae. The neurolytic most commonly used is 6% aqueous phenol. A single needle technique is satisfactory provided that good X-ray imaging equipment is available. The procedure needs minimal sedation and analgesia and is relatively straightforward to perform. In 20% of cases post-sympathectomy limb pain occurs which usually resolves in a matter of weeks and is alleviated by simple analgesics.

Gentio-femoral neuritis can occur in 5-10% of patients and is due to the spread of the neurolytic solution laterally across the anterior surface of the psoas muscle.

Lumbar sympathectomy is indicated in a variety of painful conditions but it is particularly useful in patients with ischaemic limb pain (rest pain), skin ulceration and incipient gangrene who are unsuitable for surgery. Intermittent claudication is usually not relieved nor is diabetic ischaemia or Raynaud's.

(iii) Intravenous Regional Block
Occasionally sympathetic ganglion blocks are contraindicated medically or the patient is afraid of such a technique. Another approach to block the peripheral sympathetic nervous system is to perform an intravenous regional block; this was originally described by Hannington-Kiff. He used Guanethidine which on first entering the post-ganglionic neuronal endings releases nor-adrenaline from the storage granules. The concentration of guanethidine increases and prevents the re-uptake of nor-adrenaline from the synaptic cleft. Therefore normal sympathetic tone cannot be maintained and a profound sympathetic block occurs. Other sympatheticolytic drugs have been used in this way (reserpine, ketanserin) but have not achieved the overall success of guanethidine.

2. Epidurals
The epidural injection of steroids for the treatment of chronic low back pain (LBP) and sciatica has been used for many years. Patient selection is vital for ensuring a satisfactory success rate for the procedure. Experience over the years has clarified the indications and technique most appropriate and as a result, this type of therapy has an enormous following by orthopaedic surgeons and pain clinic doctors alike.

Thorough investigation, neurological and orthopaedic evaluation are essential and although serious complications of this technique are rare, depot steroid formulations are absorbed systemically to some extent and adrenal suppression can occur.

For many years it was felt that nerve tissue could be damaged by the corticosteroid but workers have failed to show any histological damage after the epidural administration of triamcinolone. A history of previous back surgery dramatically reduces the chance of improvement with this technique probably as a result of adhesions and obliteration of the epidural space. This would prevent the steroid reaching the inflamed neural tissue.

3. Facet Joint Injection
Facet joint pain is a little known and difficult to understand cause of LBP. Injection of irritant hypertonic saline into the capsules of the facet joints in healthy volunteers produced LBP radiating to the buttocks and thighs. In facet joint disease the pain radiates from the lower part of the lumbar spine across the buttocks and into the thighs, occasionally radiating below the knee and mimicking sciatica. This pain, made worse by standing or sitting in one position for longish periods of time, is thought to be due to arthritis or damage to the lumbar facet joints. Paraspinal tenderness particularly over the sacro-iliac joint and reduced straight leg raising are common findings. The pain can be eased by movement, which is in contrast to the pain of spinal stenosis where movement exacerbates it.

Computerised axial tomography of the lumbar spine shows disease of the facet joints and confirmation of the
The blockade of aberrant nociceptive impulses arising from a neuroma can be effectively treated by local and steroid injection provided that the needle can be accurately placed. The use of a small electronic nerve-locating device will improve the chances of success.

B) STIMULATION THERAPY AND ACUPUNCTURE

1. Transcutaneous Stimulation

Transcutaneous nerve stimulation (TNS) has a very important place in the treatment of chronic pain. Melzack and Wall’s gate control theory of pain and the report by Sweet pioneered the use of nerve stimulation for the relief of pain. The success of TNS has led to great improvements in the technology and today several companies in the UK produce an extensive range of miniature battery-operated devices. These are convenient, unobtrusive, and patients are easily taught how to use them. Essentially TNS can be used to treat any localised chronic pain but the bulk of the research work has been conducted on the effect on post-operative pain. However in chronic pain patients it would appear that TNS is particularly suited to pain of neurogenic origin. These devices may appear to be expensive (approx. £80) but their use can dramatically reduce the intake of oral analgesics and non-steroidal anti-inflammatory drugs (NSAIDS).

2. Implanted Electrodes

There are certain circumstances when implanted electrode systems are indicated. These patients usually have severe neuropathic pain which has failed to respond to other modalities of treatment. The micro-electrodes, surgically implanted, directly stimulate the brain or the spinal cord and the control system is buried in a chest wall or abdominal wall pocket. The system can be telemetrically set using a transmitter. With micro-miniaturisation of components and advances in technology these techniques seem promising but they are very expensive (£5-8000) and technically complex to insert. The potential complications are such that only a few centres of excellence with extensive experience should use them.

3. Acupuncture

Acupuncture has been used by the Chinese for thousands of years for pain relief but it has only been in the last 25 years that this ancient method has achieved medical respectability. It was pain clinic physicians who took it on board with enthusiasm and it has now become an essential part of the therapy offered to patients attending the clinic. In spite of a wealth of poorly controlled trials published in recent years and much documentation of its proposed action pharmacologically and physiologically, its effect remains ill-understood. Its usefulness is not in doubt however and its lack of side-effects makes a trial of acupuncture a reasonable approach for the treatment of practically any chronic pain problem.

C) PHARMACOLOGICAL TECHNIQUES

1. Antidepressants

Well-designed studies have confirmed the usefulness of psychoactive drugs in the management of chronic pain. Amitriptyline has been used for many years in pain patients and there is much evidence that the analgesic effects of the antidepressants are related to their serotonergic effects. Newer agents such as fluoxetine, paroxetine and fluvoxamine which are all selective inhibitors of the re-uptake of 5-hydroxy-tryptamine do not appear to have the clinical usefulness of amitriptyline.
2. Anti-convulsants

The use of these drugs that specifically reduce spontaneous neuronal firing has for many years been common for pain relief of central origin. Their undoubted efficacy in the management of trigeminal neuralgia has encouraged doctors to use them for peripheral neuropathies but it has not been established that they reduce spontaneous neuronal firing in the periphery and their usefulness in conditions such as diabetic neuropathy, post-herpetic neuralgia and painful neuromas is anecdotal. Occasionally the side-effects of this class of drugs can be intolerable and patients on large doses should have regular blood tests to monitor levels of the drug and the white cell count.

3. Non-steroidal anti-inflammatory drugs

NSAID's are extensively used for chronic pain problems especially in the arthritides and musculo-skeletal pain from other causes. They are traditionally thought to work by interfering with prostaglandins and other nociceptive compounds released by tissue injury; however, some recent animal work suggests a central analgesic effect at the thalamic level[10]. Unfortunately many NSAID's have had to be withdrawn from the market because of serious side-effects.

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<tr>
<th>NSAID'S WITHDRAWN</th>
<th>SIDE-EFFECTS</th>
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<tr>
<td>feprazone</td>
<td>several</td>
</tr>
<tr>
<td>benoxaprofen</td>
<td>jaundice, photosensitivity</td>
</tr>
<tr>
<td>indoprofen</td>
<td>GIT bleeding</td>
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<tr>
<td>suprofen</td>
<td>renal failure</td>
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<tr>
<td>osmoxin</td>
<td>intestinal perforation</td>
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<tr>
<td>zomepirac</td>
<td>fatal anaphylaxis</td>
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<tr>
<td>alclofenac</td>
<td>skin rashes</td>
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<tr>
<td>fenclofenac</td>
<td>skin rashes</td>
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<tr>
<td>isoxicam</td>
<td>skin reactions</td>
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As a general rule it is wise to choose one of the many drugs available in this group which has the best track record with regard to side-effects. Although the different drugs vary in their efficacy there is little evidence to convince the clinician that any one is vastly superior to another. Most have a dose/response relationship with a ceiling effect and each patient must be individually titrated to the appropriate dose that produces the desired effect in the absence of side-effects. If a patient fails to respond to a particular class of NSAID then it is reasonable to change to a drug from a different class.

4. Cardio-vascular drugs

Beta-adrenergic blocking drugs have been known for many years to have a beneficial effect in certain migraine and atypical facial pains. Tocainide and flecanide have been used for the management of neuropathic pain on the basis of these drugs having the ability to block the calcium channels of the neural membrane. The specific calcium channels blocking properties of nifedipine and diltiazem have been used in the treatment of ischaemic limb pain. Clonidine, an alpha-2 agonist has been shown to produce good analgesia when administered epidurally. It would appear that the drug exerts its effect by a modulatory action on the spinal nociceptive processing which is mediated by an alpha-2 receptor. This effect can be antagonised in a dose-dependent way by injecting adrenergic antagonists.

D PSYCHOLOGICAL TECHNIQUES

Over the last few years there has been much more emphasis placed on this way of managing intractable pain problems. The prerequisite for any of the techniques available to the psychologist is firstly an accurate psychological profile of the patient and an interview should be supported by the many questionnaires that are available. Therapy can be divided into three major types: psychotherapy, operant conditioning and behaviour therapy. Needless to say the treatment can be very time-consuming and may not yield the success that the patient expects. Pain management programmes in which the psychologist plays a major role have been established for several years in centres in the UK and the results have been very encouraging.

CONCLUSION

The management of chronic pain is one of the most difficult and frustrating aspects of medical practice and it confounds us because pain is intangible and invisible to the doctor so that even its measurement is difficult. The psycho-social and behavioural aspects can have such an enormous impact on the patient's perception of pain that the therapeutic interventionalist may not be surprised that he is floundering in managing a complex "failed back" patient. It is unlikely that the future will bring a "magic bullet" or a universal panacea with which to treat all kinds of pain. The understanding of pain is still in its infancy and progress in elucidating the nature of the problem is painfully slow.

REFERENCES