The management of persistent pain

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CHRONIC, PERSISTENT OR LONG-LASTING PAIN affects up to one in five Australians.[1] Back pain alone is extremely costly; in Australia, health system costs for back problems were estimated to be $700 million in 1993–94,[2] while direct costs for back pain in the United Kingdom in 1998 were estimated to be in excess of £1632 million.[3]

ABSTRACT

- Persistent pain is a complex mix of physical and psychological symptoms and is ideally managed by a biopsychosocial approach. Often the relative contributions of family and personal relationships, finances, work, past pain experiences and personality outweigh those of the nociceptive or neuropathic processes from which most pain originates.
- Recent advances in our understanding of the pathophysiology of pain may lead to improved drug treatments; however, non-drug treatments — education, lifestyle modification, exercise and reassurance — should be used routinely to improve patients' quality of life.
- Patients with persistent pain that is difficult to control or has complex psychosocial influences, or who have a history of medication misuse, should be referred to a multidisciplinary pain centre. Selected patients may be offered invasive options such as nerve blocks or spinal-cord stimulation.
- The best outcomes are achieved in patients treated in group-based pain-management programs using cognitive-behavioural therapy to improve physical function, change unhelpful thinking and improve patients' understanding of their situation.

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What is pain?

Pain can be defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[4] Patients in pain present with both physical and psychological symptoms, often reflecting social and environmental influences.

Apart from the temporal characteristics (acute or persistent), pain can be classified clinically as either nociceptive or neuropathic, although in practice these may coexist.

- ***Nociceptive pain*** arises from mechanical, chemical or thermal irritation of peripheral sensory nerves (eg, after surgery or trauma or associated with degenerative processes such as osteoarthritis). Typically, the pain is described as sharp and is well localised.
- ***Neuropathic pain*** has quite different clinical features (Box 1), is less well localised and is caused by damage to the peripheral or central nervous system (ie, in conditions such as post-herpetic neuralgia and painful diabetic neuropathy).[5]

These specific clinical features may lead to a better understanding of neuropathic pain and more appropriate use of the available antineuropathic pain medications.

When pain lasts longer than 3 months or beyond the time when an acute injury would be expected to have healed, the patient's presentation becomes more complex, often, not surprisingly, with more psychological features. These include complaints of poor or non-refreshing sleep, tiredness, depression and poor concentration. Pain at this stage is often said to be "chronic" (this term has unfortunately developed some negative connotations and the terms "persistent" or "long-lasting" might be preferable).

The transmission of pain signals from the dorsal horn of the spinal cord, their modulation by descending inhibitory systems, and their continuation to the midbrain and cortex are now much better understood.[6] The clinical signs and symptoms of patients with persistent pain have neuroanatomical correlates that can be matched using functional magnetic resonance imaging of the cerebral cortex.[7] The degree of cortical reorganisation that can occur appears to be proportional to the intensity of the pain, and has been demonstrated in patients with "phantom limb" pain and chronic low-back pain.[8]

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Management of pain in general practice

Because of the complexity of persistent pain, it is essential to make a biopsychosocial diagnosis. After confirming the biomedical or organic components, an assessment of the relative contributions and dynamics of family and personal relationships, financial situation, employment record, past pain experiences and personality must be made. Patients' fear of pain and interpretation of what their pain means and its likely effect on their lives are becoming important targets for therapy. A number of psychosocial "yellow flags" have been found to be useful in predicting failure to return to work after back injury, and might also prove useful in predicting which patients will develop prolonged pain in other situations.[9] These include:

- presence of a belief that back pain is harmful or potentially severely disabling;
- fear-avoidance behaviour (avoiding a movement or activity because of a misplaced anticipation of pain), and reduced activity levels;
- tendency to low mood and withdrawal from social interaction; and
- an expectation that passive treatments rather than active participation will help.

Persistent pain can readily be considered a chronic disease, and consequently the patient needs to be "managed". Specific functional goals can be set and the patient's

expectations changed from "cure" to coping or living with less pain. Non-drug treatment strategies should be instituted early. These include reassurance, education, lifestyle modification, exercise, and reducing adverse factors (eg, weight loss for back, hip and knee pain; avoiding repetitive trauma).[10]

There is increasing clinical evidence that appropriate early aggressive management of acute pain will minimise the transition to persistent pain. Examples include decreasing the incidence of post-herpetic neuralgia by prescribing antiviral agents and amitriptyline for acute herpes zoster,[11,12] and implementing acute low-back pain guidelines (eg, advice to continue ordinary activity, avoid bed rest and use simple analgesics and short-term non-steroidal anti-inflammatory drugs [NSAIDs]).[3]

Drug treatment strategies

As many persistent pain syndromes have large psychosocial components, it is not surprising that drug treatment is not very effective unless it is administered as part of an overall management plan.

Up to 50% of patients presenting with persistent pain may have some degree of depression.[13] Supportive counselling, education and reassurance, as well as consideration of other short-term psychological therapy (eg, problem solving) from GPs or other skilled health workers, should be instituted, and, if appropriate, medication prescribed.[14] While there are many medications for the treatment of depression, the mainstay for the patient with pain has been the tricyclic antidepressant amitriptyline. Reported advantages of this medication include night-time sedation, intrinsic analgesic activity and a direct antidepressant effect.[15] While newer drugs (eg, the selective serotonin reuptake inhibitors) may be safer and more effective antidepressants, there are only limited data on their ability to relieve pain.[16]

For ongoing nociceptive pain, which often arises from degenerative musculoskeletal conditions, the regular use of simple oral analgesia such as paracetamol (up to 4 g per day) is generally safe and well tolerated. Use of intermittent short-term NSAIDs, and avoidance of long-term use of short-acting opioids (eg, codeine), is recommended.[17] For patients who do not respond to this management, a careful trial of a long-acting opioid may be considered. Evidence for efficacy of opioids in persistent pain is still scarce; however, management strategies to guide the prescriber have been published (Box 2).[18] Addictive behaviour (drug seeking and the continued use of opioids despite harm) is very uncommon while pain continues to be well controlled and function maintained.[20]

If neuropathic pain is diagnosed, there is evidence that it may be useful to trial a low-dose tricyclic antidepressant (amitriptyline, 10–25 mg at night), which can be supplemented with antiepileptic medication (carbamazepine 400–800 mg per day in two divided doses, or gabapentin 300–2400 mg per day in three divided doses) (Box 3).

With the new care planning item numbers from the Commonwealth Medical Benefits System and the focus on developing management plans for treating chronic disease, an excellent opportunity now exists to promote shared care between pain centres, general practitioners and other health professionals for these patients.

Patients should be encouraged to integrate their care plan into a healthy lifestyle, which would include maintaining their ideal weight, utilising stress management strategies and participating in regular exercise.

1: Features of neuropathic pain

- May occur in the presence of a neurological deficit (stroke, brachial plexus avulsion, spinal cord injury).
- May be unaccompanied by ongoing tissue damage.
- May occur in an area of sensory loss.
- May be burning, or shooting (ie, different to nociceptive sensations) or dysaesthetic (unpleasant abnormal sensations, such as "pins and needles").
- May occur (i) spontaneously or (ii) in response to normally non-painful stimuli (allodynia).
- May be greater than expected pain in response to a painful stimulus (hyperalgesia), or pain that increases with a repetitive stimulus (hyperpathia).

2: Points to be discussed with a patient before a trial of oral opioids[18]

- Stress that oral opioids are only one part of the treatment plan, and that data are lacking on the long-term effects of medically prescribed opioids.
- Set realistic functional goals (eg, to commence or maintain an exercise program, improve self-care ability, get out to the shops, etc).
- Explain that the aim is for controlling pain rather than no pain.
- Explain that dependence is a physiological effect of opioids and that withdrawal symptoms occur if the drug is stopped. (This should not be a problem with medically prescribed opioids.)
- Warn of the potential for cognitive impairment which may affect driving ability, especially while commencing opioid therapy and around the time of dose escalation. Point out the increased likelihood of sedation if benzodiazepines and/or alcohol are used in conjunction with opioid therapy.
- Explain the indications for ceasing treatment with opioids:
  - –lack of improvement in function, or evidence of deterioration in function;
  - –unsanctioned dose escalation and requests for early repeat prescriptions;
  - –losing prescriptions;
  - –unapproved use of the drug to treat other symptoms.
- Stress that patients must accept responsibility for:
  - –ensuring their supply of medication does not run out after hours;
  - –security of their medication;
  - –keeping review appointments;
  - –using only one doctor to supply this medication.
- Discuss side effects and their management (eg, constipation, nausea, sedation, dry mouth, urinary hesitancy, and depression of sex hormones, with associated risk of osteoporosis with long-term use).[19]

Role of pain centres

All Australian capital cities have public hospital pain centres. The waiting time to access these centres is usually long (over 6 months), but most will offer "fast track" access for cancer patients and telephone advice for other pain syndromes. Access to care in the private health system is usually

3: Drug treatment for neuropathic pain

Condition and drug used	Number needed to treat*	NHMRC level of evidence†[21]	Reference
Painful diabetic neuropathy			
Tricyclic antidepressants	3.5	I	16
Carbamazepine	3.3	II	22
Gabapentin	3.7	II	23
Post-herpetic neuralgia			
Tricyclic antidepressants	2.1	I	23
Gabapentin	3.2	II	23
Oxycodone	2.5	II	23
Trigeminal neuralgia			
Carbamazepine	2.6	I	24
Painful polyneuropathy			
Tramadol	4.3	II	25

* Number needed to treat for one person to derive at least a 50% reduction in pain.[26] † See Box 5.

4: Consider referral to a pain centre

- When a trial of opioids fails to provide pain relief
- When the patient fails to improve in function
- When the patient has difficult-to-control neuropathic pain
- When a satisfactory diagnosis can not be reached
- When there are complex psychosocial influences
- When pain is accompanied by a history of medication misuse

5: Levels of evidence (National Health and Medical Research Council)[21]

Level I: Evidence obtained from a systematic review of all relevant randomised controlled trials.

Level II: Evidence obtained from at least one properly designed randomised controlled trial.

Level III-1: Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).

Level III-2: Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case–control studies, or interrupted time series with a parallel control group.

Level III-3: Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.

Level IV: Evidence obtained from case-series, either post-test, or pre-test and post-test.

6: Goals of pain management programs

- To improve patients' understanding of their situation
- To improve their level of physical functioning
- To modify their perceived level of pain and suffering
- To provide coping strategies for dealing with their disability and distress
- To promote self-management
- To reduce or modify their future use of healthcare services

considerably shorter. Box 4 offers some indications for referral to a pain centre.

At a pain centre, an initial consultation is offered with a pain medicine specialist, physiotherapist, rehabilitation physician, occupational therapist, psychiatrist or psychologist, depending on which specific disciplines are represented at the centre. A multidisciplinary management plan will be developed in consultation with the patient and general practitioner. The key to success is patient involvement.

There are a range of specialised therapies available in pain centres to complement a multidisciplinary management plan. However, these must not be used in isolation. While the evidence base for pain medicine is slowly growing, much of it is derived from small-scale observations and may not be readily generalisable.[27]

Cognitive-behavioural therapy: Cognitive-behavioural pain management programs have Level 1 evidence for efficacy; see Box 5 for evidence levels).[28] An effective cognitive-behavioural program requires well trained and cohesive staff members who all deliver the same message to the patient. These programs, which are generally group-based, provide information about pain, exercise, and life-style modification, and assist in dispelling unhelpful beliefs, using cognitive-behavioural strategies to achieve these goals (Box 6).

Epidural corticosteroid injections: These have been traditional treatments at pain clinics, and the evidence for using corticosteroid injections in patients with "sciatica" or radiculopathic (leg) pain is becoming clearer. There is Level 1 evidence from a meta-analysis (907 patients) showing a significant short-term benefit (with greater than 75% pain relief for up to 60 days).[29] However, there is no evidence to support the use of epidural corticosteroid injections in the management of back pain without radiculopathy.[30]

Diagnostic spinal assessment: This assessment is offered in many centres for people with back or neck pain. The major nociceptive foci (eg, intervertebral disc or facet joint) in either the cervical or lumbar spine may be identified using local anaesthetic blocks. Denervation techniques for the nerves to these structures have been available for many years, but evidence of efficacy has been lacking until recently. There is now limited Level II evidence for the efficacy of radiofrequency denervation procedures in the cervical spine, with a reported median time of 263 days for return of pain to 50% of the pretreatment levels.[31] Likewise, there is limited Level II evidence for the efficacy of radio-frequency denervation procedures in the lumbar spine, with the duration of significant pain relief ranging from 3 to 12 months.[32] Treatment during this analgesia "window" must be effectively coupled with a behavioural and exercise program to ensure optimal results.

Spinal-cord stimulation: Several pain centres have developed expertise in the use of this technology, which involves placing an array of between 4 and 16 electrodes in the epidural space. Tiny variable-frequency electrical currents can then be delivered to the spinal cord from a subcutaneously placed pulse generator, similar to a cardiac pacemaker. Their action seems to involve GABAergic mechanisms at

the dorsal horn.[33] There is Level III-1 evidence supporting use of spinal-cord stimulation for patients with radicular neuropathic pain and for those with complex regional pain syndrome.[34,35] Selecting which patients will benefit most from this expensive technology remains a challenge, but data are emerging showing improved outcomes from this treatment after multidisciplinary assessment and an early integrated management plan.

Medication misuse: Assessment of patients with a history of medication (usually morphine) misuse (or in whom such misuse is suspected) has increasingly become a role of pain centres. In general, going back to first principles is required, with a new, full, multidisciplinary assessment, followed by a discussion with the patient and formulation of a management plan. Options include stopping the opioids and substituting alternative strategies, such as treatment for neuropathic pain and/or a pain management program based on the cognitive-behavioural approach. If patient acceptance of, or compliance with, opioid withdrawal is a problem, shared care between the patient's general practitioner, the pain centre and a drug and alcohol service should be considered.

Conclusion

The over-riding emphasis in managing patients with persistent non-cancer pain should be on improvement in function, and there is much that can be done by general practitioners to initiate effective treatment options for these patients. Combining non-drug treatment strategies with pharmacotherapy, backed up by a care plan that can be shared with a pain centre, will go a long way towards improving quality of life for this complex patient group.

Competing interests

I have served on medical advisory boards for Pfizer, Janssen-Cilag, Mundipharma and CSL.

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