#### Case study five

A young adult female suffered from acute burns pain. It was noted that she was allergic to NSAIDs. As she was already receiving maximal doses of morphine but pain control was still insufficient, the patient was administered patient-controlled analgesia (PCA) treatment with parenteral morphine. However, her pain was still not well controlled and she was switched to parenteral fentanyl PCA. In addition, she was given ketamine when required. The patient developed chronic pain thereafter and continued to require opioids; she was also given benzodizepines and anti-depressants. At a later stage, the patient voluntarily weaned herself off the drugs.

**Lesson:** Opioids can be used to treat acute pain, which may sometimes develop into chronic pain. Non-malignant cases may also require opioids, especially when pain is no longer manageable for the patient. It is important to resolve the balance of managing pain and achieving a good guality of life for patients; the development of trust between doctors and patients is also important for effective pain management and to curb abuse of medication.

## **Speakers**



#### Dr Yeo Sow Nam

MBBS, FFPMANZCA (Aust/NZ), FANZCA (Aust/NZ), MMed (S'pore), FIPP (US), Cert Acupuncture, FAMS

Dr Yeo Sow Nam is a Consultant and Director of Pain Management Services, and Director of Acupuncture Services, at Singapore General Hospital, Singapore. He is also a consultant anaesthetist in the Department of Anaesthesia and Surgical Intensive Care Unit at Singapore General Hospital, a visiting consultant in Pain Management at the National Cancer Centre and honorary consultant at Dover Park Hospice. Dr Yeo is a Fellow of the Australian and New Zealand College of Anaesthetists, a Fellow of the Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists and Fellow of the Interventional Pain Practice. World Institute of Pain. He is also the President of the Pain Association of Singapore. He has been a speaker at over 80 international, regional and local meetings in the last 2 years, and has authored more than 40 abstracts and original articles published in the medical and scientific press.



## Dr Noreen Chan

MB, BS, MRCP (UK), FAChPM, FAMS

Dr Noreen Chan is Medical Director and CEO of Dover Park Hospice, Singapore. She is also a Visiting Consultant to Department of Palliative Medicine, National Cancer Centre (NCC), and Department of Haemato-Oncology, National University Hospital. Dr Chan previously worked in the Department of Palliative Medicine at NCC, and helped to develop and run the inpatient consultative service at the Singapore General Hospital. She is also the Honorary Secretary of the Pain Association of Singapore. Her interests in palliative medicine include the interface between oncology and palliative care, clinical decision making and professional education at all levels.



#### Dr Serene Lim MBBS, M Med (Anaes)

Dr Serene Lim is Senior Consultant Paediatric Anaesthetist at Kandang Kerbau Women's and Children's Hospital (KKWCH), Singapore. Her special interest is in paediatric pain, an area in which she became involved after completing her Fellowship Rotation at the Boston Children's Hospital in 1995, where the Pain Program is headed by one of the world's great authorities on paediatric pain, Charles B Berde. Dr Lim is in charge of the Paediatric Acute Pain Service and Pain Link Group at KKWCH.

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## Introduction

Despite years of study, the mechanism of pain is poorly understood and the control of pain has been largely neglected. Pain is a major healthcare problem and accounts for more than 40 million medical appointments yearly. Although its definition may be highly subjective, the physical and psychological damage is particularly exacting. In fact, chronic and recurrent pain is a disease in its own right. There is an impetus for pain education for physicians so that they can accurately diagnose and effectively treat pain.

## Welcome message

Following the distribution of the last two newsletters, there has been a great deal of encouraging feedback from medical and allied healthcare colleagues suggesting that more such educational articles should be featured. Hence, in this latest issue, we will highlight common pain topics such as musculoskeletal pain, neuropathic pain and paediatric pain, and the use of opioids in chronic non-cancer pain.

We will also showcase some of my patients whose pain has been successfully managed. These case studies were presented at a refresher course at the Singapore General Hospital's annual scientific meeting. Attended by many specialists and family physicians, this was a highly interactive and educational session.

Many more projects are in the pipeline, including the forthcoming Pain Association of Singapore's (PAS) Biennial Scientific meeting to be held on 28–29 July. There will be a refresher course organized with the help of our prominent overseas speakers, which include Dr David Niv, the previous European Federation of International Association for the Study of Pain Chapters' President, and Dr Roger Goucke, Director of Pain Management Services at Sir Charles Gairdner Hospital, Perth. We look forward to your continual support and participation in the many scientific programmes that have been arranged for all our colleagues.

Dr Yeo Sow Nam President, PAS

# n and You by the Pain Association of Singapore and its Advisory Board

#### Issue 3 - July 2006

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# Neuropathic pain – an insight into an age-old problem

Dr Yeo Sow Nam



disease or surgical section of the peripheral or central nervous system" or "pain initiated or caused by a primary lesion or dysfunction in the nervous system".<sup>1,2</sup> Studies in Europe have revealed that neuropathic pain prevalence ranges from 6.0-7.7% of the population.<sup>3</sup> The leading cause of pain is low back pain (Figure 1), but the prevalence and incidence of neuropathic pain varies with different medical conditions.4-7



Nociceptive pain, on the other hand, is caused by injury to body tissues, while mixed pain involves elements of both neuropathic and nociceptive pain.8

#### Pathophysiology - the mechanisms causing neuropathic pain

Neuropathic pain can be caused by many stimuli (Figure 2).<sup>9</sup> The hallmarks of neuropathic pain are chronic allodynia (pain resulting from normally painless stimuli) and hyperalgesia (the heightened sense of pain to noxious stimuli).<sup>10</sup> These phenomena result from

various mechanisms including abnormal connections between C (pain) fibres and Aβ (touch) fibres.<sup>11</sup> Once nerves have been damaged, they may develop an increased expression of abnormal or dysfunctional sodium ion (Na<sup>+</sup>) channels.<sup>12-15</sup> Heightened sensitivity to mechanical and thermal stimuli can then result from increased conduction frequency or spontaneous ectopic discharges.

#### Recognising and assessing the neuropathic pain process

Neuropathic pain can be divided into spontaneous and stimulusevoked symptoms (Table 1).<sup>2,11</sup> Its diagnosis is largely by clinical impression of the signs and symptoms described by the patient. A

> patient's risk of developing chronic pain can be reduced by good communication with him or her, the use of effective early pain relief and thorough follow-up. There is a pressing need for improved treatment as the strong inter-relationship between pain, sleep disturbances, and anxiety and depression intensely impairs the patient's functional abilities.16-18

#### Managing neuropathic pain

The general practitioner plays a pivotal role in the ongoing management of neuropathic pain, as most patients are seen by

them. However, they are also the least confident in recognising neuropathic pain, and inappropriate drug prescriptions are worryingly common.<sup>19</sup>

Pre-emptive analgesia is the recommended first-line therapy for treatment of neuropathic pain because, once established, severe pain is more difficult to treat.<sup>10</sup> Pregabalin has been found to be very effective in treating diabetic peripheral neurophathy and postherpetic neuralgia.<sup>20</sup> Acupuncture has shown positive results, and other management options include intrathecal neurolysis or

pumps, spinal cord stimulators

	Sign/Symptom	De	
	Spontaneous symptoms		
	Spontaneous pain <sup>11</sup>	Per	
	Dysesthesias <sup>2</sup>	Abr	
	Parasthesias <sup>2</sup>	Abr	
Stimulus-evoked sympt			
	Allodynia <sup>2</sup>	Pai e.g	
	Hyperalgesia <sup>2</sup>	Hei	
	Hyperpathia <sup>2</sup>	Del	

Table 1. Signs and symptoms of neuropathic pain.

and cognitive-behavioural therapy.<sup>21,22</sup>

Chronic neuropathic pain is a disease, not a symptom. 'Rational'

3. Neuropatin Failer and starter, bar of the price inc. 4. Perturbert K. et al. Acta Artaestrestic Scalard 1997, 43:305–305, 1807

## Musculoskeletal pain

Dr Yeo Sow Nam

#### **Epidemiology of low** back pain

Musculoskeletal pain is one of the most common causes of pain and patients usually present with back or neck pain. There is a 60–90% lifetime incidence of low back pain (LBP), with an average of 5% annual incidence of LBP in any person.

LBP is caused by a variety of musculoskeletal disorders (e.g. internal disk disruption, degenerative disc disease, facet arthritis, etc.).<sup>1</sup> LBP

# Significant trauma history, or minor in

- older adults
- Nocturnal pain in supine position with history of cancer
- Bladder or bowel incontinence or dysfunction Constitutional symptoms
- iph node enlargemer
- Risk factors for spinal infection Intravenous drug use
- Major motor weakness

Figure 3. Musculoskeletal pain: history and examination.

manifests not only as pain but also translates into social and economic losses. Furthermore, contrary to popular belief,



Figure 2. Development of neuropathic pain.

#### scription (example)

sistent burning, intermittent shock-like or lancinating pain

normal unpleasant sensations e.g. shooting, lancinating, burning

normal, not unpleasant sensations e.g. tingling

nful response to a non-painful stimulus warmth, pressure, stroking

ghtened response to painful stimulus e.g. pinprick, cold, heat

ayed, explosive response to any painful stimulus

polypharmacy is often necessary with clear treatment goals. New agents and adapting new uses for existing agents will offer additional treatment options.



rates of successful recovery rapidly decline as time off work increases.

Drug	Unadjusted odds ratio (95% Cl*)	Adjusted' odds ratio (95% CI')	P (significant at 0.01)
Celecoxib	1.39 (1.11, 1.73)	1.21 (0.96, 1.54)	0.11
Rofecoxib	1.67 (1.40, 2.00)	1.32 (1.09, 1.61)	0.005
Other selective NSAIDs	1.55 (1.25, 1.92)	1.27 (1.00, 1.61)	0.046
Ibuprofen	1.40 (1.27, 1.55)	1.24 (1.11, 1.39)	< 0.001
Diclofenac	1.69 (1.53, 1.86)	1.55 (1.39, 1.72)	< 0.001
Naproxen	1.38 (1.11, 1.72)	1.27 (1.01, 1.60)	0.04
Other non-selective NSAIDs	1.40 (1.20, 1.64)	1.21 (1.02, 1.44)	0.03

Adjusted for use of aspirin, statin, anti-depressants, ischemic heart disease, diabetes, hypertension, arthritis, smoking, obesity, deprivation. ^CI (Confidence Interval)

Hippisley-Cox J and Coupland C. BMJ 2005;330:1366-1369.

Figure 4. The risk of myocardial infarction with NSAIDs and COXIBs

#### History and examination

The first step is to adopt a high index of suspicion to enable the identification of any red flags because pain may indicate an underlying disease such as tumour growth, fracture, infection and neurological damage (Figure 3). Waddell signs may also be documented to aid in identifying symptom magnification or inconsistent symptoms.<sup>2</sup> Diagnostic tools suitable for examination include laboratory-based tests, radiographs, discography and magnetic resonance imaging.

#### Treatment

It is important to recognize the type of pain being experienced. Musculoskeletal pain is usually nociceptive, and choices of medication may include nonsteroidal anti-inflammatory drugs (NSAIDs) or cyclo-oxygenase-2 inhibitors (COXIBs), membrane stabilizers, muscle relaxants or non-narcotic analgesics. Narcotics are rarely indicated and steroids are more useful for radiculitis.

Trigger-point injections are used to treat myofascial pain syndrome, for which the use of steroids is strongly discouraged.<sup>3</sup> Patients

## **NSAIDs/COXIBs** Use lowest effective dose, shortest duration

- Not for patients who have recently undergone coronary artery bypass graft surgery and revascularization procedures
- COXIBs should not be prescribed for patients with established ischaemic heart disease, stroke or congestive heart failure
- Caution for COXIBs for patients who have: hypertension, hyperlipidaemia, diabetes and smoking as well as peripheral arterial disease
- Etoricoxib should not be prescribed for patients with hypertension whose blood pressure has not been adequately controlled

Health Sciences Authority, Press release, April 2005. Available at: www.hsa.gov.sg/docs/No12\_'5fCOX-2\_'5fNSAIDs\_'5f28Apr2005.pdf, accessed May 2006.

Figure 5. HSA recommendations for NSAIDs and COXIBs.

References: Reterences: 1. Schwarzer AC, et al. Spine 1994;19:801–806. 2. Fishbain DA, et al. Clin J Pain 2004;20:399–408. 3. Simons DG, et al. Travell & Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual, Vol 1, 2nd ed. Philadelphia: Wilkins 1999;159–160. 4. Patel M, et al. Int J Epidemiol 1989;18:900–906. 5. Lee TL. Ann Acad Med Singapore 2000;29:17–21. 6. Fritzell P, et al. Spine 2001; 26:2521–2532. 7. Hippisley-Cox J, et al. BMJ 2005;331:1310–1316. 8. Singh G, et al. Abstract submitted at the European League Against Rheumatology, 8–11 June 2005, Vienna, Austria. 9. Hippisley-Cox J and Coupland C. BMJ 2005;330:1366–1369. 10. Health Sciences Authority, Press release, April 2005. Available at: www.hsa.gov.sg/docs/No12\_COX-2\_NSAIDs\_28Apr2005.pdf, accessed May

#### with chronic musculoskeletal pain have also benefited from acupuncture.<sup>4,5</sup> Treatment by vertebroplasty has been found to be very effective for osteoporotic and cancer-related spinal fractures. Surgical options also include laminectomy, fusion, discectomy and percutaneous lumbar discectomy. Although a large proportion of spinal surgeries are initially successful,<sup>6</sup> less than 25% of disc surgeries are successful after 5 years.

Perspectives on NSAIDs and COXIBs

One of the barriers to treating pain

is the concern over the risks of side effects caused by the drugs. Effective medications such as NSAIDs and COXIBs may cause serious side effects if taken indiscriminately and for long periods. NSAIDs have been most commonly associated with gastropathy and the induction of lesions and stomach ulcers.7 This has led to the development of COXIBs, but meta-analyses of adverse events associated with NSAIDs and COXIBs have indicated an equal increased risk of acute myocardial infarction (Figure 4).<sup>89</sup> Hence, the use of these drugs must be consistent with Health Service Authority (HSA) recommendations (Figure 5).<sup>10</sup>

## Managing cancer pain Dr Noreen Chan

#### Introduction

Pain is a common occurrence in cancer, affecting 60–90% of patients with advanced disease.<sup>1</sup> It is one of the most feared symptoms, but is frequently undertreated. Pain in cancer patients may result from the cancer itself, from cancer treatments – whether surgery, radiotherapy or chemotherapy - or from an unrelated problem such as arthritis.

Effective pain management is often lacking because of certain beliefs held by both healthcare workers and patients; for example, the idea that only terminal patients should receive opioids, fears of addiction or decreasing efficacy, and lack of knowledge of adequate treatment methods. The World Health Organization (WHO) has emphasized that "nothing would have a greater impact on improving cancer pain treatment than implementing existing knowledge".<sup>2</sup>

#### Pain assessment

used to treat it. Pain is classified as either nociceptive or neuropathic (Figure 8). Nociceptive pain usually responds well to morphine, whereas Pain is compounded by social, psychological and spiritual factors, as well as by physical factors. Pain should be evaluated (Figure 7) for its neuropathic pain tends to respond less well. Once the pathophysiology of the pain has been characterized and psychosocial factors taken intensity and impact on functional ability, as well as its pathophysiology. into account, a management plan can be devised. Its goal should be A detailed history that covers any concomitant medical problems, maximum pain relief with minimum side effects. Treatment should previous treatments and responses, a psychosocial assessment and a physical examination will contribute to the development of an be multimodal and consists of analgesics as well as anti-cancer effective therapeutic strategy. treatment (if appropriate), non-drug treatments (which includes education, exercise, etc.) and interventions such as nerve blocks or spinal analgesia.

#### Cancer pain management

The type of pain experienced will determine the type of medication

'OLD CART'	PAIN SCALES		
<ul> <li>Onset</li> <li>Location</li> <li>Duration</li> <li>Character</li> </ul>	Numeric & Categoric Scales No $\begin{array}{c} \bullet & \bullet & \bullet & \bullet & \bullet & \bullet \\ Pain \\ 0 & 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 \\ \end{array}$		
<ul> <li>Aggravating factors</li> <li>Relieving factors</li> <li>Therapy for pain</li> </ul>	NONE MILD MODERATE SEVERE Non-Verbal & Numeric Scales No t t t t t t t t t t t t Po Pain 0 1 2 3 4 5 6 7 8 9 10 F		

Figure 7. Methods of pain assessment

1. Ho RC. CA Cancer J Clin 1994;44:259–261. 2. Foley KM. J Clin Oncol 1995;13:2149–2151. 3. World Health Organization. WHO's pain ladder. Available at: www.who.int/cancer/palliative/painladder/en, accessed May 2006.

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<b>NATIC NOCICEPTIVE</b> ing, gnawing, well-localized, se with movement	Bone mets, liver capsule pain, chest wall	Anti-inflammatories, steroids, opioidds, clonidine, strontium-89, calcitonin, bisphosphonates
CERAL NOCICEPTIVE stant, colicky, aching, dull, o, poorly localized	Ovarian, bowel, pancreatic canceer	Opioids, anti-spasmodics, glycopyrollate, octreotide, steroids
IROPATHIC hing/stinging/biting, bing/electric ck/lancinating, allodynia, eralgesia, may be episodic	Brachial, lumbosacral plexopathies, post- herpetic neuralgia	Tricyclic anti-depressants, anti-convulsants, LA. Methadone, mexiletine, ketamine (Steroids/anti-inflammatory)

Figure 8. Types of pain and their treatment

The WHO recommends that medication for cancer pain relief should

be chosen according to a three-step ladder denoting mild, moderate and severe pain.<sup>3</sup> It is not a rigid framework but may be varied. The non-opioid analogsics, paracetamol or aspirin, can be used for mild or moderate pain. When pain persists or increases, a weak opioid such as codeine should be added. For severe pain, a potent opioid such as morphine is recommended. Adjuvant drugs may be added at any stage; these are medications which are not classified primarily as analgesics but are useful in painful conditions, particularly neuropathic pain. To control pain effectively, medication should be taken at regular intervals, avoiding 'as required' dosina.

Patients should be taught to monitor their own pain using pain scales so that they can discuss their pain with healthcare professionals. Successful cancer pain management depends on thorough ongoing clinical assessment, a systematic approach and the rational use of drugs in a multidisciplinary, multimodal approach.

## Paediatric pain

Dr Serene Lim

### Debunking the myth

The misconception that children do not feel pain has led to the unfortunate conclusion that children do not require analgesia.<sup>1</sup> In 1987, a randomized trial in pre-term babies clearly demonstrated that opioids have a positive effect on the stress response, reducing both mortality and postoperative complications.<sup>2</sup> This landmark study prompted intense interest and attention onto paediatric pain.

#### The challenge of paediatric pain

The primary reason for the inadequate management of paediatric pain is its perceived low priority against the administration of disease-related medical treatment. As pain can have periods of exacerbations and relief, certain stimuli may evoke its recurrence even after initial treatment.

The major barriers to the use of pain medication in children are fear of addiction, over-dosing and respiratory arrest. Advancements in medical science have since improved monitoring of treatment, enabling tailored therapy to be delivered to each child. The drug's potency for addressing pain adequately and quickly should also be considered (Figure 9).<sup>3\*</sup> The misguided fear about the use of opioids demonstrates a real need to re-educate healthcare practitioners and the general public, and to encourage patients and parents to focus on rehabilitation.





#### Pain assessment

Optimal pain control begins with an accurate and thorough pain assessment. A self report is ideal but is largely dependent on the cognitive abilities of the child and his/her level of gualitative appreciation. Hence, reliability of pain self-assessment in children can be uncertain. Pain scores are useful as a basic guideline for the severity of pain and, thus, doctors need to assess further the detrimental impact of

> the pain on the child's quality of life (QoL). A behavioural scale like the Face, Legs, Activity, Cry, Consolability (FLACC) scale can be employed to confirm the impact of pain on the child.

#### Pain management

Pain has been introduced as the fifth vital sign to prevent inadequacies in assessment and monitoring. Emphasis is placed on the importance of streamlining the continuum of effective pain management and a multimodal approach to pain management is preferred (Figure 10). Another aspect of pain management is non-pharmacological therapy, focusing on cognitive-behavioural therapy that features play therapy.

Finally, the goals of effective pain management are those of achieving pain relief, safety, adequate comfort and QoL for the patient and his/her families. A positive attitude is encouraged for the patient's rehabilitation and best recovery.

\* Whenever possible, the World Health Organization's pain relief ladder should be followed.

References: 1. Swafford LI and Allen D. Med Clin N Am 1968;52:131–136. 2. Anand KJ, et al. Lancet 1987;1:62–66. 3. World Health Organization. WHO's pain ladder. Available at: www.who.int/cancer/palliative/painladder/en, accessed May 2006.

#### Case study one

A 77-year-old male patient diagnosed with post-herpetic neuralgia, following a bout of shingles, presented with pain along the right C3-C4 dermatomal area. He described the pain as an 'intense electrifying sensation'. His pain score was rated 9 out of 10. The patient was started on gabapentin and this was subsequently increased. He was also given acyclovir, tramadol and topical lignocaine. His pain improved gradually but was still present.

The patient had a dorsal horn cervical epidural injection with a steroid and local anaesthetic to reduce the neurogenic inflammation caused by the virus. Pain improved by 30% and the patient was given a reduced analgesic dose. Pain relief was maintained 1 month later.

Lesson: Allodynia and hyperalgesia have been described. The limitations of drug therapy were recognized. The prescription of an anti-neuropathic agent at diagnosis of shingles infection is recommended, especially for patients with diabetes, who are at higher risk of suffering from neuropathic pain.

#### Case study two

A 78-year-old female presented with severe neck pain of 1 month's duration. Her pain score was 10 out of 10. A computerized tomography scan of her brain showed an old right putamen lacunar infarct. No acute intracranial haemorrhage was detected. Magnetic resonance imaging (MRI) of the brain revealed a 5-mm aneurysm arising from the beginning of the left terminal internal carotid artery. A cervical spine MRI showed cervical spondylosis with spinal canal stenosis at C4/5 and C5/6.

As analgesics did not offer respite, the patient was given an 'E' Facet joint injection at C2/C3 and C3/C4, following which there was immediate relief. The patient was subsequently listed for radiofrequency ablation of C2/C3 and C3/C4 because of recurrent left neck pain. A left C2/C3 facet joint block was performed later and pain subsequently improved.

Lesson: Evidence-based studies show that cervical facet joint pain can contribute to up to 51% of neck pain. Randomized controlled trials have shown the efficacy of radiofrequency lasting up to a year. This nerve ablation is not known to cause any harm to the recipient.

#### Case study three

A 39-year-old male patient presented with low back pain (LBP) and sciatica shooting down the left leg. The lumbosacral MRI revealed a diffuse disc bulge noted at L4/5 with annular tear, causing indentation of the thecal sac and mild lateral recess narrowing. The patient was initially treated with celecoxib and underwent two caudal injections. After each injection, there was an improvement in the pain score. Although his LBP and sciatica had subsided, he suffered new back pain on the left L4/L5 and L5/S1 facet joints. A facet joint block was performed with subsequent pain relief. The patient was also given baclofen and tramadol; however, the pain recurred in his left leg, which is associated with radiculopathy. The patient continued treatment with celecoxib and tramadol, and was started on gabapentin. Radiofrequency ablation of left L3-S1 facet joint was subsequently performed. Pain improved and the patient is taking fewer analgesics after the procedure.

Lesson: The patient suffered from neuropathic pain of the nerve root and nociceptive pain at the facet joint. Each injection was targeted at different sites to counter the specific pain. The key issue here was to overcome the functional difficulty and improve patient's quality of life.

#### Case study four

A 71-year-old female presented with primary rectal sigmoid cancer, sphincter preservation by anterior resection and metastases in the lung, liver and left knee. She was referred for pain on her swollen left knee, and the pain score measured 5 out of 10 at rest and 10 out of 10 on movement. The patient was administered fentanyl, morphine oral solution, arcoxia and gabapentin, but received inadequate relief. Ketamine infusion was started with a resultant improvement in pain score.

The insertion of an intrathecal catheter was offered in lieu of the escalating opioid dose. The infusion was composed of lignocaine and morphine. Ketamine infusion was shifted to oral while gabapentin was maintained. The patient was also given arcoxia and the dose of morphine oral solution was increased. Since then, patient has been taking fewer rescue doses and the pain is more tolerable.

**Lesson**: The implanted internal computerized pump delivers local anaesthetic and a minute dose of morphine directly to the nerves that supply the left knee. The patient's medication can then be suitably titrated and this also allows the patient to recuperate at home.