Pain management in primary care – current perspectives

Meyer HP, MBChB, MPraxMed, MFGP(SA)
Department of Family Medicine, University of Pretoria

Correspondence to: Prof H Meyer, e-mail: hpmeyer@kalafong.up.ac.za

Abstract

According to a 1998 *World Health Organization Survey* of 26 000 primary care patients on five continents, 22% reported *persistent pain* over the past year. Part of the problem lies with some health-care providers who have failed to keep up with the advances in pain medicine and continue to follow the *biomedical approach,* which regards a specific pathway as the only source of pain. In this model, all pain is regarded as a warning signal of tissue injury, and if conservative treatment fails, some surgical technique will be able to correct the problem.

The modern paradigm of pain management has moved from this *biomedical* to the broader *biopsychosocial approach,* where pain mechanisms now integrate input from sensory, emotional and cognitive systems.

SA Fam Pract 2007;49(7): 20-25

Introduction

The *pain processing (nociception) system* was historically conceptualised as a *"hard-wired" pain pathway* which reproduces a pain sensation in direct proportion to the extent and severity of the painful (noxious) insult. However, this concept was challenged from the 1940's and the *gate-control theory* of pain mechanisms published by Melzack and Wall in 1965, had a profound influence in the field of pain research and in the development of various forms of pain therapy.[1] This theory integrates the views of neurophysiology and psychology and states that spinal transmission of pain impulses is continuously modulated by the relative activity in the small *(A-delta and C)* fibres and the large *(A-beta)* fibres and by *descending messages* from the brain that originate in the cerebral cortex and brainstem. In subsequent years the theory has been criticised as an over-simplification and a series of "gates" at different levels of the spinal cord and in the higher centres have been postulated.

The modern *discipline of pain management* was launched by the publication of the first edition of John F. Bonica's *Management of Pain* in 1953,[2] and he established the first *interdisciplinary pain clinic* in 1947 at the University of Washington in Seattle to treat the pain of war veterans.

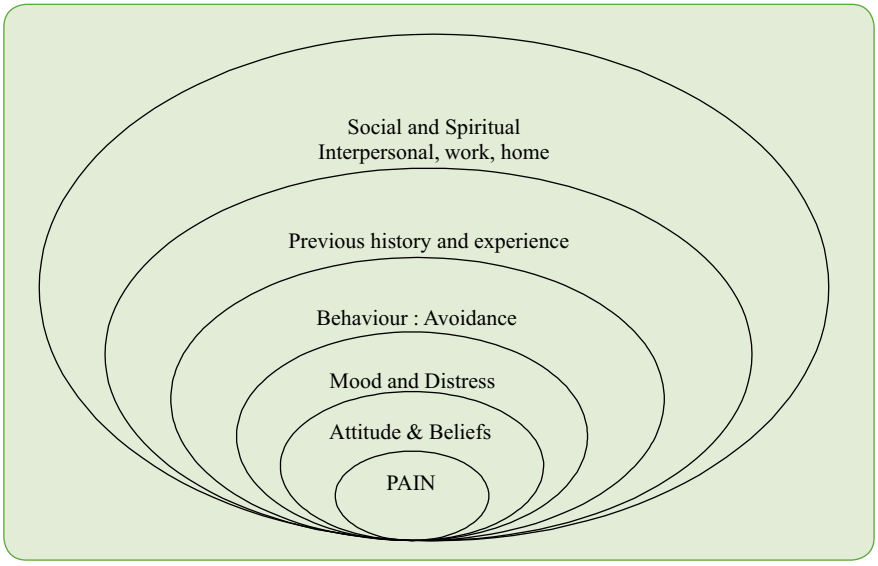
Despite many advances over the past 50 years, poorly controlled pain remains a worldwide problem. According to a 1998 *World Health Organization Survey* of 26 000 primary care patients on five continents, 22% reported *persistent pain* over the past year.[3] Part of the problem lies with some health-care providers who have failed to keep up with the advances in pain medicine and continue to follow the *biomedical approach,* which regards a specific pathway as the only source of pain. In this model, all pain is regarded as a warning signal of tissue injury, and if conservative treatment fails, some surgical technique will be able to correct the problem.[4,5]

The modern paradigm of pain management has moved from this *biomedical* to the broader *biopsychosocial approach,* where pain mechanisms now integrate input from sensory, emotional and cognitive systems.[4,6,7]

The current *definition of pain* as proposed by the IASP, reads: *"Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".*[8] This definition identifies the complex and multi-dimensional experience of pain, where the patient's physical, cognitive, emotional and behavioural characteristics mediate the pain experience.[9]

With *acute pain* of known cause, there may only be a minor contribution from the emotional and cognitive dimen-

Figure 1: Biopsychosocial model of pain[4,6,7]



sions – in patients with a *chronic pain* disorder for many years, these dimensions may play a major role in pain perception.[10]

A multitude of brain regions (known as the *"pain matrix"*) are activated following a pain stimulus. Rather than registering the pain signal to produce pain perception, the *brain matrix* constructs the pain experience by *integrating multiple inputs*, including biological (sensory) factors, present and past psychological events and socio-cultural influences.

Acute pain

Acute pain is a *normal biological response* to injury or tissue trauma and a signal of ongoing or impending tissue damage, e.g. post-operatively. It protects the organism from further injury and promotes healing after injury. Acute pain is a symptom that must be treated or its cause eliminated.[11,12] Untreated acute pain may cause unnecessary suffering and increase morbidity, it may also lengthen the recovery time after tissue injury.

There is increasing recognition that *long-term changes* may occur within the peripheral and central nervous system following the noxious input of painful stimuli. Even brief intervals of *untreated acute pain* can induce long-term neuronal remodelling and central *sensitization ("plasticity")* and may lead to chronic pain in some patients. This *"plasticity" of the nervous system* then alters the body's response to further sensory input, it becomes more sensitive to pain impulses and even innocuous stimuli may then trigger pain perception.[1,11,12,13]

Central sensitization is a complex process involving many neurochemical and molecular processes, and is induced by the release of neuropeptides such as *substance P* and *glutamate*, which then activate the NMDA-receptor-complex.[2,13,14] The subsequent intra-cellular events may lead to long-term neuronal changes, characterized by a more sensitive nervous system and *hyperalgesia*.

Acute post-operative pain may be followed by persistent pain in 10-40% of individuals, in particular after procedures such as inguinal hernia repair, thoracotomy, and breast surgery.[15] *Central sensitization* after tissue and nerve injury is also believed to be a mechanism for this phenomenon. Current data therefore support a *comprehensive and multimodal approach* to post-operative pain management.[16] Pain intensity should be assessed routinely, just as one monitors other vital signs, to ensure that acute pain is managed appropriately.

Primary types of pain[11,12]

Nociceptive pain (e.g. trauma, surgery)

Nociceptive pain occurs when intact peripheral nerve endings *(nociceptors)* are stimulated by noxious stimuli that may be mechanical, thermal or chemical. Tissue damage generates release of peptides and other components of the inflammatory soup with eventual peripheral sensitization. Peripheral sensitization is one way in which the nociceptive system can be upregulated in response to tissue injury.

Neuropathic pain

While nociceptive pain is the result of stimulation of the nervous system, neuropathic pain is due to a *lesion in the peripheral or central nervous system*, e.g. in patients with diabetic or AIDS poly-neuropathy and post-herpetic neuralgia.

Dysfunctional pain

There is a large group of chronic pain patients where no peripheral abnormality or neurological deficit can be detected. The mechanism of pain is *abnormal sensory processing* of non-painful stimuli once the central nervous system has become sensitized.[11,14,17] These include the *idiopathic pain disorders* such as irritable bowel syndrome, chronic headaches, post-whiplash disorders, fibromyalgia syndrome and others.[18]

Both neuropathic and dysfunctional pain may be present in the absence of an ongoing peripheral stimulus or "organic cause", and it is wrong to assume that these patients are only "psychological" or "hysterical".[11,17,18]

Mixed pain

These include patients with *cancer pain* and *low back pain* (in particular low back pain following surgery, or *failed back surgery syndrome*) where neuropathic, nociceptive and myofascial components may contribute to the patient's pain experience.

Chronic pain

The IASP has defined chronic pain as *"pain that persists for longer than the time expected for healing, or pain associated with progressive, non-malignant disease",* usually taken to be three months.[19]

Chronic pain often persists long after the tissue trauma that has triggered its onset, has resolved and may be present in the absence of identified ongoing tissue damage.[20] Chronic pain is a dysfunctional response which mostly does not warn the individual of underlying disease or injury and has been widely acknowledged as a *"disease in its own right".*[21]

Chronic pain may be associated with an underlying chronic disease such as arthritis. However, the largest group of chronic pain patients in the current *epidemic in developed countries,* comprises the chronic pain syndromes of unknown etiology.[12] These pain syndromes have no confirmatory laboratory evidence and are diagnosed on the basis of clinical criteria, e.g. the headache syndromes, irritable bowel syndrome, fibromyalgia and non-specific (or "simple") low back pain.

The tendency to consider chronic pain as either psychological or physical, implies a false dichotomy – both play a role in most chronic pain disorders, although the balance between organic pathology and psychosocial contributions may differ in different pain disorders. The emotional component of pain is complex and is influenced by past experiences, patient-beliefs and fears.[22,23] Negative beliefs and an attitude of hopelessness may generate *maladaptive illness behaviour* with increased pain-reporting.[22]

Box 1: Management of chronic pain – biopsychosocial

1. Goals of management
2. Interdisciplinary approach
3. Effective communication
   - *Emphasize patient's active role*
4. Pharmacological
   - *Primary analgesics*
     Paracetamol
     NSAIDS / Coxibs
     Opioids
   - *Secondary analgesics*
     Antidepressants
     Anticonvulsants
     Local anaesthetics
5. Physical therapy / exercise / manipulation
6. Sleep quality
7. Behavioural therapy
8. Occupational therapy *(Return to work)*
9. Interventional methods

Pain assessment[24,25,26,27]

Pain is a subjective, complex and personal phenomenon and can only be assessed indirectly by *patient report*.

Methods used for *acute pain* screening are insufficient to provide a comprehensive view of the multidimensional impact of *chronic pain* on the patient. In a patient with chronic pain, assessment should not be limited to *pain severity*, but at least also include pain-related *functional interference* and the *emotional impact* of the pain.

Uni-dimensional pain scales assess *pain intensity* and include numerical rating, visual analogue scales (VAS) and picture scales (facial expressions).

Multidimensional pain scales assess the effect of pain on mood, activities and quality of life, and include the McGill Pain Questionnaire and the Brief Pain Inventory.

A full *clinical examination* may provide clues to the causes of pain and formal *psychological evaluation* is indicated in a subset of chronic pain patients to assess them for maladaptive pain behaviour, somatoform disorder, etc.

Management of chronic pain syndromes

The *biomedical approach* has traditionally promised a cure by cutting or blocking the pain pathways pharmacologically or surgically. The *biopsychosocial approach* views pain as a dynamic interaction between physical, psychological and social factors, and more realistic *treatment goals* for patients include[28]:

- The reduction, mostly not elimination, of pain
- Improvement in physical / social functioning
- Improvement in mood and associated symptoms such as sleeping pattern
- Development of active coping style and self-management-skills
- A return to work
- Reduction in utilization of medical services

Evidence increasingly lends support to the use of an ***interdisciplinary approach*** where multiple therapies are provided in a *co-ordinated* manner, and where there is *active interaction* and a *common philosophy* that promotes *active patient involvement*, between participants.[28,29]

It is recommended that a *core-team* is involved in the *primary care management* of chronic pain patients. Its composition will differ from area to area, also depending on the availability of resources and the complexity of a patient's pain problem. A *core-team* may consist of a *pain management physician* (mostly a *primary care doctor* with a special interest in pain management) a *physiotherapist* and *occupational therapist*. Additional members of an *interdisciplinary team* in larger metropolitan areas may include, but are not limited to, an anaesthetist with interventional skills, a neurologist, an orthopaedic surgeon, a psychiatrist / psychologist, and a biokinetesist.

The roles of team members may also overlap and the *physiotherapist* may also be responsible for education, an exercise programme and to assist in applying the principles of *cognitive behavioural therapy*.[28]

It has been demonstrated that *interdisciplinary management*, which emphasizes *functional restoration* produces the best outcomes in the management of chronic pain patients.[30]

Education

It is important to *validate* the patient's pain complaint and to *explain* that factors that have initiated the pain problem are often different from those that maintain it. Fear-avoidance and catastrophyzing may intensify the pain-experience.

The patient should be informed about the goals of the treatment programme and certain *chronic pain myths* should be dispelled, including:[31]

- Search long enough and you will find the cause and the cure
- Abnormal scans validate and explain your pain
- Only organic pain is real
- You have to learn to live with it
- Let pain be your guide – rest when it hurts
- Hurt is equal to harm.

The outcome of pain management is often determined by what the doctor, therapist and patient expect.[31]

Physiotherapy, exercise and occupational therapy

The role of the *physiotherapist* is broad and includes education on pain mechanisms and self-management, goal-setting and a graded activity programme, pacing and helping patients to acquire problem-solving skills.[32]

An important element in physical rehabilitation involves improvement in function through *therapeutic exercises* designed individually to increase functional activity.

Passive manual methods are de-emphasized in modern physiotherapy and should be integrated in a more active and comprehensive programme. *Physiotherapists* who are too somatically focussed, e.g. on the *"degenerated disc"* may reinforce illness behaviour and perpetuate the problem.[32]

The physiotherapist should be informed on the cognitive and behavioural components of pain presentation and assist in addressing inappropriate pain-behaviour.

Occupational therapists work closely with physiotherapists in activity planning and in assessing domestic and workplace circumstances.[32] Return to work, even in the presence of some degree of pain, is an important component of chronic pain management.

Principles of pharmacological therapy[33,34,35]

- The goal of pharmacotherapy should be to improve *pain intensity and functioning* while avoiding cognitive impairment and organ toxicity.
- Many patients don't present with pure nociceptive or neuropathic pain, but rather have a *mixed pain syndrome,* therefore *rational polypharmacy* is often appropriate.
- The World Health Organization (WHO) *analgesic three-step ladder* for the rational use of analgesics in cancer pain, has also been applied for *non-cancer pain* for many years, in particular for nociceptive pain.
- There is a move away from this *empirical approach* in chronic pain pharmacotherapy, to an approach that is targeted at the particular *pain mechanism* responsible for the patient's pain (e.g. drugs that influence central sensitization).[11]
- For *continuous analgesia* consider long-acting medication on a regular basis, rather than *"as needed"*.
- Analgesics are generally more effective for *nociceptive pain*, and less effective for *neuropathic pain*.

Non-opioid analgesics

Paracetamol is still recommended as first-line therapy for osteo-arthritis.[36]

Non-steroidal anti-inflammatory drugs (NSAIDs) may be combined with paracetamol or opioids. Common side-effects include GI irritation / peptic ulceration and inhibition of platelet aggregation. *COX-2 specific agents* (e.g. *celecoxib and lumiracoxib*) reduce these risks, but are also *(similarly to older NSAIDs)* associated with renal dysfunc-

tion and potential cardiovascular side-effects, in particular in *older patients* on *long-term medication*.

Opioid analgesics

Weak opioids

Codeine phosphate is a very weak analgesic and has almost no analgesic effect by itself. Its role in chronic pain management is very limited *(if any).*[35]

The long-term use of *polycomponent codeine combinations* (containing caffeine, meprobamate and others) is strongly discouraged in chronic pain. Their potential for nephro-toxicity is greater and they are often associated with rebound pain.

Tramadol is an opioid of moderate strength and also inhibits nor-adrenaline and serotonin re-uptake from nerve endings. A number of studies have demonstrated the efficacy of *tramadol* in chronic pain conditions such as neuropathic pain, osteoarthritis, fibromyalgia and low back pain. It has a proven *synergy* with paracetamol, is not associated with peptic ulceration, renal dysfunction or cardiovascular side-effects and has a very low addictive potential.[35,36]

Strong opioids[37,38,39]

Current evidence supports the use of strong opioids in a *carefully selected* subset of patients with *chronic and resistant non-cancer pain*.

A detailed assessment should be performed by an experienced *pain management physician* before strong opioids are prescribed. Strong opioid treatment for chronic pain should not be considered life-long treatment and only *sustained – release opioids*, e.g. *transdermal fentanyl* and *sustained release oral morphine,* should be used.

Adjuvant drugs[28,33,40]

Neuropathic pain is mostly treated with medications that influence neurotransmitters, e.g. *antidepressants* and *anti-epileptic* drugs. *Opioids* are mostly reserved for patients with refractory neuropathic pain.

Antidepressants

- *Tricyclic antidepressants (e.g. amitriptyline)* are effective for neuropathic and non-neuropathic pain and its analgesic effect occurs at lower doses than its antidepressant effect. These drugs are associated with bothersome anti-cholinergic side-effects and serious cardiovascular side-effects in older patients with established heart-disease.
- *Selective serotonin re-uptake inhibitors (SSRIs)* are predominantly serotonergic drugs and are mostly *ineffective* in treating chronic pain.
- *Serotonin and norepinephrine re-uptake inhibitors (SNRIs), e.g. duloxetine* has proven efficacy in some patients with neuropathic pain and fibromyalgia (even in the absence of major depressive disorder).

Anti-epileptic drugs

Anti-epileptic drugs act at several sites that are relevant to pain perception and are believed to enhance central inhibition and limit neuronal excitation.

Of the *first generation agents, carbamazepine* is indicated for trigeminal neuralgia. It has limited efficacy in patients with diabetic neuropathy and post-herpetic neuralgia and is associated with many side-effects and toxicity.

Second generation antiepileptic drugs are better tolerated and have much fewer central nervous system side-effects, e.g. *gabapentin and pregabalin*. Pregabalin inhibits discharges from injured nerves by inhibiting calcium-channels pre-synaptically. It has a better bio-availability than gabapentin and effectivity has been proven in several trials in patients with diabetic neuropathy and post-herpetic neuralgia, as well as in fibromyalgia patients. *(It is approved as such by the US Food and Drug Administration).*[11]

Principles of behavioural therapy[22,28,31,41,42]

Several behavioural approaches may lead to long-term reduction in pain intensity and improvement in physical and social functioning. In some chronic pain patients, the *patient's belief* about the pain and its effects is a better predictor of suffering and disability than the actual disease process and / or tissue damage.

Cognitive therapy aims to help patients identify maladaptive thinking patterns and develop the ability to challenge these thoughts.

Errors of thinking include:

- I will never get better
- There is nothing I can do
- I am afraid to move
- The situation is hopeless because the pain is incurable

Engaging in pleasurable, stimulating and distracting activities are powerful means to limit disability.

Primary objectives in a programme of cognitive behavioural therapy include:

- Change view of pain from overwhelming to manageable
- Change from passive and helpless to active and competent
- Be aware of the association between negative thoughts and maladaptive pain behaviour
- Teach specific coping skills

Interventions[28,33,43]

Less invasive methods

- *Myofascial trigger point therapy* may provide pain relief and facilitate patient participation in active physical therapy, if it is correctly performed in selected patients with *myofascial pain syndrome,*[44,45] as part of a comprehensive pain management programme.
- *Nerve block therapy* may be useful to allow patients to participate in active rehabilitation. *Sympathetic nerve blocks* may be useful in some visceral pain states and in some patients with sympathetically maintained pains.[28,43]
- *Epidural steroid injections* may provide temporary pain relief in patients with radicular low back pain.
- *Pulsed radiofrequency* is a non-destructive procedure that may relieve chronic neuropathic pain in selected patients – however, more evidence is needed before official recommendation for this procedure in guidelines will be appropriate.[45]

More invasive methods

- These include *surgical procedures* such as *microvascular decompression* for trigeminal neuralgia and *joint-replacement surgery* for severe osteoarthritis. *Spinal surgery* should be reserved for patients who are strictly selected by an interdisciplinary team. Neurosurgical procedures include *micro-DREZ-otomy* for patients with intractable pain after plexus brachialis avulsion injuries.
- *Spinal cord stimulation* has evolved as a reversible, non-destructive and low-morbidity technique for chronic intractable pain associated with ischaemia and certain refractory neuropathic pain syndromes. It is however an expensive option.
- *Epidural* and *intrathecal drug delivery systems* have been used successfully over many years in a carefully selected group of patients with intractable pain when other therapies have failed.

Summary

The last 20 years have seen an explosion of both basic science and clinical research in the field of pain medicine. It is now clear that factors other than the injuring stimulus influence pain perception and that untreated acute pain as well as many psycho-social factors may contribute to the neuroplasticity *("central sensitization")* that may occur in response to an initial pain stimulus and lead to chronic pain.

Once *central sensitization* has taken place, relatively innocuous stimuli may activate pain perception *(hyperalgesia).* This has lead to the recognition of pain as the *"fifth vital sign"*, which should be monitored with the same vigilance as blood pressure, temperature, pulse and respiratory rate, e.g. in the management of patients after surgical or other forms of trauma.

Although John F Bonica brought recognition to the *multi-disciplinary approach* to pain management, the publication in 1965 of the *"gate control theory"* by Melzack and Wall revolutionized the concept of pain and pain management. The recognition of chronic pain not only as a symptom, but as a *disease itself,* has been a major conceptual change. This has meant a shift in the management of chronic pain to the *multi-(inter-) disciplinary biopsychosocial approach* where there is communication between team members and an emphasis on active patient-participation and functional improvement.

This approach includes *educational interventions* as well as *cognitive behavioural* approaches and supervised *exercise therapy*. Appropriate *pharmacological treatment* must be evidence-based and outcomes must include improvement in the patient's ability to function, not only pain-relief. *Invasive therapy* should be conservatively selected after comprehensive assessment and an appropriate period of comprehensive conservative management.

See CPD Questionnaire, page 34

This article has been peer reviewed

References

1. Melzack R, Wall PD. Pain mechanisms: a new theory. Science 1965; 150: 971-9.
2. Bonica JJ. The management of Pain. Philadelphia: Lea and Febiger, 1953.
3. Gurejo O, von Korff M, Simon G, Sater R. Persistent pain and well-being – a WHO study in primary care. JAMA 1998; 280: 147-51.
4. Merskey H, Loeser JD, Dubner R, Waddell G. in: The Paths of Pain 1975-2005. Seattle: IASP Press, 2005. p 379-90.
5. Deyo RA. Low back pain. Sci Am 1998; August: 29-33.
6. Main CJ, William A. ABC of psychological medicine: Muskulo-skeletal pain. Br Med J 2002; 325:534-7.
7. Justins DM. Pain 2005 – an updated review. Seattle: IASP Press, 2005. p 80.
8. Merskey H. The definition of Pain Europ J of Psychiatry 1991; 6:153-9.
9. Katz L. The multidimensional nature of chronic pain: An integrative model for the interdisciplinary team. CME 2000; 18(2): 139-43.
10. Johnson MI. The physiology of the sensory dimensions of clinical pain. Physiotherapy 1997; 83(10):526-36.
11. Woolf CJ. Pain: Moving from symptom control towards mechanism – specific pharmacologic management. Ann Int Med 2004; 140:441-51.
12. Shipton EA. Pain: Acute and chronic. London: Arnold, 1999. p 1-36.
13. Carr DB, Goudas LC. Acute pain. The Lancet 1999 ; 353 :2051-8.
14. Bennett RM. Emerging concepts in the neurobiology of chronic pain. Mayo Clin Proc 1999; 74:385-98.
15. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. The Lancet 2006; 367:1618-25.
16. Brown AK, Christo PJ, Wu CL. Strategies for postoperative pain management. Best Pract Res Clin Anaesthesiol 2004; 18(4): 703-17.
17. Nielson LA, Nielson TG. Central sensitization in Fibromyalgia and other musculoskeletal disorders. Curr Pain Headache Rep 2003; 7:355-61.
18. Diatchenko L, Nackley AG, Slade GD, et al. Idiopathic pain disorders – pathways of vulnerability. Pain 2006; 123:226-30.
19. Classification of chronic pain: Descriptions of chronic pain syndromes and definitions of pain terms. Pain (Suppl) 1986; 3:1-226.
20. Holdcroft A, Jagger S. The Chronic Pain Patient in: Core topics in Pain. London: Cambridge University Press, 2005. p 117-20.
21. Niv D, Devor M. Position paper of the European Federation of IASP chapters (EFIC) on the subject of pain management. European Journal of Pain 2007; 11:487-9.
22. Baumann SE. Chronic Pain. CME 1994; 12(9):1129-36.
23. Turk DC. Remember the distinction between malignant and benign pain? Well, forget it. Clin J Pain 2002; 18:75-6.
24. Carduno N, Kapur D. Measuring pain. Br J Anaesthesiol 2002; 2(1):7-10.
25. Karoly P, Ruehlman LS, Aiken LS, Todd M. Evaluating chronic pain impact among patients in Primary Care. Am Acad Pain Med 2006; 7(4):289-97.
26. Knox H, Todd MD. Pain Assessment instruments for use in the Emergency Department. Emerg Med Clin North Am 2005; 23: 285-95.
27. Holdcroft A, Jagger S. Pain measurement in Humans in: Core Topics in Pain. London: Cambridge University Press, 2005. p 72-93.
28. Ashburn MA, Staats PS. Pain: Management of Chronic pain. Lancet 1999; 353(9167): 1-11.
29. Ashburn M, Rice L. Interdisciplinary approach to pain management in: The management of Pain. New York: Churchill Livingstone, 1998: 235-48.
30. Caraggee EJ. Persistent low back pain. New Engl J Med 2005; 352:1891-8.
31. McIndoe R. A behavioural approach to the management of chronic pain. A self management perspective. Austr Fam Phys 1994; 23(12):2284-92.
32. Holdcroft A, Jagger S. Overview of treatment of chronic pain: Core topics in Pain. London: Cambridge University Press, 2005. p 219-234.
33. Anon. Management of chronic pain syndromes: Issues and interventions. Pain Medicine 2006; 6(S1):1-21.
34. Feinberg SD. Prescribing analgesics – how to improve function and avoid toxicity when treating chronic pain. Geriatrics 2000; 55(11):48-55.
35. Camu F, Vanlersberghe A. Pharmacology of systemic analgesics. Best Pract Res Clin Anaesthes. 2002; 16(4):475-88.
36. Schnitzer TJ. Non-NSAID pharmacological treatment option for the management of chronic pain. Am J Med 1998; 105:45-51.
37. Ballatyne JC. Mao J. Opioid therapy for chronic pain. New Engl J Med 2003; 349: 1943-53.
38. Kalso E, Allan L, Delemijn PLI, Faura CC, et al. Recommendations for using opioids in chronic non-cancer pain. Europ J Pain 2003; 7:381-6.
39. Recommendations for the appropriate use of opioids for persistent non-cancer pain. A consensus statement on behalf of the Pain Society, the Royal College of Anaesthetists, the Royal College of General Practitioners and the Royal College of Psychiatrists. The British Pain Society, 2004.
40. Maizels M Mccarberg B. Antidepressants and antiepileptic drugs for chronic non-cancer pain. American Fam Phys 2005; 71(3):482-90.
41. Eccleston C. Role of psychology in pain management. Br J Anaesth 2001; 87:144-52.
42. Malzack R, Wall PD. A cognitive – behavioural approach to pain management in: Handbook of pain management. London: Churchill Livingstone, 2003. p 533-41.
43. Krames ES. Interventional pain management. Med Clin North Am 1999; 83(3): 787-808.
44. Graff-Radford SB. Myofascial pain: Diagnosis and management. Curr Pain Headache Rep 2004; 8:463-7.
45. Jensen TS. Pulsed radiofrequency: A novel treatment for chronic cervical radicular pain? Pain 2007; 127:3-4.