

PORTFOLIO VERTICAL THEMES

OVERVIEW ESSAY:

PAIN

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Introduction. Pain is a common everyday experience, with as many as 87% of patients experiencing moderate or severe intensity at some time during their stay in hospital¹ and 20-25% of the general population in Scotland reporting significant or severe pain lasting many months^{3, 4}. It is essential in alerting us to actual or potential tissue damage⁵. Failure of this mechanism can allow gradual damage to occur which may result in loss of function (e.g. Charcot's joint)⁶ and in the acute situation can even result in delayed diagnosis of life-threatening conditions⁶. But if it is possible to have pain without tissue damage or vice versa, what is pain? The International Association for the Study of Pain (IASP) defines it as “*an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.*”⁷. The inseparable emotional experience is very distressing but is functional in eliciting a behavioural response to remove the stimulus, limit further injury and optimises recovery⁵.

The assessment and management of pain and its impact on patients depends on its duration- *acute pain* (of recent onset) is thus discussed separately from *chronic pain* (of more than 3 months duration). Although each pain problem needs to be considered individually, division into types of pain based on aetiology is useful for management decisions: *nociceptive*, due to stimuli from somatic or visceral nociceptors; *neuropathic*, due to damage to nerves (although use of this term differs^{5, 8}); and *psychogenic* (of psychological origin). Pain is, however, influenced by many of factors, and a biopsychosocial model of *total pain* is used, particularly in palliative care literature^{2, 9} to describe the experience which results from the interplay of physical, psychological, social and spiritual pain. But how well do we understand the way in which this experience comes about, and how can we use this to treat pain?

Pain physiology and pharmacology. The perception of acute pain reflects activation of a nociceptors, afferent transmission to the spinal cord and relay via dorsal horn to higher centres⁸. Feedback and modulation are features of each level of transmission and are important targets for therapy. Pain physiology is an area of active research and only a simplification of current theories can be given here, many of which are still debated. A schema of the neuroanatomy of pain is given in *Figure 1*. Nociceptors respond to noxious chemicals and stimuli with a relatively high threshold compared to other cutaneous sensory fibres responding to heat, cold or mechanical stimulation, thus being selective to noxious stimuli. C-fibre nociceptors (burning pain) particularly evoke the affective-emotional aspects of pain and A-fibre nociceptors (pricking pain, sharpness and perhaps aching pain⁵, responding with higher frequencies) prompt rapid withdrawal from noxious stimuli⁸. Local inflammation, neural autocrine and paracrine signalling and spinal reflexes affect nerve terminal depolarisation and thus the sensitivity of the injured and surrounding area (hyperalgesia- a heightened response to noxious stimuli- and allodynia- a response to non-noxious stimuli)⁵. Local anaesthetics can be used to reduce signal conduction along peripheral nerves and NSAIDs and

steroids reduce synthesis and release of inflammatory mediators both in peripheral tissues and spinal cord. The relay of the signal on to supraspinal centres is modulated by both intrinsic and supraspinal signals. Spinal opioids and α_2 -adrenergic agonists (acting on endogenous receptors) and anti-inflammatory drugs (reducing inflammatory mediators) thus inhibit this relay. Signals from large-fibre sensory neurons inhibit those of adjacent nociceptive neurons⁵ (gate theory), and this is how transcutaneous electrical nerve stimulation (TENS) and acupuncture may work. Projections from the dorsal horn nuclei ascend via the anterior or lateral spinothalamic tracts to synapse in many brainstem nuclei and the thalamus, relaying to cortical centres. Systemic opioids, paracetamol and anxiolytics have their effects on higher centres¹⁰, affecting pain perception or descending spinal modulation and psychological therapies work on the relationship between cognitive factors and pain perception¹¹.

The Neuromatrix. Recent conceptions beyond the spinal cord have moved towards a highly complex understanding of pain perception, the “neuromatrix”¹². This includes

influences from: (1) cutaneous, visceral and other somatic receptors sensory inputs; (2) other sensory inputs that influence the cognitive interpretation of the situation; (3) cognitive and emotional inputs from other areas of the brain; (4) inhibitory modulation inherent in all brain function; (5) stress-regulation systems, including cytokines as well as the endocrine, autonomic, immune and opioid systems. Many of these components have been investigated using functional imaging¹³. This conception brings us closer to the integration of sensory and emotional components of pain in the IASP definition and to an understanding of the way in which the brain integrates sensory, cognitive and emotional aspects into the experience of “total pain”.

Chronic pain pathophysiology. The persistent activation of pain pathways and its role in chronic pain are not fully understood, but multiple levels of the pathway are likely to be involved. Peripherally, changes are observed in neurotransmitter, ion channel and receptor conditions as a result of inflammation or nerve damage, leading to hyperalgesia and allodynia as described above. Dorsal root and spinothalamic tract neurons have been shown to switch between different modes⁵: 1. *physiological*, 2. *suppressed* (leading to analgesia, induced by opiates), 3. *sensitised* (leading to hyperalgesia in response to repeated signals, reduced by pre-emptive analgesia and affected by

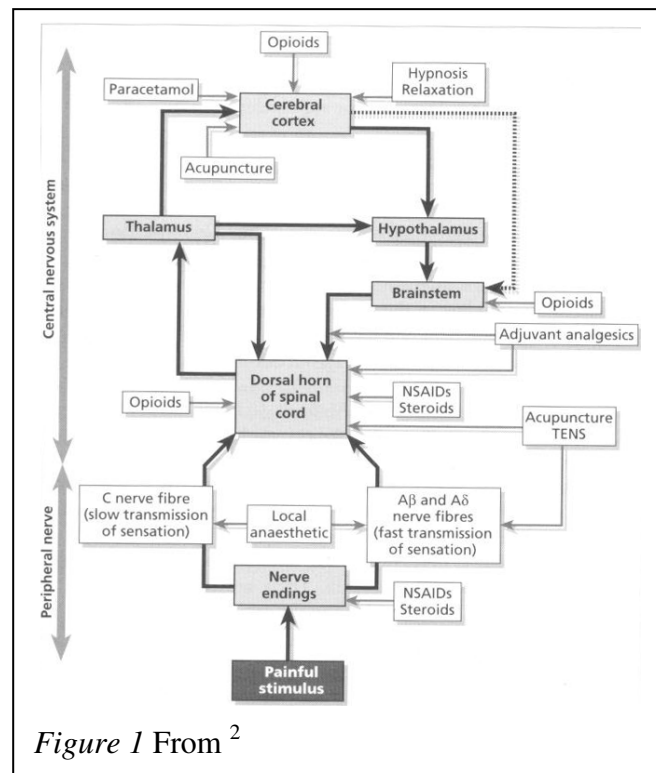


Figure 1 From ²

anticonvulsants, ketamine and dextromethorphan due to NMDA receptor inhibition¹⁰) and 4. *reorganised* (leading to allodynia). 2 and 3 are variations in membrane potential, transmitter and receptor levels leading to suppressed or heightened perception of pain. Structural reorganisation such that A β -fibres input tactile signals into pain pathways leading to allodynia is primarily a problem following nerve injury and amputation, and there is little evidence of successful therapy to preventing this⁵. Cognitive aspects such as coping and pain-related anxiety are also involved¹¹.

Assessment and management. As pain is by nature a complex experience, the assessment of pain is fraught with difficulties, however, if the measurements are done properly, remarkably sensitive and consistent results can be obtained¹⁴. As pain is a subjective experience which does not correlate well with any objective measure so far used, the patient's description of their pain is the best measure. A description of pain by its site, character, intensity, duration, onset, course, radiation, associated symptoms and precipitating and relieving factors is classically used in medicine to help to determine the origin of pain¹⁵. The earliest pain measures used categorical scales using descriptive words for the severity of the pain¹⁶. Validated questionnaires exist to quantify physical pain using a wide range of descriptors, categorical, numerical and visual analogue scales e.g. the McGill Pain Questionnaire¹⁷ and its abbreviated version. Many more cover a range of domains such as functional/disability, coping/psychological/mood, social, and sleep¹⁸. Various forms of assessment have been developed for situations where detailed questionnaires are inappropriate due to urgency, rapid changes or limited cognitive or communicative ability. In postoperative pain, simple unidimensional "physical" pain scores are usually used and patients are often asked to deep breathe, cough and move. The worst pain is scored and recorded¹⁹. WOMAC visual analogue and Likert scales are used in the functional assessment of osteoarthritis, quantifying self-reported pain in various situations e.g. walking on flat, on stairs, sitting, lying, etc.²⁰

Important aspects of pain management. *Non-opioid analgesics* such as paracetamol, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) are the first line of management in mild to moderate pain and are used as adjuncts in the management of severe or postoperative pain. NSAIDs are useful for their anti-inflammatory as well as their analgesic effects, but do affect gastrointestinal mucosa and platelet function as a result of their anti-prostaglandin activity. Although generally well tolerated, their adverse effects may be serious, most often in the elderly⁹. Potential side-effects include gastric irritation and bleeding, fluid retention, headache and renal failure in patients with renal impairment¹⁰. *Opioid analgesics* are most commonly used in the management of severe acute pain and chronic cancer-related pain. Immediate-release (IR) morphine tablet or elixir is used to find the dose which controls pain but without unacceptable side-effects such as constipation, dry mouth (the two most common), nausea, vomiting, sedation^{9, 10}. Adjuvant analgesics can be used to minimise the dose required and thus the side-effects. Patients can then convert to controlled-release

morphine with additional IR “break-through” doses as required^{10, 21}. Alternatives such as transdermal fentanyl patches and methadone are used in chronic pain management⁹. *Adjuvant analgesics* are used for types of pain which are less responsive to paracetamol, NSAIDS and opioids, primarily chronic pain and cancer pain. Nerve pain may be responsive to gabapentin, tricyclic antidepressants or anticonvulsants^{9, 10}. Steroids may be helpful to reduce intracranial pressure⁹ or pains caused by local oedema such as nerve compression as well as helping “total pain” in terminal patients by giving an energy boost. *Surgery* may remove structures impinging on nerves, e.g. disc prolapses or cancer pain, or replace structures which are required for function but causing pain, e.g. total knee arthroplasty. *Physiotherapy* is widely used in chronic pain management programmes and are involved in patient education and encouraging realistic and gradual increases in mobility and activity²². *Radiotherapy* may be used in painful bone metastases and to reduce tumour sizes when these impinge on surrounding structures. *Massage, heat & cold pads, exercises, chiropractic and osteopathy* used predominantly in sports injury and chronic pain. *Psychological techniques* such as relaxation, biofeedback and visualisation are an important part of any chronic pain management programme²². *TENS, acupuncture, massage* and many other complementary and alternative therapies are very popular with chronic pain patients²³, though in many cases there is a lack of evidence as to their efficacy¹⁴.

Scenarios. Mr J.M²⁴. had stage IV small-cell lung cancer and was suffering greatly due to chest pain, exhaustion, breathlessness and a depressive reaction to being informed that further chemotherapy was no longer a viable option but the best supportive care would be provided from now on (or caused by his chemotherapy, brain radiotherapy or paraneoplastic syndrome^{5 p.1086}). His management focused on optimising physical comfort and social support, oxygen and adequate analgesia using step 2 of the WHO analgesic ladder²: co-codamol 30/500 TT QID and tramadol 50mg PRN.

Mr. P²⁵ underwent revision of his right knee arthroplasty which failed to relieve his pain. He was taking co-proxamol and ibuprofen PRN prior to the operation and had limited mobility. After anaesthesia was established, pre-emptive sciatic and femoral nerve blocks with local anaesthetic²⁶ were performed prior to the operation. This was combined with post-operative patient-controlled analgesia (PCA) monitored by the acute pain team followed by oral analgesia as the patient recovered. Optimally, transfer from PCA to CR oral opioids (e.g. 20mg morphine BD) is delayed until 24h after gastric emptying has resumed and combined with short-acting opioids and NSAIDS or paracetamol^{21, 27}. He went home on simple oral analgesia with physiotherapy follow-up.

If, after 3 months, adequate pain control is not established, referral to chronic pain outpatient clinics may be appropriate. Here a multidisciplinary management team is required to deal with the many aspects of this difficult problem²². This team consists of *physicians* trained as anaesthetists (mainly

providing pharmacological and physical interventions), *clinic nurses* (administer questionnaires and possibly alternative interventions e.g. at WGH, Edinburgh), *physiotherapists*, *clinical psychologists* and *occupational therapists* (assist in the assessment of the needs of the patient in terms of self-care and the installation of aids and devices in their homes).

Conclusions & Reflections. It is inherent in the definition of pain that it is an unpleasant experience and thus the role of doctors is to help to relieve this misery as well as treat any underlying conditions where appropriate. As pain is a potent cause of anxiety and suffering, this may be the patient's primary concern even when there are potentially more life-threatening components to their condition. Thus pain relief is extremely important to patients, as evidenced by surveys of patient satisfaction¹⁴. Inadequately controlled post-operative pain has marked physiological effects, increasing comorbidity and slowing recovery and may predispose to the development of chronic pain^{5, 28}. Chronic pain is often accompanied by disability, fear, anxiety and depression, all of which in turn may affect the pain^{29, 30}. Due to this and its chronicity it may have a profound effect on employment³¹, daily activities³² and family life³³. Improvements in pain relief are needed, but are unlikely to come in the form of a magic pill which eliminates all pain without side effects. For acute pain, what we have already is very effective, but the way we use it is still sub-optimal¹⁴, and much progress has still to be made in both acute and chronic pain medicine.

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