The multiple definitions of breakthrough pain

Developments in pain assessment have led to a much greater understanding of the different types and definitions of pain. However, the definition of breakthrough pain is still unclear — for some, breakthrough pain is transient pain on a background of treated pain; for others, it is a flare up of a previously treated pain or painful event. Therefore, breakthrough pain is an umbrella term that requires further definition.

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Since Melzack and Wall's gate theory opened the door onto the concept of pain modulation, excitation or inhibition, and control, the field of pain research and treatment has exploded.[1] Pain was considered to be one dimensional by many clinicians until the validation of the McGill Pain questionnaire.[2,3] This demonstrated that pain description was useful and could reliably map onto the cause of pain, that is neuropathic, inflammatory, ischaemic or visceral. More importantly, it was the first tool to validate and discriminate between the afferent (neural), affective (emotional) and evaluative (intensity) components of pain. This allowed the development of a huge number of pain-assessment tools, all attempting to define, localise, and quantify the multidimensional aspects of the pain experience.

More recent work using functional magnetic resonance imaging (fMRI) has allowed the hitherto "black-box" of the brain to be explored.[4] This work further unpicks old clinical concepts of psychogenic pain/higher functional pain, all of which implied that pain existed only in the patient's imagination.

fMRI has in many ways exploded this concept. The elegant demonstration of the neural networks linking affective areas of the brain (limbic, hypothalamus) with memory recall (hippocampus), location, intensity and attention-to areas (cortex, insular), has given a physical basis to McGill's descriptors.[5,6] The large body of neural physiology and pharmacological research further enhances this. It has demonstrated the complex feed-forward and negative feedback pathways in the dorsal horn; extensive modulation of inputs; integration within the brain; and ascending and descending pathways.[7–9]

The explosion of understanding in receptor structure, role of neurotransmitters, secondary messenger pathways, regulation pathways, and DNA-altered expression have all contributed to the enhanced clinical assessment and treatment of pain.

Multidisciplinary pain

The theory of pain as a multidimensional sensation is widely accepted, and it has allowed a better understanding of the clinical patterns demonstrated. The multidimensional assessment encompasses intensity, affective, descriptive, functional components, reflecting the higher centre neural networks and clinical experience. For example: intensity might be severe, but described as tingling, burning, affective, excruciating, fearful, and limiting walking and sleeping. Most clinicians acknowledge the value of pain assessment and diagnosis as a pathway to appropriate treatment, referral and management. The development of multidisciplinary teams with doctors, international anaesthetists, nurses, psychologists, physiotherapists, acupuncture and more

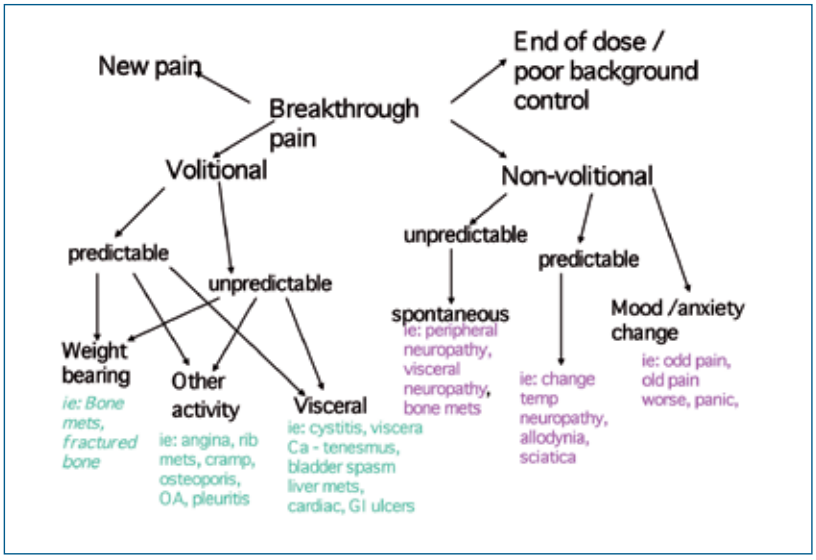

Figure 1: A schematic representation of some of the diagnostic categories that can be hidden within the term "breakthrough pain"

have further extended pain management from acute to chronic conditions.[10,11] It is worth noting that although pain is the single most common reason for patients seeking GP or hospital attendance, pain assessment and adequate treatment remain poor in all care settings.[12] Only 2% of chronic pain patients are ever referred to pain specialists, which is low by any standard given the personal, social and healthcare costs.[13] Better education around causes of pain, pain pathways, assessment and treatment algorithms may help.

It is on this background of increased knowledge that clinicians have become better at assessing and categorising background or tonic pain (ongoing pain, usually continuous, distinct from flares of pain). This enables a better assessment of cause and possible treatments. Thus, a peripheral neuropathic pain is often correctly diagnosed as pain in a dysesthetic area, with characteristics of burning, tingling, and intensity rating (often on a 0–10 scale), radiation along the neural pathway. Diagnosis of neuropathic pain allows treatment algorithms to be tried.[14]

Breakthrough pain

Until recently, any pain that was in addition to the background pain or that burst through the treatment regime was termed "breakthrough pain". This was a beautifully simple description. All clinicians believed they knew what they meant. The problem arises now that the treatment of pain varies depending on cause, and thus breakthrough pain needs definition by type and causation to select the correct treatment.[15]

Breakthrough pain has been variously defined as "transient increase in pain...in a patient who has stable persistent pain treated with opioids".[16] Therein lies a host of problems. Does the patient have to have background pain to have breakthrough pain? Are opioids a requirement to define treated background pain? This definition provides no information about how the patient experiences the pain.

The variety of terminology that has crept in illustrates the problem: episodic pain, incident pain, transitory pain, pain flare, end-of-dose pain, and general breakthrough pain.

To give a flavour of the problem, consider the following clinical scenarios. A spontaneous shooting pain of neuropathy, starts in seconds, lasts seconds and is overwhelmingly intense. The flare of pain on weight bearing of a limb with a metastases or broken bone is interesting because it can be eliminated by immobilisation. Severe bladder spasm secondary to a tumour or infection may be volitional (associated with urination) or spontaneous, or lastly a general chest ache that cuts in prior to the next dose of long-acting pain killers being due. None of these pains are the same and none will require the same treatment, yet all are described as breakthrough pain.

Causes

The confusion over breakthrough pain persists as it is merely an umbrella term, in the same way that pain was just pain in the 1960s. Now that we are more sophisticated in defining "pain" (background), the same level of science, diagnosis and appropriate treatment should be applied to the modern throw-away term: breakthrough pain.

Schematically, breakthrough pain can be broken down into appropriate subgroups, which in turn may lead to more appropriate

treatment regimes (Figure 1). Thus, for the above examples, spontaneous neuropathic pain is best treated by systemic neuropathic agents to attempt to reduce the frequency and severity of the spontaneous flare; fast-acting drugs are inappropriate. In the movement-induced pain of a broken limb, clearly stabilisation and surgery are required; in metastatic bone pain, treatment of background pain is with radiotherapy, bisphosphonates, opioids with the addition of fast-acting opioids taken before movement pain; or in the case of end-of-dose failure, an increased background analgesia rather than short-acting opioids.[15,17]

Further subtle complications arise when breakthrough pain is applied to everything. Does the "breakthrough pain" have to be linked or part of a background pain state, as in neuropathy? Or can it be any pain, new or old that happens to "breakthrough" analgesia, such as cystitis pain on top of controlled cancer pain, or can it be a recrudescence of an old pain that has flared up, such as increasing pleural effusion worsening of pre-existing pleuritic pain. Does there have to be background pain? Patients with bone metastases may often be pain free at rest, not requiring opioid analgesia, but experience excruciating pain on weight bearing. A similar transition may be seen in a patient with exertional angina. Alternatively, it could be just a bad day, when pain seems to "breakthrough" but it is hard to pin down or treat. Depression or bad news can also reduce internal inhibition, allowing ongoing pain to "breakthrough" and be consciously experienced and expressed.

Conclusion

Despite breakthrough pain being beautifully simple, summing up of what individual clinicians think they mean, it could be argued that it has had its time.

Pain, regardless of whether it is background or transitory in nature, should be defined, categorised and diagnosed. Umbrella terms at best lead to poor management, and at worst dangerous medicine and total confusion. Perhaps we should just describe what is presented, diagnose it is if possible, and work with the team and patient to create an acceptable individualised, management plan. Leave "breakthrough" with the umbrellas in the stand.

Conflict of interest: Dr Urch has received honoraria for advisory board work for Grünenthal Pharma

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Key points

- Is there background pain? Check adequately treated and consider end-of-dose failure
- Is the pain transient?
  - Define: character, location, radiation, precipitating factors, relieving factors, temporal features
  - Try to define: cause and type of pain, and treat accordingly
- Neuropathy, treat background neuropathy; bone pain, treat cause (fracture, infection or cancer)
- Select analgesic profile to mirror pain flare (eg, rapid onset, very short-acting opioids [ie, oral morphine] for cancer or non-cancer pain flares or those lasting longer than one hour; or inhaled anaesthetics [ie, for non-cancer, ultra quick acting]) or non-pharmacological methods
- Pre-emptive analgesia or prevention where possible
- Document assessment, proposed treatment and re-assess.

Breakthrough pain is an umbrella term that needs better definition