

Chapter 1

Introduction

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You can't find it (inner peace) in that darkness of pain...I can't emphasize that the pain blinds you to all of that, blinds you to all that's positive. I mean the real bad pain...it just closes you down. You just can't get through it...it's an iron door and it's one thing you don't wanna go through...you just wanna, wanna stop.

(Coyle 2004)

1.1 Introduction

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Over the last 20 yrs, there has been an increasing interest in the phenomenon of breakthrough pain. This upsurge in interest has been generated by a greater awareness of the problem of breakthrough pain (secondary to improvements in the management of background pain), and has been fuelled by an increasing range of pharmacological options for the treatment of breakthrough pain (Colleau 1999).

The focus of this book is on cancer-related breakthrough pain in adults. However, breakthrough pain is also reported to be common in children with cancer (Friedrichsdorf et al 2007) and in adults (and presumably children) with non-malignant diseases associated with acute/chronic pain (Zeppetella et al 2001; Portenoy et al 2006).

1.2 Definitions

- Pain

The standard definition of pain is 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' (Merskey and Bogduk 1994).

- Background pain

Background pain refers to 'constant or continuous pain of long duration' (Ferrell et al 1999). It should be noted that the phrase 'long duration' refers to a period of ≥ 12 hr/day (Ferrell et al 1999).

The term background pain is widely used in the United Kingdom. However, other terms are used in the medical literature to describe the same phenomenon, including 'basal pain', 'baseline pain', and 'persistent pain' (Ferrell et al 1999).

- Breakthrough pain

A recent definition of breakthrough pain is 'a transitory exacerbation of pain experienced by the patient who has relatively stable and adequately controlled baseline pain' (Portenoy *et al* 2004).

Breakthrough pain is a widely used term, although other terms such as 'episodic pain', 'exacerbation of pain', 'pain flare', 'transient pain', and 'transitory pain' (Colleau 1999) are also used in the medical literature to describe the same phenomenon.

'Breakthrough pain' is an English term, and an equivalent term does not exist in certain European languages (e.g. French, Italian, Spanish) (Colleau 1999). On the basis of this fact, an Expert Working Group of the European Association for Palliative Care (EAPC) has suggested that the term 'breakthrough pain' should be replaced by the terms 'episodic pain' or 'transient pain' (Mercadante *et al* 2002). However, the term breakthrough pain is still extensively used in clinical practice and is almost exclusively used in the medical literature.

1.3 Classification

Breakthrough pain is usually classified according to its relationship to specific events:

- Spontaneous pain (also known as 'idiopathic pain')—this type of pain occurs unexpectedly.
- Incident pain (also known as 'precipitated pain' or, when appropriate, 'movement-related pain')—this type of pain is related to specific events and can be subclassified into three categories:
 1. Volitional incident pain—is precipitated by a voluntary act (e.g. walking).
 2. Non-volitional incident pain—is precipitated by an involuntary act (e.g. coughing).
 3. Procedural pain—is related to a therapeutic intervention (e.g. wound dressing).

In the past, 'end-of-dose failure' was often considered to be a subtype of breakthrough pain. (End-of-dose failure describes an exacerbation of pain that occurs prior to the next dose of the background analgesic, and reflects declining levels of the background analgesic.) However, now many experts believe that end-of-dose failure is not a subtype of breakthrough pain, since they perceive that end-of-dose failure represents 'inadequately controlled breakthrough pain'. Table 1.2 shows the prevalence of breakthrough pain subtypes in English-language studies applying standard criteria for breakthrough pain (Portenoy & Hagen 1990; Fine & Busch 1998; Portenoy *et al* 1999; Zeppetella *et al* 2000; Gómez-Batiste *et al* 2002; Hwang *et al* 2003;).

Table 1.1 Prevalence of breakthrough pain in studies applying standard criteria for breakthrough pain

Study	Population	Prevalence of breakthrough pain	Comments
Portenoy & Hagen (1990)	Hospital inpatients (pain-team referrals) – USA n = 90	63%	Criteria for BTP outlined in this study. 90 patients assessed; 63 patients reported controlled background pain; 41 patients reported BTP.
Fine & Busch (1998)	Palliative care patients (home setting) – USA n = 22	86%	Only patients with pain eligible. 22 patients assessed; 22 patients reported background pain; 19 patients reported BTP.
Portenoy <i>et al</i> (1999)	Hospital inpatients – USA n = 178	51%	Only patients on regular opioid analgesics eligible. 178 patients assessed; 164 patients reported controlled background pain; 84 patients reported BTP.
Zeppetella <i>et al</i> (2000)	Hospice inpatients – UK n = 414	89%	381 patients assessed (33 patients not assessable); 245 patients reported background pain; 218 patients reported BTP.
Fortner <i>et al</i> (2002)	Cancer patients (home setting) – USA n = 1000	63%	Telephone survey of cancer patients. 1000 patients assessed; 256 patients reported regular analgesic usage; 160 patients reported BTP.

Table 1.1 (Contd.)

Gómez-Batiste <i>et al</i> (2002)	Palliative care patients (various settings) – Spain n = 407	41%	397 patients assessed (10 patients not assessable); 163 patients reported BTP.
Fortner <i>et al</i> (2003)	Cancer patients (outpatient setting) – USA n = 373	23%	Non-specific data relating to the patients' pain scores/pain medications were used to diagnose presence of BTP. 373 patients assessed; 144 patients reported background pain; 33 patients were deemed to have BTP.
Hwang <i>et al</i> (2003)	VA hospital patients (in/outpatient setting) – USA n = 74	70%	Only patients with pain eligible. 74 patients assessed, 74 patients reported background pain; 52 patients reported BTP. After a week of treatment, BTP prevalence decreased from 70% to 36%.

BTP = breakthrough pain; VA = Veterans Affairs.

1.4 Epidemiology

Pain is a common problem in patients with cancer. Indeed, the prevalence of pain has been reported to be 30–40% amongst patients with early disease (receiving anti-cancer therapy), and 70–90% amongst patients with advanced disease (Foley 2004).

Similarly, breakthrough pain is a common problem in patients with cancer. The prevalence of breakthrough pain has been reported to be 19–95% amongst various groups of patients (Zeppetella & Ribeiro 2003). This disparity reflects a number of factors, including differences in the definition utilized, in the methods utilized, and in populations studied (Mercadante *et al* 2002). Furthermore, the reporting of breakthrough pain is affected by certain language/geographical variables (see below).

Many authors have adopted the diagnostic criteria for breakthrough pain employed by Portenoy and Hagen (1990). These criteria are (a) the presence of stable analgesia in the previous 48 hr; (b) the presence of controlled background pain in the previous 24 hr (i.e. average pain intensity of none, mild, or moderate for over half of the previous 24 hr); and (c) the presence of 'temporary flares of severe or excruciating pain' in the previous 24 hr.

Table 1.1 shows the prevalence of breakthrough pain in English-language studies applying standard criteria for breakthrough pain (Portenoy & Hagen 1990; Fine & Busch 1998; Portenoy *et al* 1999; Zeppetella *et al* 2000; Fortner *et al* 2002, 2003; Gómez-Batiste *et al* 2002; Hwang *et al* 2003). It should be noted that these figures represent the prevalence of breakthrough pain in selected populations of cancer patients, rather than the prevalence of breakthrough pain in the general population of cancer patients.

Interestingly, the International Association for the Study of Pain (IASP) survey of cancer pain characteristics and syndromes found that pain specialists from English-speaking (North America, Australasia) and Northern/Western European countries reported more breakthrough pain than pain specialists from South American, Asian, and Southern/Eastern European countries (Caraceni & Portenoy 1999; Caraceni *et al* 2004).

Breakthrough pain appears to be more common in patients with advanced disease (Colleau 2004), in patients with poor performance status (Caraceni *et al* 2004), in patients with pain originating from the vertebral column (and to a lesser extent other weight-bearing bones/joints) (Caraceni *et al* 2004), and in patients with pain originating from the nerve plexuses (and to a lesser extent nerve roots) (Caraceni *et al* 2004).

Table 1.2 Prevalence of breakthrough pain in studies applying standard criteria for breakthrough pain

Study	Breakthrough pain subtypes			Comments
	Paroxysmal pain	Incident pain	'End-of-dose failure'*	
Portenoy & Hagen (1990)	27%	43%	18%	12% pains were 'mixed' in nature (incident and end-of-dose failure). Incident pain precipitants: movement 22%; coughing 12%; sitting 4%; touch 2%.
Fine & Busch (1998)	No data	~ 50%	No data	No further details in paper.
Portenoy <i>et al.</i> (1999)	38%	49%	13%	Incident pain precipitants: movement 27.8%; defaecation 5.7%; urination 3.8%; coughing 3.7%; sitting 3.7%; breathing 1.9%; eating/drinking 1.9%.
Zepetella <i>et al.</i> (2000)	59%	24%	17%	No further details in paper.
Gomez-Batiste <i>et al.</i> (2002)	32%	52%	15%	Incident pain precipitants: movement 38%; eating/drinking 3%; defaecation 2%; coughing 2%.
Hwang <i>et al.</i> (2003)	17%	64%	19%	Data based on initial assessment of patient. Incident precipitants: movement 44%; coughing 4%; eating/drinking 4%; defaecation 2%; sitting 2%.

* 'End-of-dose failure' is now generally not considered to be a subtype of breakthrough pain (Mercadante *et al.* 2002).

1.5 Aetiology

The aetiology of the breakthrough pain is often the same as that of the background pain (Portenoy & Hagen 1990; Portenoy *et al* 1999). Thus, breakthrough pain may be due to (a) a direct effect of the cancer; (b) an indirect effect of the cancer (i.e. secondary to disability); (c) an effect of the anti-cancer treatment; or (d) an effect of a concomitant illness (Zeppetella & Ribeiro 2003). Indeed, breakthrough pain may be experienced by patients with all stages of cancer (at diagnosis, during active treatment, during remission, during relapse/progression, following cure) (Portenoy & Hagen 1990; Portenoy *et al* 1999). Table 1.3 shows the aetiology of breakthrough pain in relevant published studies (Portenoy & Hagen 1990; Portenoy *et al* 1999; Zeppetella *et al* 2000).

Not surprisingly, the pathophysiology of the breakthrough pain is also often the same as that of the background pain. Thus, breakthrough pain may be (a) nociceptive; (b) neuropathic; or (c) mixed (nociceptive and neuropathic). Table 1.3 shows the pathophysiology of breakthrough pain in relevant published studies (Portenoy & Hagen 1990; Portenoy *et al* 1999; Zeppetella *et al* 2000).

1.6 Clinical features

Breakthrough pain is not a single entity, but a spectrum of very different entities. The clinical features vary from individual to individual, and may vary within an individual over time (Portenoy 1997). Nevertheless, breakthrough pain is often reported to be frequent in occurrence, acute in onset, short in duration, and moderate-to-severe in intensity. Moreover, the clinical features of the breakthrough pain are often related to the clinical features of the background pain (Portenoy *et al* 1999).

Breakthrough pain may result in a number of other physical, psychological, and social problems. Indeed, the presence of breakthrough pain can have a significant negative impact on quality of life (Portenoy *et al* 1999; Hwang *et al* 2003). The degree of interference seems to be related to the characteristics of the breakthrough pain: patients with spontaneous pain (Portenoy *et al* 1999) and patients with severe pain (Swanwick *et al* 2001) may experience particular problems.

Table 1.3 Aetiology/pathophysiology of breakthrough pain

Study	Aetiology			Pathophysiology		
	Cancer	Cancer treatment	Concomitant disease	Nociceptive pain	Neuropathic pain	Mixed pain
Portenoy & Hagen (1990)	76%	20%	4%	53%	27%	20%
Portenoy et al (1999)	65%	35%	0%	38%	10%	52%
Zeppetella et al (2000)	71%	11%	18%	75%	9%	16%

Not surprisingly, breakthrough pain is associated with increased use of health care services (i.e. increased outpatient visits, increased inpatient admissions) (Fortner *et al* 2002). The result of the increased use of health care services is an increase in direct costs (e.g. prescription costs) and in indirect costs (e.g. transportation costs) for both the health service and the patient and their carers (Fortner *et al* 2003).

1.7 Conclusions

The quotation at the start of the chapter exemplifies the negative effects of poorly controlled cancer pain (Coyle 2004), whilst the subsequent quotation (from the same patient) reinforces the positive effects of well-controlled cancer pain (Coyle 2004). Breakthrough pain is a major challenge to health care professionals (as well as to their patients). Nevertheless, in many cases, it is possible to eradicate the breakthrough pain (Hwang *et al* 2003). Moreover, in all cases, it should be possible to ameliorate the breakthrough pain. The following chapters will address the issues of the assessment, the general principles of management, and the specific options for management of cancer-related breakthrough pain.

Once the pain was relieved it was the most beautiful experience of my life, to be able to participate and control the pain.

(Coyle 2004)

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