

Consensus Panel Recommendations for the Assessment and Management of Breakthrough Pain

PART I ASSESSMENT

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INTRODUCTION: DEVELOPMENT OF THE CONSENSUS PANEL RECOMMENDATIONS

The consensus recommendations detailed in this article are intended to guide clinicians in the assessment and effective management of breakthrough pain (BTP). Although BTP can occur in patients with acute as well as chronic pain syndromes, these recommendations focus on BTP associated with chronic cancer-related and non-cancer-related pain, with an emphasis on pharmacological management.

Several approaches were taken to survey the medical literature. PubMed, a search engine for selected peer-reviewed journal articles and which is part of the National Library of Medicine, was examined for the period from 1990 through October 2004. The search for management-related references

was initiated after all references with pain (as a major focus) and drug therapy were identified. References related to headache were excluded.

All articles with the terms breakthrough or episodic or flare or incident or transient or rescue were identified. These two searches were combined to identify the references common to both. This subset was then limited to those in English and human and clinical trial or meta-analysis or practice guideline.

A similar approach was also used for assessment-related references in PubMed. The Cumulative Index to Nursing & Allied Health Literature (CINAHL) database was also searched via a strategy similar to that used for PubMed.

Relevant references were identified by searching guidelines and summaries from the following sources: Agency for Health Care Research and Quality Clinical Guidelines and Evidence Reports, Bandolier, Cochrane Database of Systematic Reviews, American College of Physicians (ACP) Journal Club, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Institute for Clinical Systems Improvement, National Guideline Clearinghouse, and U.S. Preventive Services Task Force.

The abstract of each reference was reviewed; if the abstract was considered potentially relevant, the complete reference was obtained and reviewed in detail. The Consensus Panel members, who provided recommendations based on the review of the literature and their experience in pain management, prepared and evaluated a summary of each reference as it related to BTP.

Two teleconferences were held on September 30, 2004, and November 5, 2004, to discuss the scope of the project and to search for terms and key words, definitions, outlines, sections, and subsections, particularly the assessment and management of BTP. From these findings, the Consensus Panel developed and subsequently reviewed a draft of the manuscript prior to the live meeting on December 4, 2004, in Orlando, Florida. During the live meeting, the Expert Panel achieved consensus recommendations for the assessment and management of BTP.

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Breakthrough Pain: Assessment

Case Study: T. G.

T. G. is a 62-year-old woman with stage IV breast cancer. A recent bone scan has demonstrated several new metastatic bone lesions. On physical examination, the most painful area is her right hip and anterior thigh. This pain is worsened with any weight-bearing activities such as standing and walking.

She is being referred to radiation oncology to receive external beam radiation for pain control and to prevent a possible pathological fracture. Her current pain medication is oral sustained-release morphine sulfate 90 mg every 12 hours, which she has been taking for the past six months.

BACKGROUND

This case represents a common scenario seen in clinical practice. Almost 50% of all Americans seek medical care each year for pain, making pain the single most frequent reason for a physician consultation in the U.S.^{1,2} Pain is inadequately controlled in many of these patients. In some patients such as T. G., the pain that was established at the baseline examination persists, affecting her quality of life and functioning, often even with drug therapy. Furthermore, such patients also experience BTP, which affects 19% to 95% of all patients with pain, depending on the population surveyed and the definition of BTP used.³⁻¹¹

Despite the considerable variability in how BTP is defined, it is clear that BTP is associated with significant patient morbidity, including decreased functioning^{10,12,13} and increased levels of depression and anxiety.^{12,13} BTP may also predict a poor medical outcome.^{3,4,14-16} It is associated with lower patient satisfaction with opioid therapy^{9,15} and significantly increased utilization of health care compared with patients without BTP.⁶ BTP is a major component of the public health problem related to the undertreatment of pain, which has become a national quality-of-care issue and is a priority concern of the Agency for Healthcare Research and Quality.¹⁷

To help address this situation, we present this two-part series to emphasize the importance of BTP as a clinical entity.

Part 1 describes the definition, clinical spectrum, and assessment of BTP. Part 2 focuses on the management of BTP.

TERMINOLOGY

“Breakthrough,” “episodic,” “incidental,” and “transient” pain are some of the terms most commonly used to refer to the pain flares that occur beyond baseline persistent pain. Complicating matters is the fact that no widely accepted definition exists for any of these terms; in fact, several definitions of BTP have been proposed.^{7,18-22}

To be practical, we chose to use the term “breakthrough” pain and have defined it as a transient exacerbation of pain that occurs in patients with otherwise stable, baseline persistent pain. This definition requires the presence of baseline persistent pain and stresses the importance of worsening pain intensity and a *transient* profile. Although baseline persistent pain might result from an acute pain syndrome, our consensus recommendations relate to persistent *chronic* pain. The chronic pain may be either cancer-related or non-cancer-related in origin (e.g., arthritis, low back pain, or diabetic neuropathy).

Although most of the research on BTP has focused on patients with cancer, we and others believe the limited evidence suggesting that non-cancer-related BTP shares many common features with cancer-related BTP.²³ Consequently, we have developed these consensus recommendations to include both cancer-related BTP and non-cancer-related BTP and have based our recommendations on the results of clinical trials and our collective clinical experience.

BTP and baseline persistent pain generally share the same etiologic mechanism, but this is not always the case. Furthermore, from our definition, baseline persistent pain must be *stable*, because *unstable* baseline persistent pain suggests the need for more aggressive around-the-clock management, which differs from BTP management.

Finally, the pharmacological management of baseline persistent pain typically consists of around-the-clock analgesics, and usually an opioid, but the analgesic treatment of baseline persistent pain is not required to satisfy our definition of BTP.

Three subtypes of BTP have been defined: (1) incident pain, (2) idiopathic pain, and (3) end-of-dose pain (Table 1).

Table 1 Subtypes of Breakthrough Pain (BTP)

	Characteristics	Usual Management
<i>Incident, predictable</i>	Consistent temporal causal relationship with predictable motor activity, such as movement, defecation, micturition, breathing, or coughing	Immediate-release opioid, acetaminophen, tramadol on an as-needed basis prophylactically; rest; ice; patient education
<i>Incident, unpredictable</i>	Inconsistent temporal causal relationship with motor activity, such as sneezing, bladder spasm, or coughing	Immediate-release opioid on an as-needed basis
<i>Idiopathic</i>	Not associated with a known cause; generally of longer duration than incident pain	Immediate-release opioid on an as-needed basis
<i>End-of-dose</i>	Occurring before a scheduled dose of an around-the-clock analgesic; more gradual onset and longer duration than incident or idiopathic BTP	Increase in dose and/or frequency of around-the-clock analgesia

Breakthrough Pain: Assessment

Incident pain (pain with activity or movement) appears to be somewhat more common than *idiopathic* or *end-of-dose* pain.^{5,7,11,12,24} Most causes of incident pain are predictable and are relatively responsive to pretreatment with pharmacological therapy or other treatments. Unpredictable incident pain (pain occurring spontaneously) is less responsive to pharmacological therapy because of its rapid escalation and its inability to be pretreated.^{15,16}

Idiopathic pain is not associated with any known cause. Pain that rapidly intensifies is sometimes called *crescendo* pain. Idiopathic pain generally lasts longer than incident pain.¹¹ Idiopathic BTP that worsens in a patient with cancer often suggests progressive disease, because analgesic tolerance is not generally the cause of progressive pain.²⁵

End-of-dose pain occurs before a scheduled dose of an around-the-clock analgesic.^{7,12} Characteristically, this form of pain has a more gradual onset of intensity and a longer duration than the other types of BTP. Because end-of-dose pain occurs as a result of an inadequate dose of analgesic or a dosing interval that is too long, the analgesic regimen used to treat baseline persistent pain should be reassessed and modified as necessary.

Case Study (continued)

T. G. has predictable, severe incident BTP upon any movement from a supine position or with attempts at ambulation. Sometimes she also has idiopathic BTP. She has begun experiencing sharp, shooting pains in her right hip and down her leg, which seem to have no specific precipitating cause.

BTP encompasses a wide spectrum of characteristics, with no apparent significant differences between cancer-related and non-cancer-related BTP (Table 2).^{26,27} Typically, the onset of BTP is abrupt, with a time to peak pain severity of 3 to 5 minutes, and then resolving within 15 to 30 minutes. Patients with baseline persistent pain often have a higher median peak pain level and a longer duration of BTP than people without baseline persistent pain.^{5,10,12,24}

Several episodes of BTP can occur on a daily basis; more than four episodes per day may warrant reassessment of the cause as well as the approach to management of the baseline persistent pain. The cause of the BTP is often, but not always,

the same as that of the baseline persistent pain.¹² *Neuropathic* BTP (e.g., postherpetic neuralgia, reflex sympathetic dystrophy) is often of shorter duration, but it occurs more frequently than *nociceptive* BTP (e.g., sprains, fractures, bruises, burns, inflammation).^{9,28} Approximately 50% of BTP episodes are incident in nature.

ASSESSMENT

The assessment of pain begins with an attempt to find a correctable cause of BTP, such as an unrecognized vertebral compression fracture. The pain must be thoroughly assessed and the pattern must be understood as much as possible so that baseline persistent pain can be differentiated from BTP. Because the management of each type of pain differs significantly from the other, the dual focus of the pain assessment is an important determinant of effective long-term pain management.

Case Study (continued)

T. G. is having difficulty sleeping at night and has been experiencing at least two or three episodes of waking resulting from pain.

The patient is the best source of information about BTP. The most important step a clinician can take is to ask the patient specific questions about BTP. Because some patients might not understand the term "breakthrough pain," it may be helpful to initiate the discussion by asking the patient to describe a recent episode of severe pain.

Case Study (continued)

To facilitate the discussion with T. G., the clinician should ask various questions to establish the presence (or absence) of BTP and its characteristics (Table 3).²⁹

It is important to know the duration and intensity, as well as the onset, of BTP in selecting the appropriate pharmacological option and the route of administration for treating BTP (see Part 2 in the forthcoming June issue of *P&T*). Similarly, knowing the character, location, and pathophysiology of the BTP helps to differentiate the causes of nociceptive, neuropathic, and mixed pain (e.g., migraine), which can affect the choice of an analgesic or adjuvant analgesic. Understanding the

Table 2 Characteristics of Breakthrough Pain

	Average	Range
Time to peak severity	3–5 minutes	10 seconds to 180 minutes
Severity	Severe or excruciating	Mild to excruciating
Duration	15–30 minutes	1 second to more than 24 hours
Number of episodes per day	1–5	Less than 1 to 3,600
Precipitated by event	55%–60%	52%–77%
Predictable	50%–60%	41%–81%

Data from references 5–11, 18, 24, 26, and 27.

Breakthrough Pain: Assessment

Table 3 Assessing the Presence of Breakthrough Pain (BTP)

- Do you have episodes of severe pain or BTP?
- How many episodes of BTP do you have each week? Each day?
- How long is it from the time the pain first occurs to when the pain is at its worst?
- How long does each episode of BTP last (minutes, hours)?
- On a scale of 0 to 10, with 0 being no pain and 10 being the worst pain you can imagine, how much does an episode of BTP hurt when it occurs?
- Describe where the BTP occurs. What does it feel like?
- Is the BTP similar to or different from your baseline persistent pain?
- Does your BTP occur with movement or other activity, spontaneously (not associated with any activity), or just before you are supposed to take your next dose of pain medicine?
- What impact does the BTP have on your daily responsibilities at home/work? Are you able to do the things that you want/need to do?
- Are there any things that you avoid doing or that you are able to do only with severe pain?
- What do you do to relieve the BTP?
- What types of treatments have you used? How long did you use them? Were they effective? Are they still effective?
- What drugs have you used to relieve the BTP? What were the doses? Were they effective? Are they still effective?

The presence of end-of-dose pain should generally lead to a reassessment of the etiology and the management of the baseline persistent pain. For incident pain, the use of an analgesic or an adjuvant analgesic with a slower onset, taken in advance of the pain-provoking event, may be possible. Similarly, preventive measures are sometimes helpful, especially when the pain is caused by predictable precipitating factors. For example, cough-induced BTP that results from allergic rhinitis should be aggressively managed with antiallergy therapies, such as nasal steroids and antihistamines.

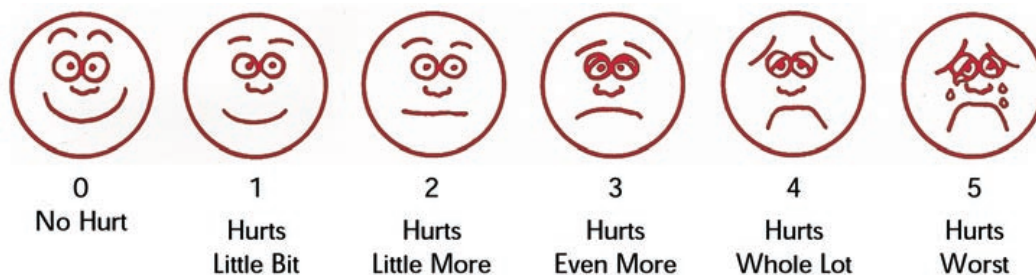
In addition to the history and physical examination, computed tomography or magnetic resonance imaging may be helpful in providing a detailed assessment of the nervous system and soft-tissue structures. However, because these imaging studies do not provide information about the functional status of the structure or its role in the pain syndrome, these findings must be carefully evaluated.

Several assessment tools have been used to evaluate BTP, although none has been validated for this type of pain. Because the patient is the best source of information, assessment tools that quantify the patient's perception of pain may be the most useful.

impact of BTP on the patient's functional status and quality of life is especially important in determining the goals of treatment because complete resolution of BTP is rarely possible.

The clinician should identify the source as well as the subtype of BTP, which will help determine the appropriate pharmacological and nonpharmacological management options (see Table 2, Part 2, in the forthcoming June issue of *P&T*). Corrective measures, such as bracing, vertebroplasty, and radiation therapy, should be implemented as appropriate.

Unidimensional instruments such as the Numerical Rating Scale, the Visual Analogue Scale, and the Wong-Baker FACES Pain Rating Scale, may be helpful. The Wong-Baker Scale (Figure 1) is suitable for patients of all ages (except the very young), for those of all cultures, and for those who are cognitively impaired. A shortcoming of these and similar unidimensional scales is that they assess only pain severity.



Explain to the person that each face is for a person who feels happy because he has no pain (hurt) or sad because he has some or a lot of pain. Face 0 is very happy because he doesn't hurt at all. Face 1 hurts just a little bit. Face 2 hurts a little more. Face 3 hurts even more. Face 4 hurts a whole lot. Face 5 hurts as much as you can imagine, although you don't have to be crying to feel this bad. Ask the person to choose the face that best describes how he is feeling.

The rating scale is recommended for persons age 3 and older.

Brief word instructions: Point to each face using the words to describe the pain intensity. Ask the child to choose the face that best describes own pain and record the appropriate number.

Figure 1 Wong-Baker FACES Pain Rating Scale. (From Wong DL, Hockenberry-Eaton M, Wilson D, et al. *Wong's Essentials of Pediatric Nursing*, 6th ed. St. Louis: Mosby, 2001:31. Courtesy of Elsevier.)

Breakthrough Pain: Assessment

Name Mary Johnson
Day Thursday
Date June 10, 2004

1 DAILY PAIN CHART Connect the points on your Daily Pain Chart so your medical team can see when and why your pain level changed. Every day, start a new chart.

2 DAILY PAIN LOG

MEDICINES: NAME/DOSE

#1 Hydrocodone/acetaminophen 12 mg/650 mg oral every 6 hrs

#2 Morphine 10 mg every 4 hrs as needed

#3 Hydrocodone/acetaminophen 3 every night

#4 gabapentin

#5 gabapentin

NON-MEDICINE THERAPY (other than prescription medicines)

hot bath

ACTIVITIES/EXERCISE

walked dog

COMMENTS AND MORE INFORMATION: Make notes for and about visits with your healthcare provider, side effects from treatments you may be experiencing, and any problems you are having coping with your pain. You may also want to write more about some of your answers on the previous page.

I forgot my morning medicine. I did a little too much yesterday and had to take it easy today. I felt a little sad today, but was able to reach a friend to talk. My pain is pretty well under control, but I need help with my breakthrough pain.

Name Mary Johnson
Day Thursday
Date June 10, 2004

3 DAILY PAIN SUMMARY

Did you have pain today? NO YES

Did you avoid or limit any of your activities or cancel plans today because of pain or changes in your pain? NO YES: What activities?

Did you take all your pain medicine today according to instructions? NO YES

Even though you took your pain medicine for persistent pain on schedule, were there times during the day that you experienced unrelieved breakthrough pain? NO YES

How many times did this happen today?
1 2 3 4 5 6 7 8 9 10 more than 10

Did any specific activity start your breakthrough pain? NO YES: What activities?
walking my dog

What was your average level of pain today?
0 1 2 3 4 5 6 7 8 9 10

Other than prescription medicine, did you do anything else today to relieve the pain?
 NO YES (Check any that you used.)

Non-prescription drugs (e.g., acetaminophen, ibuprofen)
 Herbal remedies
 Hot or cold packs
 Exercise
 Changing position (such as lying down or elevating your legs)
 Physical therapy
 Massage
 Acupuncture
 Rest
 Psychological counseling
 Talk to trusted friend, family, clergy
 Prayer, meditation, guided imagery
 Relaxation technique (hypnosis, biofeedback)
 Creative technique (art or music therapy)
 Other (describe):
took a hot bath

Check any of these common side effects that you've noticed after taking your pain medicine.

Drowsiness, sleepiness
 Nausea, vomiting, upset stomach
 Constipation
 Lack of appetite
 Other (describe):

Did you skip any of your scheduled pain medicines today? NO YES: Why?
I forgot

Did you call your doctor's office or clinic between visits because of pain? NO YES

Overall, are you satisfied with your pain management? YES NO (Explain what makes you satisfied or not satisfied. Use Log section.)

What pain level overall would you find acceptable?
0 1 2 3 4 5 6 7 8 9 10

Put an "X" on the body diagram to show each place you've had pain today.

Figure 2 Pain diary. (From the American Pain Foundation. Available at: www.painfoundation.org/downloads/Notebook.pdf.³¹)

Multidimensional scales, such as the Brief Pain Inventory, may be more useful because they characterize BTP more extensively; however, they are time-consuming and a health care provider must usually be involved for their completion.³⁰ A *pain diary*, in contrast, can be used to collect multidimensional information and is designed for completion by the patient over the course of a day or longer. Consequently, a patient's pain diary is probably more reliable than memory for accurately reflecting the pattern of symptoms in relation to activities and other variables. The diary is useful both in the initial patient evaluation and as an ongoing guide to modify treatment.

Figure 2 shows a sample of a completed pain diary, developed by the American Pain Foundation.³¹ A blank copy of a pain diary is available at the Foundation's Web site (www.painfoundation.org). A disadvantage of this diary is the time necessary to interpret the relatively large amount of information.

Following initiation or changes in the management of BTP, particularly with an opioid, it is critical that the patient be reassessed using the "four A's" of chronic pain medicine: (1) analgesia, (2) activities of daily living, (3) adverse events, and (4) aberrant drug-related behavior.³² In addition to the tools used in the initial assessment of BTP, the Pain Assessment and Documentation Tool, developed by the National Pain Education Council, may be helpful in guiding further changes to therapy.

Case Study (continued)

An assessment of T. G.'s pain reveals that her baseline persistent pain, especially at night, is not being adequately controlled. Her pain intensity upon waking from sleep is a 5 or 6 (on a scale of 1 to 10) during the night. She has great difficulty returning to sleep because of the pain. She has not demonstrated any morphine-related adverse drug effects, so the choice is made to schedule her evening dose of morphine closer to her bedtime and to increase the dose to 120 mg. The morning dose is continued at 90 mg.

T. G. says that her pain increases to 8 or 9 (on a scale of 1 to 10) whenever she tries to walk. This is especially difficult for her when she is trying to prepare a meal. She also experiences intense sharp, shooting pains three or four times a day while sitting and not moving (e.g., while she is reading or watching television). This pain becomes severe within a matter of minutes and lasts for 10 to 15 minutes; sometimes it lasts as long as 45 minutes. Both types of BTP are related to her baseline persistent pain.

T. G.'s pain-management plan must address the predictable incident BTP with movement as well as the idiopathic BTP that has no precipitating cause.

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Disclosure

Dr. Bennett reports no relationships with respect to his participation in this project.

Dr. Burton reports that he receives Research Support from Elan, Celgene, and Glaxo; he is on the Speakers' Bureau of and has been a Consultant for Medtronic, Inc., and Merck.

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Dr. Fortner reports no relationships with respect to his participation in this project.

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