Panic Attacks and Panic Disorder

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Panic disorder is a devastating condition with a higher prevalence in female patients and young adults. Panic disorder is frequently associated with major depression, agoraphobia, substance abuse, suicide attempts, and impaired quality of life. Only one half of the subjects with panic disorder seek care for their attacks, and those who do seek care tend to present to primary care and emergency department settings. If treated appropriately, panic disorder has a favorable prognosis.

KEY WORDS. Panic disorder; family practice; emergency medicine; diagnosis; health care services; health care utilization. *(J Fam Pract 1996: 43:275-282)*

To someone who has never experienced a panic attack, it is difficult to appreciate its emotionally devastating nature. An objective description of its symptomatology cannot capture the trauma it causes.

The definition of panic attack is based on diagnostic criteria in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV)[1] (Table 1). Panic attacks have a distinctive constellation of symptoms, beginning spontaneously and rapidly peaking in intensity. The initial symptoms tend to be cardiopulmonary, with dyspnea often reported. Fear of dying, going crazy, or losing control, which may be a learned response, occurs late in the attack.[2] Although there is considerable symptomatic variability both within and between subjects with panic, panic attacks tend to be a uniform phenomenon.[3,4] Because isolated panic attacks may occur in otherwise normal patients who are under extreme duress, the occurrence of panic attacks is not uniquely diagnostic of panic disorder.

Panic disorder is defined by recurrent panic attacks with at least 1 month of panic-induced behavior change or persistent concern about the attacks or their consequences (Table 2). To meet the criteria for panic disorder, the attacks cannot be the direct result of a general medical condition or of substance abuse. In addition, since panic attacks are seen in a variety of mental disorders, they are not indicative of panic disorder if they are better explained on the basis of a mental disorder other than panic disorder.

The onset of panic disorder tends to occur in young adulthood (ages 20 to 40), but 26% of cases are reported in subjects younger than 20 years of age.[5] Recent studies suggest that panic beginning late in life, in those over 50 years old, may produce less depression and agoraphobia.[6] Panic disorder is familial in nature, and its onset usually occurs during times of stress, hormonal instability,[7] or cocaine use.[8] Recent evidence suggests that both panic disorder[9] and infrequent panic[10] may be linked to childhood sexual abuse, raising the possibility that panic disorder may represent a form of posttraumatic stress disorder.

From an epidemiologic standpoint, panic disorder occurs more frequently in women than in men. Panic attacks may be more prevalent in African-Americans and in subjects with little education, but they are unrelated to overall socioeconomic status.[11]

THE IMPORTANCE OF PANIC

The generalist nature of primary care implies that every disorder is relevant to the primary care physician. Disorders that are *truly* important, however, are identified by their prevalence, severity, and treatability. Only treatable severe disorders that are prevalent in primary care settings are critical to primary care physicians.

In the community, the lifetime prevalence of panic disorder is up to 3.8%.[11] Similarly, the lifetime prevalence of infrequent panic is 5.6%.[11] In family practice settings, the prevalence of current panic disorder and infrequent panic are 13% and 9%, respectively.[12] A study performed in a private family practice office found a panic prevalence of 4.5% with an incidence of 0.015 cases per patient-year

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TABLE 1

Criteria For Panic Attack

Note: A Panic Attack is not a codable disorder. Code the specific diagnosis in which the Panic Attack occurs (eg, 300.21 Panic Disorder With Agoraphobia).

A discrete period of intense fear or discomfort, in which four (or more) of the following symptoms developed abruptly and reached a peak within 10 minutes:

(1) palpitations, pounding heart, or accelerated heart rate
(2) sweating
(3) trembling or shaking
(4) sensations of shortness of breath or smothering
(5) feeling of choking
(6) chest pain or discomfort
(7) nausea or abdominal distress
(8) feeling dizzy, unsteady, lightheaded, or faint
(9) derealization (feelings of unreality) or depersonalization (being detached from oneself)
(10) fear of losing control or going crazy
(11) fear of dying
(12) paresthesias (numbness or tingling sensations)
(13) chills or hot flushes

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(Unpublished data. Katerndahl DA). This suggests that in a 3000-patient practice, 45 patients will develop new-onset panic attacks each year.

Not only is panic disorder prevalent in primary care settings but it also represents a serious disorder as measured by comorbidity, quality of life, and economic costs. In terms of comorbidity, panic disorder is so closely linked to agoraphobia that the DSM-IV makes a distinction between panic disorder with agoraphobia and panic disorder without agoraphobia. It is believed that subjects with panic disorder may begin to fear situations in which they have experienced a panic attack. Soon, they develop anxiety in anticipation of those situations and eventually avoid them. Of the subjects with panic disorder, 65% have some degree of phobic avoidance.[13]

Panic disorder is also associated with depression. The rate of major depression in subjects with panic disorder is 48%.[13] Irrespective of the presence of affective disorders, panic disorder is also linked to suicidality. The rates of suicidal ideation and suicide attempts (19% and 8%, respectively) seen in subjects with panic disorder are higher than those seen in subjects with major depression.[14] Either through a kindling phenomenon with repeated withdrawals or through attempts to self-medicate for their panic, there is an increased prevalence of substance abuse in subjects with panic disorder. Alcoholism is seen in 37% of subjects with panic disorder, and illicit drug abuse is present in 31%.[13] Quality of life is poorer in subjects with panic disorder: not only is self-perceived physical and emotional health rated poorer[15] but also 26% of subjects have moderate to severe social impairment.[16] Financial dependency (25%)[15] and panic-related work disability[17] are common in subjects with panic disorder. Compared with other anxiety disorders, panic disorder results in the worst outcomes and the most psychosocial impairment for affected patients.[18] Economically, panic disorder is responsible for high health care costs as well as work disability costs of over $33,000 per patient.[17]

Panic disorder is a severe condition prevalent in primary care settings; but to be considered of critical importance, it must also be treatable. Panic disorder is eminently treatable through a variety of pharmacologic and nonpharmacologic means. With response rates of over 90% in some studies,[19] panic disorder is considered to have "the most favorable prognosis of any major psychiatric condition."[20] In light of its severity, its prevalence in primary care, and its treatability, knowledge about panic disorder is of critical importance to primary care physicians.

PRESENTATION TO THE HEALTH CARE SYSTEM

Although patients with panic disorder are heavy utilizers of the health care system,[21] only 59% of community-dwelling subjects with panic have ever sought care from the health care system for their attacks.[22] Although a number of factors differ between those who seek care and those who do

not, only three factors independently predict care seeking: treatment experience, panic-related inability to work, and having to get someone else to drive.[22] The subject's interpretation of the panic attack appears to be most critical in the care-seeking decision. Almost one half of those seeking care did so based on their own cognitive assessment, eg, they thought they were dying. Similarly, one third of those who never sought care failed to do so because of their interpretation of their symptoms, eg, attributed them to a known condition other than panic disorder.[22]

Seventy-four percent of patients who seek care do so for their self-perceived worst attack. However, 64% of patients present when their attacks increase in frequency, and 54% seek help following their first panic attack. Presenting complaints are generally somatic symptoms rather than anxiety. One study found that 8 of 10 patients presenting with unexplained panic-related symptoms met criteria for panic attacks.[23] Forty-three percent of emergency department patients with atypical chest pain had panic attacks and 16% were found to have panic disorder.[24] One third of cardiology patients with chest pain but normal coronary arteries had panic disorder.[25] In a study conducted in a family practice office setting, 26% of patients presenting with chest pain had panic disorder, and an additional 24% had infrequent panic attacks (Unpublished data. Katerndahl DA, Trummell C. Prevalence and recognition of panic states in STARNET patients presenting with chest pain).

Although previous tertiary-based studies suggested that patients with panic disorder frequently utilize multiple sites to seek care for their attacks,[26,27] community-based work found that 58% of those seeking care did so from only one site. Only 12% of patients used more than three sites. As Table 3 shows, 85% of patients initially seeking care use medical settings. Of those presenting, 43% use the emergency department. Of those ever seeking care, however, the family physician's office is the most frequent site of presentation (35%), followed by the emergency department (32%) and mental health settings (26%). Only 13% of subjects have ever sought care outside the health care system.[28]

Certain factors independently predict site-specific care-seeking. The family physician's office tends to be used when chest pain accompanies the attacks, when panic causes the patient to take time off from work, when the patient believes that dyspnea needs treatment, and when panic is appraised to be neither self-induced nor temporary. Different factors predict presentation to the emergency department: subjects who are male, are dependent on alcohol, and require someone else to drive for them tend to use the emergency department.[28] Other studies have found that the presence of chest pain during panic is associated with presentation to both the emergency department and a personal physi-

TABLE 2

Diagnostic Criteria for 300.01 Panic Disorder Without Agoraphobia

A. Both (1) and (2):

(1) recurrent unexpected Panic Attacks

(2) at least one of the attacks has been followed by 1 month (or more) of one (or more) of the following:

(a) persistent concern about having additional attacks

(b) worry about the implications of the attack or its consequences (eg, losing control, having a heart attack, "going crazy")

(c) a significant change in behavior related to the attacks

B. Absence of Agoraphobia

C. The Panic Attacks are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication) or a general medical condition (eg, hyperthyroidism).

D. The Panic Attacks are not better accounted for by another mental disorder, such as Social Phobia (eg, occurring on exposure to a specific phobic situation), Obsessive-Compulsive Disorder (eg, on exposure to dirt in someone with an obsession about contamination), Posttraumatic Stress Disorder (eg, in response to stimuli associated with a severe stressor) or Separation Anxiety Disorder (eg, in response to being away from home or close relatives).

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TABLE 3

Sites Selected by Patients Seeking Treatment for Panic Attack

Treatment Site	% of Patients Presenting at Any Time (N=97)	% of Patients Presenting for Episode of Initial Contact (n=53*)
Medical health care settings	19	85
Emergency department	32	43
Minor emergency center	11	7
Clinic	9	7
Physician's office		
General/family physician	35	35
General internist	3	6
Cardiologist	9	6
Otolaryngologist	3	6
Ambulance	19	15
Mental health care setting	26	35
Psychiatrist	24	22
Psychologist	10	13
Social worker	5	4
Mental health clinic	11	7
Alternative care settings	13	19
Telephone help line	10	6
Clergy	8	7
Folk healer/*curandero*	8	7
Chiropractor	6	6

NOTE: Subjects may have presented to >1 site so percentages may not total 100.

*Only the 57 patients who presented to at least one site were included. Four of these subjects did not respond to this question.

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cian.[29] Thus, patients seeking care for their panic attacks preferentially use the emergency department and the family physician's office, especially if chest pain is a prominent feature of the attacks.

DIAGNOSIS OF PANIC DISORDER

Previous work suggests that anxiety disorders in general[30] and panic disorder in particular[26] are frequently unrecognized by clinicians. Sheehan[26] found that of 57 newly diagnosed tertiary care patients with panic disorder, all had seen at least one physician and 70% had seen at least 10 physicians without having received a diagnosis. Ninety-five percent of those seeking medical care had seen a psychiatrist. Only 2% of emergency department patients with atypical chest pain and panic were recognized as having "anxiety."[24] Similarly, another study found that only 28% of family practice patients with chest pain and panic were recognized by their physicians as having "anxiety" (Unpublished data. Katerndahl DA, Trummell C. Prevalence and recognition of panic states in STARNET patients presenting with chest pain). A community-based study[29] found that only 47% of those seeking care for their panic attacks had ever been told that they had a panic attack. Fewer than one half of those with panic attacks had their condition diagnosed correctly by emergency department or family physicians. Recognition was associated with increased utilization of general medical settings. Physicians in these settings were more likely to recognize panic if (1) panic symptoms were severe, (2) phobic avoidance was present, or (3) panic reduced work capacity.

The diagnosis of panic disorder is based on DSM-IV criteria (Table 2). Although provocative tests are used in research settings, none of these tests has sufficient sensitivity and specificity to be used clinically. Two recently developed screening instruments, Symptom Driven Diagnostic System–Primary Care (SDDS-PC) and Primary Care Evaluation of Mental Disorders (PRIME-MD), are advocated for use in primary care settings. Although there is evidence that both are valid, their reliability is only fair.[31,32]

It is important that physicians distinguish between panic disorder and hyperventilation syndrome. Although hyperventilation may be important in panic disorder,[33,34] hyperventilation syndrome lacks the clear-cut diagnostic criteria that characterize panic disorder. Hyperventilation provocation tests using room air are poor inducers of panic attacks,[35] and hyperventilation syndrome

fails to respond to anxiolytics or antidepressants.[36]

The significance of subsyndromal panic, either infrequent panic attacks or limited-symptom attacks, is still unclear. Although little research has been done on limited-symptom attacks, studies comparing panic disorder with infrequent panic suggest that the prevalence of comorbid psychiatric conditions is similar in both panic groups.[37-39] With respect to disability and quality-of-life measures, however, subjects with infrequent panic tend to be intermediate between controls and those with panic disorder.[40] Thus, recognition of infrequent panic is important, and may represent management implications similar to those of panic disorder.

Table 4 is a list of medical conditions thought to be associated with panic or panic-like attacks. These conditions must be considered with a thorough history and physical examination before instituting a management plan. Routine laboratory testing is unnecessary and may actually be detrimental, despite patients' tendency to believe in a somatic cause for their attacks. Following a normal coronary angiogram, patients with panic disorder reported greater disability and more symptoms than controls while continuing to believe that their chest pain was cardiac in origin.[41] Although panic disorder is associated with mitral valve prolapse, the presence of the latter in patients with panic disorder does not alter either the clinical course or the treatment response.[42] A drug screen, however, is appropriate in any patient in whom substance abuse is suspected.

TABLE 4

Conditions Associated with Panic Symptoms

Psychiatric disorders
Major depression
Agoraphobia
Simple phobia
Social phobia
Generalized anxiety disorder
Obsessive-compulsive disorder
Substance abuse
Posttraumatic stress disorder
Cardiovascular disorders
Mitral valve prolapse
Paroxysmal supraventricular tachycardia
Endocrine disorders
Hyperthyroidism
Hypoglycemia
Menopause
Pheochromocytoma
Carcinoid syndrome
Neurologic disorders
Temporal lobe epilepsy
Cerebral tumor
Parkinson's disease
Sleep disorders
Narcolepsy
Sleep apnea
Drug-related disorders
Antidepressant withdrawal
Sedative-tranquilizer withdrawal
Stimulant (cocaine, cannabis, PCP) use
Metronidazole use
L-dopa use
Neuroleptic use
Organic solvent exposure
Miscellaneous
Wilson's disease
Acute intermittent porphyria
Hyperventilation syndrome

MANAGEMENT

The goal of therapy is a panic-free state. Once the diagnosis is made, management begins with patient education. At the time of diagnosis, patients have often sought care unsuccessfully. Although they may have been told that "it's all in your head" and may question their own sanity, they are generally convinced that they suffer from a physical disorder. Patient education begins with a discussion of the role of neurotransmitters in psychiatric disease. Labeling their symptoms as "panic disorder" may reassure patients of the legitimacy of their illness. Discussion of the favorable prognosis further elicits cooperation. Family physicians report that patients with panic disorder usually accept the diagnosis.[43] Information concerning consequences of panic—phobic avoidance, suicidal ideation, and substance abuse—should be elicited. Physicians need to address the impact panic has on the patient's family, social relation-

ships, and work. Because panic disorder has been linked to childhood sexual abuse, a childhood history should eventually be obtained.

If an associated disorder is found (Table 4), treatment should be directed at this condition. Avoidance of caffeine and other stimulants is important, along with tobacco and cannabis, which also may exacerbate panic disorder. Dietary inositol (12 g/day) may decrease the frequency of panic attacks.[44] Some patients with panic disorder may be sensitive to fluorescent lighting, sleep deprivation, and emotional conflict.[45] Unless exercise is known to exacerbate their panic, patients should be advised to exercise to reduce their general anxiety levels.[46]

Although insight therapy and individual psychotherapy are not helpful for patients with panic disorder, other forms of behavioral therapy are. Applied relaxation and respiratory training are appropriate. Cognitive behavioral therapy is as effective as pharmacotherapy and may have a lower relapse rate.[47] During individual or group cognitive-behavioral therapy, patients re-create their self-perceived worst panic symptom and attempt to train themselves to experience it without the sense of an impending attack.[48,49] Exposure therapy, in which patients expose themselves to phobic situations for increasingly longer periods of time, is recommended for all patients with panic disorder. Family physicians who are confident of their counseling skills tend to provide counseling to patients with panic disorder.[43] In addition, family and community support groups may be important adjuncts to management, especially in patients with phobic avoidance.

Although no medication will abort a panic attack once it has begun, a variety of medications will prevent the onset. Recent research has demonstrated the effectiveness of serotonin reuptake inhibitors (SSRIs).[50] Although fluoxetine (20 to 40 mg/day), fluvoxamine (50 to 200 mg/day), and paroxetine (20 to 60 mg/day) have been studied most frequently, other SSRIs also may be effective. During the initial phase, characterized by transient excitation, lower doses should be used. Headache, nausea, and impotence are common side effects of SSRIs.

Tricyclic antidepressants are effective in up to 90% of patients with panic disorder. Beginning with an initial dose of 25 to 50 mg at bedtime, patients should be titrated up to maximum doses of 300 mg/day. Imipramine shows a plasma level–response relationship up to plasma levels of 140 ng/mL.[51] Although imipramine has been the most studied among the tricyclic antidepressants, desipramine and clomipramine are also effective. Patients should be warned of transient excitation when initiating imipramine therapy. As with SSRIs, adequate doses of tricyclic antidepressants may require at least 3 weeks before treatment response occurs. Cardiotoxicity and anticholinergic side effects are major concerns associated with the use of tricyclic antidepressants.

Although neuroleptic agents are contraindicated in patients with panic disorder, high-potency benzodiazepines are as effective as tricyclics and may produce a more rapid response. The literature recommends high doses (alprazolam 3 to 10 mg per day, clonazepan 2 to 6 mg per day, and lorazepan 4 to 8 mg per day), but experience in primary care patients suggests that lower doses may be effective. The new sustained-release alprazolam derivative, adinazolam-SR, also may be effective.[52] Based on plasma levels in the context of side effects and remission rates, the optimal alprazolam dose may be 2 to 3 mg per day. Clonazepam may produce less sedation and fewer withdrawal symptoms. Alprazolam-related memory impairment may continue even when the patient is medication-free.[53] Although abuse of alprazolam has been limited to patients with a prior history of substance abuse, chronic benzodiazepine use will lead to physical dependence. Consequently, slow tapering is necessary when attempting to discontinue the medication.

Monoamine oxidase inhibitors (MAOIs) may be even more effective for panic disorder than tricyclics. Of major concern, however, is a possible interaction between these drugs and tyramine-containing foods that may lead to hypertensive crisis. Therefore, MAOIs are not first-line agents for panic disorder. When used, the initial dose of phenelzine is 15 mg at bedtime, which is increased up to 60 mg/day. The new reversible monamine oxidase-A inhibitors may represent safer alternatives.[54]

Although sodium valproate, clonidine, and verapamil may have some antipanic activity, beta-blockers, buspirone, and bupropion do not. These agents may be helpful only in dealing with comorbid social phobia and generalized anxiety disorder.

Some clinicians combine a high-potency benzodiazepine with an antidepressant to ensure a rapid response, intending to withdraw the benzodiazepine after 1 to 2 months. This approach, however, is not recommended because once patients respond to the benzodiazepines, they resist eliminating them. To date, only paroxetine and alprazolam have Food and Drug Administration approval for the treatment of panic disorder.

The therapeutic approach used in any particular patient should be individualized based on the patient's age, comorbid conditions, and concurrent medications. In addition, it is important to seek input from the patient concerning the proposed treatment plan. Patients with panic disorder frequently fail to adhere to dosing schedules, often undermedicating themselves. Physicians should consider patient preferences to maximize adherence to the recommended therapeutic regimen. Depressed patients with panic disorder should be started on either an SSRI or a tricyclic antidepressant. Elderly patients traditionally have poor tolerance for tranquilizers and the anticholinergic side effects of tricylic antidepressants while being at risk for cardiotoxicity. Consequently, they should not be treated with a tricyclic antidepressant or benzodiazepine. Patients with a history of substance abuse similarly should avoid benzodiazepine use. Cognitive therapy should be strongly considered for patients who are pregnant or who cannot tolerate medications. Patients whose condition was initially diagnosed in the emergency department setting should be referred to their family physician unless a mental health provider is available on site. Pharmacotherapy should not be instituted in the emergency department. Patient education should be provided and exposure therapy encouraged.

Once the patient is panic-free, medication should be continued for at least 6 to 12 months. Benzodiazepines and tricyclic antidepressants should be tapered to avoid withdrawal symptoms. Relapse is common after discontinuation of medication. If this occurs, medication may need to be reinstituted. Three-year follow-up studies have found, however, that the majority of patients continued to do well after short-term treatment with alprazolam, imipramine, or group therapy.[55,56]

Family physicians tend to refer patients with panic disorder when they lack confidence and when local resources are adequate.[43] Patients must be prepared for referral and accept it. Mental health referral should be considered for patients who are suicidal or actively abusing drugs or alcohol. Referral also should be considered if the physician is unfamiliar with an indicated therapy or the patient fails to respond. Finally, patients with full-blown agoraphobia or a history of childhood sexual abuse may need more intensive psychological counseling than the family physician can provide.

SUMMARY

Panic disorder is a prevalent condition resulting in frequent use of the health care system. Without diagnosis and treatment, panic disorder is a chronically disabling disorder associated with significant comorbidity and decreased quality of life. Treatment is highly effective and can restore patients to normal functioning. As part of the Panic Disorder Education Campaign, the National Institute of Mental Health provides a Panic Hotline (800-647-2642) to offer physician and patient information about panic disorder.

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