

# Panic Disorder in the Medical Setting

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Most patients with panic disorder have their initial contact with the health care system in a general medical setting. Only 35% of patients have their first contact in a mental health care setting, and of these, only 22% are evaluated initially by a psychiatrist. Thus, family practitioners, cardiologists, gastroenterologists, and other specialists need to become familiar with the signs, symptoms, and differential diagnosis of panic disorder. Early diagnosis of panic disorder by nonpsychiatrists—before unnecessary tests are ordered—would substantially decrease the costs associated with this condition.

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There are multiple reasons why physicians who are not psychiatrists need further education about panic disorder. Perhaps one of the most compelling reasons is that patients are seen primarily by physicians in general medical practice. Fully 50% to 60% of patients with psychiatric illnesses are seen and treated exclusively in general medical settings.<sup>1,2</sup> This is also true for patients with anxiety disorders. According to the National Ambulatory Medical Care Survey, of 90,000 primary care patient visits, 11% were for anxiety, 11.2% were for headache and dizziness, and 7.5% were for abdominal pain, all of which probably were symptoms of an anxiety disorder.<sup>3</sup> When 350 primary care physicians were asked about their patients, they rated anxiety as the most common psychiatric problem seen in their practice.<sup>4</sup> The commonality of this problem is certainly the primary explanation for why 80% of benzodiazepines prescribed in recent years have been by primary care physicians.<sup>5</sup>

## PANIC DISORDER IN GENERAL PRACTICE

The importance of unrecognized and misdiagnosed panic disorder in general medicine is expertly reviewed by Katon.<sup>6</sup> He and his colleagues have reported that 20% of patients in a primary care setting met strict DSM-III-R (*Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*) criteria for panic disorder (life-

time).<sup>7</sup> Another 18% met the criteria if they were slightly liberalized, much like the new panic disorder criteria in the DSM-IV. Katon et al.<sup>7</sup> also have demonstrated that panic disorder plays a large part in the utilization of health care services in general medicine. Among "high utilizers" of health care services (those who represent the top 10% of patients in frequency of seeing physicians), 58% had either panic disorder, generalized anxiety disorder, or affective illness, with 22% having panic disorder.

This problem is compounded by the high level of nonrecognition of psychiatric problems, including panic disorder, by general practitioners. Fully one third to one half of psychiatric problems in primary care are not recognized or diagnosed properly.<sup>8,9</sup> Psychiatric illness also leads to at least a doubling of nonpsychiatric health care utilization.<sup>10</sup> This is perhaps especially true for anxiety disorders, since patients with panic disorder and agoraphobia are among the highest users of health care services.<sup>11</sup>

Primary care physicians need to be able to correctly diagnose and treat patients with panic disorder, since they are the primary physicians who treat these patients, both initially and later. As seen in Table 1,<sup>12</sup> most patients with panic disorder have their first contact with a health care professional in general medical practice, and almost half of the patients are treated in that setting. Thirty-five percent of patients are seen first by a general internist or family practitioner, and a similar percentage are treated in that setting. Forty-three percent of patients with panic disorder are first seen by an emergency room physician, and 15% of patients are initially brought to the emergency department in an ambulance. Thirty-five percent of patients have their initial contact with a mental health professional. However, only 26% of patients receive care in that setting, with most of these patients being treated by a psychiatrist. The 19% of patients who are initially seen at alternative, nonprofessional sites are a concern; 13% of these patients receive treatment at these sites.

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**Table 1. Settings in Which Patients With Panic Disorder Are Treated\***

	First Contact (%)	Later (%)
Medical	85	49
Emergency department	43	32
Minor emergency room center	7	11
Office		
General or family practitioner	35	35
Cardiologist	6	9
Otolaryngologist	6	3
Ambulance	15	19
Mental health	35	26
Psychiatrist	22	24
Psychologist or social worker	17	15
Alternative	19	13

\*From reference 12, with permission.

### WHY PANIC DISORDER IS MISDIAGNOSED

It is not surprising that panic disorder is frequently misdiagnosed by primary care physicians. Studies suggest that patients are correctly diagnosed 95% of the time if their anxiety and depressive symptoms are the principal presenting complaints. However, only 48% are correctly diagnosed if patients initially report primarily somatic symptoms.<sup>13</sup> This pattern of presenting symptomatology with a strong somatic focus has been termed *somatization* and is one of the primary diagnostic dilemmas in this area. Problematically, most patients with panic disorder (90%) report primarily somatic symptoms.<sup>14,15</sup> These patients often have seen 10 or more physicians<sup>14</sup> and have spent more than a decade in the health care system before they are correctly diagnosed.

Katon<sup>15</sup> studied the physical symptomatology of 55 primary care patients referred to him for evaluation. These patients had an average of 12 to 14 symptoms, the most common being cardiac symptoms (reported by 39% of patients). Chest pain was common (22%), as were tachycardias and arrhythmias (25%). One third of the patients reported primarily gastrointestinal symptoms. Epigastric pain with a history of peptic ulcer disease (15%) and epigastric pain relieved by antacids were common. Thirteen percent of patients reported diarrhea as their primary symptom; presumably many of these patients had irritable bowel syndrome. Neurologic symptoms were prominent in 44% of the patients. Headache was a principal symptom in 20%, dizziness in 18%, and syncope and pseudo-seizures in 9%. Pulmonary symptoms were also common, particularly shortness of breath (13%) and asthmatic symptoms (5%). Katon reported that 15% of the patients had a history of alcoholism. Only 11% of the 55 patients initially described their symptoms as psychological. The types of presentations described by Katon are associated with misdiagnosis in more than half of the patients and agree with data on underrecognition and misdiagnosis of panic disorder in primary care settings.

The extent of unrecognized panic disorder is most striking among cardiologists.<sup>16</sup> A patient with atypical chest pain has a high likelihood of having panic disorder, especially if the workup for coronary artery disease is negative. In one study,<sup>17</sup> 16% of emergency department patients with chest pain actually had panic disorder, and 43% of these patients met the criteria for panic attacks. In another study, 90% of patients at a chest pain clinic had panic disorder<sup>18</sup>; among the patients who were found not to have coronary artery disease, 98% had panic disorder. Perhaps most striking are the findings of Carter et al.,<sup>19</sup> who reported that almost 30% of the patients admitted to the coronary care unit at a university hospital had panic disorder and no evidence of coronary artery disease. Among patients whose coronary artery disease workup was negative, 55% had panic disorder. These data from patients reporting acute chest pain are similar to those of Beitman et al.<sup>20</sup> In their study, 30% to 50% of ambulatory patients with chest pain and negative workups for coronary artery disease had panic disorder.

The prevalence of unrecognized panic disorder in gastroenterology is also striking. Lydiard et al.<sup>21</sup> studied patients with well-characterized irritable bowel syndrome and found that 29% met the criteria for panic disorder. Interestingly, both syndromes generally resolve if the patient is treated for panic disorder.<sup>22</sup> The cost implications of misdiagnosis and mistreatment of patients with panic disorder who report primarily cardiac, gastrointestinal, neurologic, or pulmonary symptoms have not been well studied. However, this area clearly is an important potential source of reducing health care expenses.

### DIFFERENTIAL DIAGNOSIS

The multiple physical symptoms reported by patients with panic disorder are the principal difficulty to correctly diagnosing these patients in general practice. Katon et al.<sup>23</sup> have demonstrated that patients not only have symptoms in multiple organ systems but average more than 14 physical symptoms in a medical review of systems. This leads patients to appear to have either organic illness, somatization disorder, or hypochondriasis. Between 41% and 71% of patients spuriously meet the criteria for somatization disorder.<sup>24,25</sup> They also exhibit a tremendous overlap with hypochondriasis.<sup>26</sup>

The most important issue, however, is that effective treatment of panic disorder can alleviate these multiple physical symptoms.<sup>14</sup> This underscores the importance of correctly diagnosing panic disorder, somatization, and hypochondriasis. Patients with somatization disorder can be identified by their histories. These patients often have chaotic lives with multiple relationships and marriages, which are frequently abusive in nature. They also typically abuse alcohol or other substances and have a history of being physically or sexually abused as children.<sup>27-29</sup>

### **Differential Diagnosis of Panic Disorder From Other Psychiatric Illnesses**

Patients with panic disorder often abuse alcohol in an attempt to relieve their symptoms.<sup>30,31</sup> Epidemiologic and clinical studies show that patients with panic disorder tend to use alcohol to manage anxiety symptoms. How frequently this moves from increased drinking to alcoholism is controversial and currently under study. Cocaine abuse can produce panic disorder that lasts beyond the cessation of cocaine use.<sup>32</sup>

One of the most common psychiatric differential diagnoses for panic disorder is depression. More than 60% of patients with panic disorder experience clinical depression in their lifetime.<sup>33,34</sup> One third of patients with panic disorder also have comorbid depression.<sup>33,34</sup>

Posttraumatic stress disorder, especially of the civilian type, has a considerable symptom overlap with panic disorder. It can be differentiated by a history of a trauma, such as assault, rape, or a car accident. Similarly, social phobia shares many symptoms with panic disorder, and panic attacks occur in similar situations in both syndromes. There also is considerable comorbidity of the two syndromes.

### **Differential Diagnosis of Panic Disorder From Medical Conditions**

General practitioners are beginning to emphasize early diagnosis of panic disorder rather than the previous practice of extensive workup of the common physical symptoms—workups that usually are fruitless. However, general practitioners rightfully question whether there are actual medical complications of panic disorder and whether rare medical conditions might be missed if workups were less extensive. Data suggest there may be a small increase in the incidence of hypertension and peptic ulcer disease among patients with panic disorder.<sup>23</sup> Death from cardiovascular causes also may be increased in patients with panic disorder.<sup>35,36</sup> If so, this increase is fairly small, and the common concern of patients with panic disorder—that they have cardiovascular disease—is almost always unfounded. However, if the increase in cardiovascular deaths among patients with panic disorder is substantiated, it might be related to the reported increases in blood pressure and the poor health habits of these patients, who typically do not follow a regular exercise program.

### **SUBSTANCES THAT EXACERBATE PANIC DISORDER**

Several substances can exacerbate panic symptoms; among these is caffeine. Boulanger et al.<sup>37</sup> reported that two of three patients with panic disorder had discontinued caffeine use even before their disorder was correctly diagnosed. Withdrawal from alcohol and sedative use also can exacerbate anxiety symptoms,<sup>38</sup> as can the use of mari-

juana, cocaine, and amphetamines.<sup>32,39,40</sup> The risk of an exacerbation of panic symptoms is also greater among patients who use sympathomimetic agents and asthmatic patients who use aminophylline.

### **MEDICAL CONDITIONS THAT MIMIC PANIC DISORDER**

The medical conditions listed in Table 2 can mimic panic disorder and may lead to a misdiagnosis. The classic case is hyperthyroidism, which can resemble panic disorder in many ways. Although hyperthyroidism is fairly uncommon, it is the justification for obtaining thyroid function tests on a new patient with panic disorder.<sup>41</sup> Similarly, symptoms of angina or cardiac arrhythmias can sometimes resemble those of panic disorder, as can those of chronic obstructive pulmonary disease or, rarely, pulmonary embolus.

Patients often believe their anxiety symptoms are related to hypoglycemia, although this is almost never the case. A report of hypoglycemia should be evaluated skeptically and as a likely explanation for anxiety symptoms only in patients whose symptoms are postprandial or associated with hunger and in those with known endocrine abnormalities that might predispose them to glucose abnormalities. Physicians may think the patient's symptoms resemble those of a pheochromocytoma, but this too is a rare and unlikely cause of panic disorder. Pheochromocytoma should be seriously considered only in patients who also have hypertension, headache as a predominant symptom, flushing, postural hypotension, and an absence of typical panic disorder symptoms.<sup>42,43</sup>

Certain endocrine problems, especially parathyroid abnormalities and Cushing's disease, can be associated with anxiety symptoms. Epilepsy, particularly temporal lobe epilepsy, can resemble panic disorder. However, patients with temporal lobe epilepsy have episodes associated with loss of consciousness or memory loss and characteristic automatisms. Although rare, electrolyte disturbances and anemia are sometimes associated with symptoms similar to those of panic disorder.

### **SUGGESTED MEDICAL WORKUP**

In patients with symptoms of panic disorder, a thorough medical and psychiatric history coupled with a family history and medication and drug history are preferred over an extensive physical or laboratory workup. A routine physical examination and a neurologic examination are also important, as are the limited laboratory tests listed in Table 3. An electrocardiogram may be indicated for patients with significant cardiovascular symptoms but can usually be omitted in patients younger than age 40.

Diagnosing panic disorder early should be the goal of the general practitioner, rather than arriving at the diagno-

**Table 2. Medical Conditions That Mimic Panic Disorder**

Anemia
Angina
Arrhythmias
Chronic obstructive pulmonary disease
Cushing's disease
Electrolyte disturbance
Epilepsy, particularly temporal lobe epilepsy
Hyperthyroidism
Hypoglycemia
Parathyroid disorders
Pheochromocytoma
Pulmonary embolus
Transient ischemic attacks

sis after ruling out what could be a long list of potential but unlikely medical syndromes. If the symptoms are typical and the patient is young, the diagnosis of panic disorder as a likely explanation for the symptoms can be made after the history and physical examination. The patient should be educated that panic disorder is a medical and probably genetic condition of the autonomic nervous system that can be effectively treated. The physician should reassure the patient that the laboratory tests are being performed to rule out unlikely other causes of particular symptoms.

### COST ISSUES

The high prevalence of panic disorder, coupled with underrecognition, misdiagnosis, and mistreatment, is associated with considerable waste in the health care system. In 1976, Clancey and Noyes<sup>44</sup> reported that 71 patients with anxiety symptoms had 358 tests or procedures, for an average of 7.5 tests per patient; these tests included electrocardiograms (38% of patients), electroencephalograms (24%), and upper gastrointestinal studies (25%). Inappropriate tests are still an issue today.

Beitman et al.<sup>20</sup> presented preliminary but striking figures of the waste associated with coronary angiograms performed on patients with panic disorder in whom these tests were not indicated. Forty-three percent to 58% of patients with normal coronary arteries had panic disorder; avoiding unnecessary angiograms or stress tests would yield a remarkably large potential savings if these patients were diagnosed early and unnecessary tests avoided.

A similar case can be made for the use of echocardiograms to try to rule out mitral valve prolapse. Echocardiograms are reported to be "abnormal" in 35% to 50% of patients with panic disorder. Typically, the abnormalities involve prolapse greater than some arbitrary figure on the echocardiogram and are not associated with either physical findings of mitral valve prolapse or functional consequences.<sup>45-47</sup> Most patients with panic disorder do not have a meaningful abnormality of the mitral valve, and the echocardiogram is often misleading in evaluating and treating these patients.

**Table 3. Suggested Medical Workup for Patients With Symptoms of Panic Disorder**

Medical, psychiatric, and social history
Physical and neurologic examinations
Family history
Medication and drug history
Electrocardiogram (patients > age 40)
Laboratory tests
Complete blood count
Chemistry panel
Thyroid function test
Others specifically indicated

Although even less well studied, the expensive endoscopic studies of patients with panic disorder who also have irritable bowel syndrome are also a waste of health care dollars.

### CONCLUSION

Considerable progress in the diagnosis and treatment of patients with panic disorder has been made in the past 20 years. However, this progress has not been adequately conveyed to nonpsychiatrists, particularly cardiologists, gastroenterologists, neurologists, and primary care physicians, who actually see the majority of these patients. This underrecognition is especially unfortunate because of the waste of health care resources through unnecessary medical care and because patients with panic disorder generally respond so well to appropriate treatment. Hopefully, current educational efforts will make effective treatment available to more patients across the various branches of medicine.

*Drug name:* aminophylline (Mudrane and others).

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# Discussion

## Role of the Primary Care Physician

**Dr. Jefferson:** My impression is that general practitioners are aware of the high prevalence of panic disorder and depression in primary care, given the enormous efforts made to educate physicians about these psychiatric illnesses. Even then, they may not recognize these disorders in their own patients. However, even if the primary care physician identifies these conditions, treatment may still be inadequate. What is the likelihood of instituting some type of program that would make a difference in treating these patients?

**Dr. Ballenger:** Right now, evolving changes in the health care system should provide a financial motive for primary care physicians to treat patients in managed care who have panic disorder, rather than refer them to a psychiatrist. Managed care plans also provide financial incentives for ordering fewer diagnostic tests.

**Dr. Rosenbaum:** Do you think the financial incentive overrides the need to provide good patient care?

**Dr. Ballenger:** It certainly shouldn't and probably doesn't in most cases. However, we have yet to arrive at an effective way of changing the practices of our primary care colleagues. For instance, my group is making a considerable effort to develop a computerized management system for psychiatric problems. It should not only help them make the diagnosis, but also should help them select appropriate treatment.

**Dr. Jefferson:** Yet, should primary care physicians be treating panic disorder? When should they refer the patient to a mental health professional?

**Dr. Ballenger:** Ideally, the primary care physician should refer the patient to a psychiatrist, rather than a cardiologist. Tests done by a cardiologist typically are wasted on a patient with panic disorder and contribute to the increased costs of health care. Referral to a cardiologist also delays effective treatment of the patient. However, the primary care physician may have medicolegal concerns about referral to a psychiatrist and may believe they are legally more at risk if they do not refer to a cardiologist a patient with mitral valve prolapse or prominent cardiovascular symptoms.

**Dr. Pollack:** We need to provide primary care physicians with data on the typical characteristics of a patient with panic disorder. For example, a female patient younger than age 40 without significant findings on physical examination and no family history of cardiac disease but a positive family or personal history of anxiety disorders should be referred to a psychiatrist first. These physicians need guidelines for making the diagnosis.

**Dr. Marshall:** They also are faced with the dilemma of making the diagnosis early in the course of the illness in a patient who has primarily physical symptoms. It is very difficult to do that.

**Dr. Ballenger:** Managed care plans need to develop protocols for diagnosing panic disorder based on the expert opinion of psychiatrists. Such protocols would recommend referral to a psychiatrist if the patient met certain criteria. This could provide the medicolegal protection the primary care physician requires.

For most patients, I believe involvement of a competent psychiatrist or referral results in better care. I am not impressed that these patients are well treated by primary care physicians, primarily because they require more time than is usually available.

**Dr. Shear:** A study of the treatment of depressed patients by primary care physicians supports that point. In this study, the primary care physicians were told that the patients had major depressive disorder. The patients were then randomly assigned to treatment by the primary care physician or a mental health professional, from whom they received drug or psychosocial therapy. Seventy percent of the patients responded to either the psychosocial therapy or to medication prescribed by study-monitored physicians. However, fewer than 30% of patients responded to "care as usual" from the primary care physicians; most of these patients were not prescribed an antidepressant in adequate doses for adequate periods of time.

**Dr. Rapaport:** If primary care physicians do not treat depressed patients appropriately, those with panic disorder will be treated even less well, since this condition is more difficult to treat. The amount of physician contact needed by a patient with panic disorder is substantial.

**Dr. Charney:** Whether patients are referred to psychiatrists or treated by the primary care physician is driven by economics in many parts of the country. At our institution, we are finalizing a contract with a managed care organization that will provide 45 psychiatrist hours per month for about 35,000 lives. As a result of this capitated contract, we need to train the primary care physicians to diagnose and treat our patients. Yet, because we are operating on a capitated system, the primary care physicians frequently want to refer patients to us, but we are going to train them to use us more efficiently.

**Dr. Davidson:** That type of contract could result in primary care physicians finally deciding to treat patients. There is a fairly large subgroup of patients with panic disorder who could easily be treated by primary care providers.

**Dr. Rosenbaum:** Yet a system that encourages each side to dump on the other does not work in the patient's best interests.

**Dr. Jefferson:** The goal should be an integrated system in which mental health is not separate from the whole system. In such a setting, nothing would be gained by referring or not referring a patient. Instead, the question becomes, What is the most efficient way to treat the patient?

**Dr. Ballenger:** The difficulty, however, is whether the primary care physician can treat the patient with panic disorder. Although they may be motivated to do so because of financial incentives, their training in this area may be inadequate. All the data I have seen do not support the premise that primary care physicians effectively treat patients with panic disorder.

**Dr. Shear:** As psychiatrists, we work with a select group of primary care physicians who have an interest in what we have to say. The rest of the primary care providers have little interest in the recommendations of mental health professionals. The physicians who do care probably do not do as well as they should in treating patients with panic disorder.

### Importance of Comorbid Disorders

**Dr. Rosenbaum:** Panic disorder is quite separate from medical illness, although sometimes the line is blurred. Chronic obstructive pulmonary disease (COPD) can mimic panic disorder, yet patients with COPD may be predisposed to panic disorder. The rates of panic disorder are higher in these patients, so COPD may be a risk factor. Conversely, panic disorder may be a risk factor for COPD.

**Dr. Pollack:** We have been using serotonin selective reuptake inhibitors (SSRIs) to treat dyspnea in patients with COPD who do not have full-blown panic disorder or depression. We found that the SSRI decreases dyspnea and

increases functional capacity and sense of well-being, even though the patients are not being treated specifically for Axis I depression or panic disorder.

**Dr. Rosenbaum:** This is not simply an issue of differential diagnosis. The issue is whether the panic disorder is causing something else. The stress response and release of catecholamines presumably can actually damage cardiac myofibrils, resulting in contraction-band myopathy. In a vulnerable patient, repeated panic attacks could, over time, damage the heart and cause idiopathic cardiomyopathy. Thus, panic disorder is a biopsychologic disorder that if left untreated can damage other systems.

**Dr. Ballenger:** That is theoretically very interesting, but I worry that it might lead some patients to undergo unnecessary cardiac biopsy.

**Dr. Davidson:** That is a real dilemma. Although we tell patients that no one has ever died from a panic attack, in fact patients may have died from the physical effects of a panic attack.

**Dr. Ballenger:** Even so, all the data we currently have indicate that it is a very rare occurrence.

**Dr. Shear:** In addition to the possible physical effects of a panic attack, evidence indicates that panic disorder can worsen an existing physical condition, such as asthma.

**Dr. Rapaport:** You also have to consider the role of corticosteroid withdrawal in both patients with COPD and those with asthma. Even with a "normal" tapering of steroids, patients can experience a significant increase in anxiety symptoms and memory problems. This derealization phenomenon may have a role in panic attacks.

**Dr. Jefferson:** The issue of hypertension may have some bearing on treatment selection. At least two reports have indicated that the use of tricyclic antidepressants in patients with panic disorder may be associated with the development of hypertension or just an overall increase in blood pressure and heart rate.