REVIEW ARTICLE

Panic Disorder and Asthma

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ABSTRACT

The presence of asthma is a risk factor for the development of panic disorder. The co-occurrence of panic disorder and asthma is greater than would be expected based on their individual prevalence rates. This may be due in part to the important role of respiratory factors in panic disorder. Panic and anxiety can directly exacerbate asthma symptoms through hyperventilation, and are associated with patients' overuse of as-needed asthma medications, with more frequent hospital admissions and longer hospital stays, and with more frequent steroid treatment, all of which are independent of degree of objective pulmonary impairment. This paper reviews the literature on the relationship between panic and anxiety on the one hand, and the experience and management of asthma on the other.

ANXIETY

Anxiety is a ubiquitous phenomenon. It is one of the most common presenting symptoms to both primary care and behavioral health care (1). As a symptom, anxiety is present across a range of psychiatric diagnoses. It is at the core of many disorders, from specific phobias like those of animals or of heights, to obsessive compulsive disorder, to generalized anxiety disorder, and of course, to panic disorder. In addition, it is present to a more or lesser extent in such disparate disorders as bulimia, substance abuse, major depression, sexual dysfunctions, schizophrenia, and various adjustment disorders. Finally, it has been esti-
estimated that 11% of visits to primary care physicians are for complaints of anxiety in the absence of a medical cause (2).

A panic attack is defined as a sudden onset (less than 10 min) of fear accompanied by an intense urge to escape and by at least 4 of a list of 13 symptoms, such as dyspnea, chest pain or discomfort, choking or smothering sensations, rapid heartbeat, sweating, trembling or shaking, nausea, and numbness/tingling sensations. Infrequent panic attacks are fairly common; however, individuals experiencing recurrent panic attacks together with significant impairment in functioning resulting from the attacks are diagnosed with panic disorder and represent approximately 1.7%–2.6% of the general population (3).

Despite the apparent low prevalence of panic disorder, it is a costly disorder—both emotionally and financially. Individuals with panic disorder report seven times more physician visits and more than twice as many work days lost than those in the general population. The economic cost for missed work has been estimated at $619.00 per full-time employee; medical expenses—beyond psychiatric visits—are approximately 2.5 times more for those with panic disorder than for those without panic disorder (4). Such patients often undergo numerous unnecessary and expensive medical tests (5). In addition to the economic cost, panic disorder and the occurrence of panic attacks are correlated with a high risk of substance abuse and suicide among patients with mood disorders (6–8).

**ASTHMA**

The symptoms of asthma are remarkably similar to those of panic disorder. Asthma symptoms include wheezing, shortness of breath, chest tightness, recurrent cough, congestion, as well as hyperventilation. Between 2 and 15 million adults in the United States have a diagnosis of asthma (9). Between 1980 and 1987, asthma prevalence rates increased 29%, while the death rate from asthma increased 31% (10). Like panic disorder, asthma also is a costly disorder. The total healthcare cost for asthma during 1985 was estimated at $4.0 billion (11).

**RELATIONSHIP OF ASTHMA TO PANIC DISORDER**

The study of panic disorder among asthmatics can contribute to improved medical outcome for this subgroup of patients. The adverse effects of panic and anxiety on the course and outcome of asthma add to the cost and suffering. These effects include more intensive steroid regimen prescriptions, more frequent hospital readmissions, and longer hospital stays (12–14). The number of shared symptoms (e.g., dyspnea, choking and smothering sensations, chest pain, etc.), however, makes diagnosing panic disorder in the presence of asthma a challenging task; but it is essential for optimum management of both illnesses (15). A study comparing panic attacks to asthma attacks determined that hyperventilation–hypocapnia were more commonly identified by subjects with panic disorder, whereas airway obstruction-related symptoms were more frequently endorsed for asthma attacks. Three symptoms that best differentiated the groups (i.e., sensitivity greater than 0.90 and specificity greater than 0.70) were wheezing, mucous congestion, and coughing, all being more characteristic of asthma attacks than panic attacks (16).

The diagnosis of panic disorder among asthma patients is difficult, and it is in part this reason that the vast majority of studies have studied panic symptoms, panic–fear, or state/trait anxiety among asthma patients, rather than the full-blown disorder. Nevertheless, because individuals with panic disorder display the highest levels of general anxiety symptoms relative to other anxiety disorders (17,18), it is reasonable to assume that many of the findings reviewed here with respect to high anxiety or high panic–fear will generalize to samples that comprise asthma patients with full-blown panic disorder. Restricting a comparison group of asthmatics to those with full-blown panic disorder would almost certainly accentuate group differences that have al-
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ready been observed between highly anxious asthmatics and their nonanxious counterparts. Still, the most productive strategy for best characterizing the debilitating effects of panic disorder on asthma morbidity, as well as for delineating the role of respiratory disease in panic disorder, is to study full-blown, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)-defined panic disorder in this population.

Given the unpredictable and life-threatening nature of a respiratory disease such as asthma, it is not surprising that the comorbidity of panic disorder and asthma is greater than would be expected based on their individual prevalence rates (19,20). This may be due in part to the important role of respiratory factors in panic disorder; to the aversive stimuli associated with asthma attacks, which can lead to anticipatory anxiety and phobic-like avoidance; or to some as yet unspecified facilitative process (21); or to all of these factors.

In a study by Carr (22), 22.6% of 93 asthmatic individuals reported having experienced panic attacks, and 9.7% reported panic attacks frequent enough to meet Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-IIIR) (23) criteria for panic disorder. Using structured clinical interviews, Yellowlees and his colleagues diagnosed panic disorder in 12% of an asthmatic sample (20). Shavitt and colleagues (21) reported a 13.1% point prevalence of agoraphobia using a structured interview in a sample of 107 asthmatic outpatients. In a study of the temporal relationship between these two disorders in 51 asthma patients, 90% of the asthmatics with panic disorder were diagnosed with asthma first. In addition, the morbidity risk for panic disorder in families of asthmatics with panic disorder (13.5%) was significantly higher than in families of asthmatics without evidence of panic (2%) (24). These rates are well above the 1.7-2.6% prevalence rates reported for the general population (3) and suggest that unpredictability—and at times uncontrollable—dyspnea is a significant etiologic factor in panic disorder, as suggested by Ley (25).

In contrast to the above, a study of a much larger sample size (n = 123) found the prevalence of panic disorder among asthmatic patients to be higher than in the general population, but similar to the rate observed in nonasthmatic medical patients (26).

RESPIRATORY DYSFUNCTION IN PANIC DISORDER

The majority of panic disorder patients experience breathing-related problems. Among panic sufferers, most of the diagnostic symptoms for a panic attack can be reproduced by hyperventilation (25,27,28) or by inhalations of carbon dioxide (29,30). Many theories of panic disorder consider hyperventilation and abnormalities in respiratory physiology to be paramount. For example, Gorman and colleagues suggested that respiratory drive in panic patients is controlled by abnormally sensitive carbon dioxide receptors in the central nervous system (CNS) (31). More recently, Klein argued that panickers possess an abnormal suffocation detector that processes asphyxia-related cues (32,33). According to Klein, hyperventilation among panic disorder sufferers is a result of the body’s adaptive attempts to reduce panicogenic carbon dioxide.

Ley initially proposed that panic attacks were a reaction to the perceived uncontrollability or unpredictability of the somatic effects of hyperventilation-induced hypocapnia (34). Ley’s revised dyspnea–fear theory attributes the fear experienced during what he classifies as hyperventilatory panic attacks to an “innate emotional–respiratory-response mechanism (25,27).” In contrast to Klein, Ley describes hyperventilation as a cause of some panic attacks. Rachman and colleagues also discussed the theoretical importance of dyspnea in panic disorder (35).

In addition to the panicogenic effects of voluntary hyperventilation and carbon dioxide inhalation among panic patients, further evidence of abnormal respiratory physiology in panic disorder comes from studies demonstrating higher respiratory rates and lower venous carbon dioxide in panic disorder patients relative either to nonpanic anxiety disorder patients or to normal controls (36). Moreover, a number of studies have documented acute
changes in pCO₂ (reflecting hyperventilation) during naturally occurring panic attacks (37–39). These findings suggest that biological factors, particularly those involving respiratory physiology, are central to the etiology of panic disorder. More recently, however, Bass argued that hyperventilation rarely accompanies panic, and that it is more likely to be a consequence than a cause of the panic. Bass also argues that “breathing therapy” works not by normalizing pCO₂, but by slowing respiratory rate (40).

There are several ways that factors specific to asthma may cause panic. These include hyperreactivity of CNS centers controlling respiratory drive, which can produce hyperventilation, as well as reactions to asthma medications. Adrenergic-agonist, theophylline, and steroid medications all have been implicated in provoking anxiety and other negative emotional states (41). Thus, a vicious cycle (42) may be initiated by asthma attacks, which can increase CO₂ because increased CO₂ can trigger a panic attack among certain individuals; and panic attacks can in turn exacerbate asthma via cooling of the airways (43).

Classical conditioning may also play an important role in the link between asthma and panic. Because some asthma attacks can be particularly severe and life-threatening, it may require only one such experience before mild sensations of dyspnea—through a process of classical conditioning—come to serve as reliable triggers (i.e., conditioned elicitors) of anxiety-induced hyperventilation and panic, which in turn may exacerbate asthma (44). A study from our laboratory (45) showed that anxiety was strongly related to verbal reports of bronchoconstriction (i.e., dyspnea), independent of actual airway changes. Such a discrepancy between verbal reports of dyspnea and objective pulmonary measures in eliciting fear may reflect stimulus generalization associated with the aforementioned process. That is, experiences with intense (and possibly life-threatening) bronchospasm can function as an unconditioned stimulus for fear, with the fear-response later elicited by more subtle, private, and transitory respiratory stimuli that are not grossly evident in pulmonary function tests. Similarly, in another study from our labora-

tory (46), the relationships among panic–fear, pulmonary function, trait anxiety, and dyspnea were examined in panic disorder patients, asthmatics, and nonpanic/nonasthmatic controls. Within-group regression analyses showed that dyspnea (i.e., verbal reports of breathing difficulties) was a significant predictor of panic–fear symptoms among asthmatics. Future research is needed to determine what specific personal and historical experiences contribute to the link between verbal reports of fear and of dyspnea. It may be a function of measurement source (i.e., verbal), or may indicate a personal history of life-threatening attacks. As will be discussed, panic measures are not associated with more severe asthma when severity is indexed by objective pulmonary impairment instead of self-reported dyspnea.

**PSYCHOLOGICAL EFFECTS OF ASTHMA**

In light of the high prevalence of panic among asthmatics, together with the strong correlation between reports of breathing difficulties and of panic, it would appear that respiratory difficulties in general, and symptoms of asthma in particular, can have a profound effect on the development of panic disorder. This relationship is more complex than it at first appears, however. For example, we had 86 asthmatics complete two measures of panic–fear (illness-specific panic–fear and generalized panic–fear), a measure of dyspnea frequency, and a measure of “catastrophic cognitions” about bodily symptoms (47). Several asthma variables (ratings of dyspnea frequency and pulmonary function test results) and several “cognitive” variables were grouped separately and used to predict the panic–fear measures. Hierarchical regression analyses showed that the cognitive variables predicted significant variance in both panic–fear scales after partialling out the effects of demographic and asthma variables. By contrast, the asthma variables were not associated with generalized panic–fear when the cognitive measures were statistically controlled.
Similarly, in a study of 93 asthmatics (22) anxiety sensitivity index (ASI) scores, but not pulmonary function, were significantly related to panic disorder. In that same study, we compared the asthmatics (with and without panic disorder) to 10 panic disorder subjects without asthma and to 32 nonanxious, nonasthmatic controls on the ASI, the Body Sensations Questionnaire, and the Agoraphobic Cognitions Questionnaire. Whereas subjects with panic disorder (asthmatic and nonasthmatic) displayed significant elevations on these measures compared to those without panic disorder, the presence of asthma alone had no effect. That is, asthmatic subjects (those without panic disorder) showed no greater concern about bodily sensations than did nonasthmatics. Thus, asthma is associated with a higher risk of panic attacks and panic symptoms, and asthma is associated with a real risk of life-threatening bronchoconstriction; but asthma alone is not associated with elevations in self-reported catastrophic cognitions, as might be predicted by cognitive models of panic (48).

**PHYSIOLOGICAL FINDINGS**

In a study of physiological and airway reactivity to psychologically stressful laboratory tasks, we obtained similar results (49). Using the forced oscillation technique, we assessed airway impedance responses to psychologically stressful laboratory tasks among 61 subjects with asthma only, 10 with asthma and panic disorder, 23 with panic disorder only, and 18 normal controls. As expected, asthma patients displayed higher airway impedance relative to nonasthmatics. Interestingly, those with DSM-IIIR (23)-diagnosed panic disorder had significantly lower airway impedance (i.e., better pulmonary function) relative to nonpanickers. This panic vs. no-panic group difference was found in the asthmatic group as well, indicating that the presence of asthma did not differentially affect this difference.

Another comparison of asthmatic patients with and without panic disorder found that baseline levels of forced expiratory volume at 1 sec (FEV<sub>1</sub>) and bronchial responsiveness to histamine were not significantly different. Although panic disorder patients reported significantly higher levels of perceived breathlessness during induced bronchoconstriction compared to matched controls, this was not associated with a significantly greater drop in FEV<sub>1</sub>. The authors concluded that the higher prevalence of panic disorder in asthma is non-specific and probably due to selection bias (26).

**DOES ASTHMA FACILITATE THE DEVELOPMENT OF PANIC DISORDER?**

The presence of asthma is a risk factor for the development of panic disorder. Among panic disorder patients, the presence of hyperventilation symptoms, the panicogenic effects of carbon dioxide, the high frequency of breathing-related complaints, together with the beneficial effects of breathing retraining techniques in this population (50,51) all underscore the essential role of respiratory disturbance in panic disorder. The nature of this role or the mechanism by which asthma contributes to the development of panic disorder, however, has not been delineated. Some have suggested that cognitive misinterpretations can explain this relationship (48). Cognitive theorists argue that panic measures are better predicted by cognitive measures than by objective pulmonary function test results (22,52).

Asthma is a disease that can present an individual with numerous triggers, such as shortness of breath, choking sensations, and chest pain, all of which can be "catastrophically" interpreted. This would seem to explain the increased likelihood of panic attacks in this population. The problem with the cognitive model is that one might expect asthma severity to be highly predictive of panic, because more severe asthma would present a given individual with a greater frequency of somatic symptoms (relative to an asthmatic person with less severe asthma) that would then be subject to misinterpretation. By contrast, our research found that panic disorder is associated with better, not worse, pulmonary function (49). Still, asthma can be highly variable and unpre-
dictable, rendering the meaning of pulmonary function tests or forced oscillation results obtained during any single laboratory session difficult to interpret. Further, the cognitive measures in these studies are not being measured during the panic episodes.

Another weakness of cognitive explanations is that causal inferences are being drawn from correlational designs. Self-reports of “cognitions” are correlated with self-reports of panic attacks, with catastrophic cognitions interpreted as causing panic (48). What remains to be explained, however, are the external events (independent variables) that cause verbal reports of both panic and catastrophic thoughts (an environment-behavior relationship). It is also necessary to delineate the experiences contributing to the development of the correlation between catastrophic thinking and panic attacks (a behavior-behavior relationship).

HOW PANIC EFFECTS ASTHMA

The vast majority of studies have examined measures of panic-fear or state/trait anxiety, rather than of full-blown panic disorder. Two types of panic-fear have been delineated in the literature: panic-fear in response to the symptoms of asthma, termed illness-specific panic-fear and measured by the Asthma Symptom Checklist (53), and a more generalized panic-fear (derived from the Minnesota Multiphasic Personality Inventory [MMPI]), which is believed to reflect a stable personality trait (54). The effects of both types of panic-fear on the course of asthma are significant. They include more intensive steroid regimen prescriptions, excessive use of as-needed medication, more frequent hospital readmissions, and longer hospitalizations (53,55–57). These effects are generally independent of objectively measured pulmonary impairment.

It has been suggested that some illness-specific panic-fear is a good thing, serving as a call for action on the part of the asthma patient (53). Patients reporting low illness-specific panic-fear may ignore early warning signs of a symptom flare-up, which can lead to hospitalization when preventive action could have been taken (58). Extremely high illness-specific panic-fear, however, often leads to overuse of as-needed medication, and is associated with maladaptive and disruptive anxiety during an asthma attack (59,60). Also, as Kinsman and colleagues indicated, high illness-specific panic-fear can lead to hyperventilation-induced asthma exacerbations because of rapid breathing associated with the fear response (60).

Both high and low generalized panic-fear (MMPI panic-fear) are maladaptive to the course of asthma (57,61). Patients with low MMPI panic-fear are similar in their coping to those with low illness-specific panic-fear: they minimize their symptoms and are reluctant to use preventive medication (55). High MMPI panic-fear is characterized by high anxiety, helplessness, and dependence in response to a variety of situations beyond those just related to breathing difficulties (60). Furthermore, high MMPI panic-fear is associated with worse medical outcome for asthmatics, including longer and more frequent hospitalizations. MMPI panic-fear scores are independent of objective medical indicators and highly stable across several months of intensive inpatient medical treatment (55,61). Kolbe and colleagues found that serious management errors in acute severe asthma are common and that most of these errors relate to patient self-management behavior (62). Serious errors included delayed or nonsummoning of emergency ambulance services because of panic during the index attack.

There is also evidence that asthmatics who show the greatest autonomic reactivity (as might be expected among asthmatics who experience panic attacks), indexed by blood pressure, electromyogram (EMG) activity, and finger pulse amplitude, also show the greatest airway reactivity in response to psychological stress (e.g., bogus suggestions that the individual is inhaling a potent bronchoconstrictor) (63). Thus, panic disorder may directly contribute to increased asthma morbidity by the responsiveness of such individuals to emotional triggers. Moreover, the medications most often used to treat anxiety and panic (i.e., benzodiazepines) can worsen pulmonary function (64). In a study on the role of panic
attacks in asthmatic children, however, the investigators observed improvements in asthma and reductions in asthma medications subsequent to the treatment of panic attacks by alprazolam and by cognitive therapy in more than 20 patients (42).

The studies described here reflect how panic and anxiety can adversely influence asthma directly through the effects of panic symptoms (e.g., hyperventilation), and indirectly through patient behavior (e.g., overuse of medications, self-management behavior). Interestingly, panic–fear reactions and anxiety in the asthma patient have also been found to influence the behavior of the physician. In one study, prescription decisions of physicians rated high in “sensitivity” were significantly influenced by the asthma patient’s level of panic–fear (53). In a more recent study of 42 adult asthmatics, panic–fear accounted for 25% of the variance in steroid prescribing among all physicians in an asthma outpatient clinic (65). Whereas Kinsman’s study (53) found that objective pulmonary measures also contributed significantly to predicting physician prescription behavior, this more recent study found no relationship between pulmonary function performance (FEV1, peak flow; and forced vital capacity) and prescription decisions (65). The relationship between patient behavior and physician prescription writing exists even among asthmatic children. In a study of 34 asthmatics ages 9–15 years, steroid prescriptions were significantly associated with the child’s panic–fear score but not with clinical status or asthma severity, defined as the number of episodes in the past year (66).

In summary, panic and anxiety can directly exacerbate asthma symptoms through hyperventilation, and are associated with an overuse of as-needed asthma medications, with more frequent hospital admissions and longer hospital stays, and with more frequent steroid treatment, all of which are independent of degree of objective pulmonary impairment.

The correlation between high panic–fear—as measured by the Asthma Symptom Checklist—and a diagnosis of panic disorder (22), together with the relationship between panic–fear and asthma morbidity, is suggestive of the detrimental effects of panic disorder on asthma. There remains, however, little research examining full-blown panic disorder in this population. Basic research on individuals comorbid for panic disorder and asthma is sorely needed. We know that panic–fear measures are associated with poor asthma outcome. But what effect does full-blown panic disorder have on the short- and long-term course of asthma? In a detailed examination of the antecedents of 406 asthma attacks among nine individuals, Knapp and Nemetz identified “fear of having an asthma attack” as a commonly occurring trigger of asthma attacks (67). The fear of asthma attacks possibly reflects a classically conditioned response to subtle respiratory sensations as described earlier, and it is remarkably similar to the vicious cycle described among panickers, who develop anticipatory anxiety in response to a variety of innocuous bodily sensations (including those associated with anticipatory anxiety itself). Thus, interventions developed for treating panic disorder might also serve to improve asthma outcome in asthmatics suffering from panic attacks. To date, however, no studies have examined the treatment of panic disorder among individuals with asthma. This represents a major gap in the literature.

A central component in the treatment of panic attacks is exposure, both to external situations or activities and to internal physiological sensations (51). It is unknown at present if exposure can be safely conducted with panic patients who also have asthma, or whether exposure to asthma triggers can be included. A number of studies examined the effects of systematic desensitization and of progressive muscle relaxation for patients with asthma (68,69). Unfortunately, most of these studies focused predominantly on pulmonary outcome variables—where the outcome appears to be rather equivocal for relaxation techniques—rather than on anxiety and panic measures (70).

Although high anxiety and the presence of panic appear to be correlated with poor asthma outcome, Kinsman and colleagues warned against the assumption that anxiety reduction in asthma is universally warranted (71). Not all asthmatics respond to anxiety with airway obstruction. This was clearly
demonstrated by a study from our laboratory, which demonstrated an improvement in pulmonary function in response to psychological stress (49). Several studies of airway reactivity to psychological stress demonstrated that some asthmatic individuals (particularly those with labile airways) respond with bronchoconstriction (63). This airway response was even more pronounced among those who displayed the most autonomic reactivity to the psychological stressors. Thus, Kinsman suggested that outcome studies of this subgroup might show better response to anxiety management relative to outcome studies that include all asthmatics. Whatever the anxiety management might involve, it should be emphasized that early detection of panic disorder among asthma patients is crucial, because this may decrease additional morbidity caused by the comorbidity of panic and asthma (21).

Another consideration in the treatment of anxiety among asthmatics, as Kinsman indicated, is that some degree of anxiety about breathing difficulties is adaptive. Among medically healthy panic sufferers, a good deal of treatment focuses on disputing “catastrophic interpretations” of bodily sensations, such as dyspnea and chest pain (48). However, research has shown that asthmatic individuals with significantly low levels of panic-fear display inadequate medication management, which can often lead to high rates of rehospitalization (72). Thus, healthcare providers who are treating asthma in the context of panic disorder need to train patients to discriminate effectively between asthma-related and anxiety-related somatic symptoms.

CONCLUSION

The presence of airways disease appears to contribute significantly to the risk of developing panic disorder. The presence of high anxiety and panic-fear adversely affect the course of asthma, leading to higher hospitalization rates, longer hospital stays, more intensive medication regimens, and excessive use of as-needed medication. It is essential that clinical researchers examine (a) what那些 anxiety reduction procedures should include; (b) which asthmatic patients should be treated; and (d) how treatment of panic disorder affects asthma medication usage, emergency visits, and hospitalizations.

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