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From Relias

Issues Relevant to Treating Patients with Anxiety Disorders in the Emergency Department

"The suspense: the fearful, acute suspense … the racking thoughts that crowd upon the mind, and make the heart beat violently, and the breath come thick, by the force of the images they conjure up before it; the desperate anxiety to be doing some¬thing to relieve the pain, or lessen the danger, which we have no power to alleviate; the sinking of soul and spirit, which the sad remembrance of our helplessness pro¬duces; what tortures can equal these; what reflections of endeavours can, in the full tide and fever of the time, allay them!"

— *Charles Dickens,* Oliver Twist, *1838*

Anxiety disorders are the most prevalent mental health problem worldwide. As practicing emergency physicians know, anxiety is common in emergency department (ED) patients. Abar and colleagues, using a convenience sample of adult ED patients aged 45 to 85 years, observed that 10% demonstrated severe anxiety on a validated screening questionnaire.[1] Dark and colleagues analyzed the 2009-2011 National Hospital Ambulatory Medical Care Survey to identify that anxiety was the primary reason for about 1% of ED visits.[2]

Untreated anxiety is associated with psychosocial and occupational impairment and is a risk factor for developing other mental health disorders and suicide. Early and appropriate intervention is key to modulating these outcomes.[3,4]

The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) delineates specific diagnostic criteria for each disorder contained under the general umbrella of anxiety disorders. These include generalized anxiety disorder (GAD), social anxiety disorder (SAnD), panic disorder (PD), specific phobias, agoraphobia, separation anxiety disorder, anxiety disorder unspecified, selective mutism, substance/medication-induced anxiety disorder, and anxiety disorder due to another medical condition.[5]

Close to 30% of the U.S. adult population will experience at least one of these conditions at some point in a lifetime.[6] However, before viewing anxiety as a disorder, it is useful to reflect that anxiety is a universally experienced human emotion. References to this state appear throughout human history, with pictographs, mythology, and primitive writings depicting anxiety and associated states. The term, derived from the Germanic "angh" (to narrow or constrict) with echoes in the archaic Greek term "anchein" (to strangle or suffocate), illustrates an early

EXECUTIVE SUMMARY

- Anxiety disorders are the most prevalent mental health problem worldwide.
- The diagnosis may be complicated, since patients often delay seeking treatment until the development of somatic symptoms. More than one-third of patients turn to self-medication and more than 80% have a comorbid diagnosis, such as major depressive disorder.
- The typical course is chronic and persistent, with complete remission in only about 20% of patients at five years.
- The Generalized Anxiety Disorder-7, a seven-item questionnaire, is the most commonly used screen, with a score of 8 or greater calling for further evaluation.
- Treatment includes self-help groups, cognitive behavioral psychotherapy, and psychopharmaceuticals.
- Medications typically include selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, buspirone, tricyclic antidepressants, gamma aminobutyric acid agonists, and benzodiazepines. The use of cannabidiol is controversial.
- Panic disorder and social anxiety disorder have specific diagnostic criteria requiring more targeted therapeutic approaches.

understanding of the association of anxiety with tightness and/or constriction in the chest or throat — a phenomenon still recognized today as part of an anxiety response.[7]

Interestingly, anxiety often is adaptive, assisting in sending signals of approaching danger and helping mobilize focus and necessary energy. Anxiety can be appropriately associated with avoidant behavior or other compensatory strategies, all of which may help an individual function at optimal levels.

But if an anxiety response begins to interfere, rather than assist, with a desired level of functioning, the concept of a disorder becomes relevant. The majority of patients with disorders of anxiety frequently seek care presenting with somatic symptoms, such as insomnia, chest pain, or gastrointestinal complaints. In many cases, the perception of anxiety is "masked" by such symptoms; a comprehensive history, physical examination, and appropriate medical workup are critical to accurate diagnosis and appropriate treatment.[3,4,6]

Treatment for anxiety disorders involves psychotherapy and/or psychopharmaceuticals, with medical investigations demonstrating similar overall efficacy for each approach.[3,4,6] This article reviews three common disorders of anxiety — generalized anxiety disorder, panic disorder, and social anxiety disorder — with a focus on issues relevant to when these patients are seen in the ED.

Generalized Anxiety Disorder

A 45-year-old retail worker and separated mother of a young teen, with no chronic medical conditions, presents with insomnia and daytime fatigue worsening over the last year, and frequent headaches and forgetfulness starting about two months ago. She notes that her work performance is slipping, and that she has less patience at home, stating, "Now that I have a teenager, there's more to worry about." She explains that she also is worried "something is wrong with me … maybe I have a brain tumor?" She is asking about medication for sleep.

GAD is a chronic disorder of anxiety with progression of symptoms over time. Hallmarks of this disorder are:

• excessive worry about a variety of events or topics; the worry is experienced as being difficult or unable to be controlled, for at least six months;

• three or more of the following symptoms (only one symptom in children is needed to diagnose): restlessness/feeling on edge, easy fatigue, concentration difficulty, irritability, muscle tension, sleep disturbance;

• an impairment in functioning related to the worry and/or somatic symptoms;

• the symptoms are not better explained by another medical problem, mental illness, or substance use.[8]

The diagnosis of GAD may be complicated, since patients often delay seeking treatment or medical advice until somatic symptoms emerge. Additionally, more than one-third of these patients will turn to self-medication (drugs and/or alcohol) for symptom management, and more than 80% will have a comorbid diagnosis, such as major depressive disorder or another anxiety disorder. A careful history with an accurate time line often is critical in diagnosis and appropriate treatment focus.[9]

Epidemiology

GAD has a worldwide lifetime prevalence of 3.7%, with higher prevalence in higher-income countries (4.1% lifetime prevalence in the United States), and occurring with greater frequency in middle-aged, widowed, or divorced women. The typical course is chronic and persistent. Symptom management and functional improvement are the main goals of treatment. Studies show complete remission occurs in only about 20% of patients at the five-year mark.[9-11]

Genetics play a role in the expression of most mental illnesses; GAD is not an exception. Twin studies indicate heritability influences about 31% of emergence, with psychosocial and other environmental factors affecting the remaining portion. There is an overlap of heritability with separation anxiety disorder, PD, and the phobias. Research in pharmacogenetics points to a promising role in identifying genetic

Table 1. GAD-7 Anxiety

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3
Column totals	___ +	___+	___ +	___ =
			Total score	_____

Source: Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

Scoring GAD-7 Anxiety Severity
This is calculated by assigning scores of 0,1,2, and 3 to the response categories, respectively, of "not at all," "several days," "more than half the days," and "nearly every day." GAD-7 total score for the seven items ranges from 0 to 21.
0-4: minimal anxiety
5-9: mild anxiety
10-14: moderate anxiety
15-21: severe anxiety

factors predictive of a response to selective serotonin reuptake inhibitors (SSRIs).[12]

Differential Diagnosis and Screening Tools

A comprehensive history, employing nonjudgmental interview techniques with open-ended questions, is key to accurate diagnosis and treatment. Screens are useful in pointing an interview toward a specific direction but are not to be used as a stand-alone diagnostic tool.[9-11]

As with most anxiety disorders, checking for medical disorders that may exacerbate or mimic anxiety symptoms is an important component of the initial workup. Thyroid disease, vascular disease, disorders causing dysregulation of blood glucose, withdrawal from pharmaceuticals (including antidepressants and antianxiety agents) and withdrawal from substances of abuse (including caffeine) are among the differential. Check for subtle signs suggestive of neurological dysfunction, especially in the elderly presenting with cognitive impairment.[13]

Common medications that may cause or worsen anxiety include analgesics, antihypertensives, anticholinergics, antihistamines, levodopa, SSRIs, opioids, and muscle relaxants. A careful history examining the temporal relationship between the onset or worsening of anxiety symptoms and starting/stopping medication is helpful in elucidating such a relationship.[9-11,13] Check also for comorbid substance use or abuse, since this will have implications for the direction of treatment.[9-11,13]

The Generalized Anxiety Disorder-7 (GAD-7), a seven-item questionnaire, is among the most commonly used screens for GAD. (*See Table 1.*) This screen is completed by the patient or can be administered by a social worker or mental health counselor. The maximum score on the GAD-7 is 21. In general, a score of 8 or higher should lead to further evaluation for anxiety and a score of 15 or higher is indicative of severe anxiety. The final item on the GAD-7 asks for a subjective evaluation of level of functioning. Although this item is not used for scoring, it is useful for following a response to treatment over time.[14,15] Another general method to screen patients for GAD is simply to ask, "How often do you worry too much about minor matters?"

Treatment

Guidelines for the prevention and treatment of anxiety disorders are based on the "stepped care" model, starting with the least intensive intervention for mild symptoms and

Table 2. SSRI/SNRI Recommended Doses for GAD, PD, and SAnD[4,13,25]

Medication	Drug Class	Dose Range	First-Line?	FDA-Approved for GAD?	FDA-Approved for PD?	FDA-Approved for SAnD?
Paroxetine (Paxil, Pexeva)	SSRI	10 mg to 50 mg (start low; advise against sudden discontinuation)	Yes	Yes	Yes	Yes
Sertraline (Zoloft)	SSRI	50 mg to 200 mg (start as low as 25 mg)	Yes	No*	Yes	Yes
Escitalopram (Lexapro)	SSRI	5 mg to 20 mg (start low)	Yes	Yes	No	No
Citalopram (Celexa)	SSRI	10 mg to 40 mg (start at 10 mg)	Yes	No	No	No
Fluoxetine (Prozac)	SSRI	10 mg to 60 mg (start low; long half-life: low potential for withdrawal)	Yes	No	Yes	No
Fluvoxamine CR (Luvox CR)	SSRI	100 mg to 300 mg per day, divided doses	Yes	No	No	Yes
Duloxetine (Cymbalta, Drizalma)	SNRI	60 mg to 120 mg (start at 30 mg)	Yes	Yes	No	No
Venlafaxine XR (Effexor XR)	SNRI	75 mg to 225 mg (start at 37.5 mg)	Yes	Yes	Yes	Yes

SSRI: selective serotonin reuptake inhibitor; SNRI: serotonin-norepinephrine reuptake inhibitor; GAD: generalized anxiety disorder; PD: panic disorder; SAnD: social anxiety disorder; FDA: Food and Drug Administration

*Supported by large clinical trials

only progressing to further treatment if clinically indicated. Most stepped care models for GAD start with "watchful waiting," including frequent re-evaluation and self-monitoring while improving lifestyle factors (exercise and diet, for example) that are affecting symptoms.

If there is no clinical improvement, the next step typically is a referral to a self-help group or internet-based cognitive behavioral psychotherapy (CBT). If there still is an inadequate response, psychopharmaceuticals and/ or more intensive psychotherapy — in part, depending on patient preference — are recommended. The final step in the sequence, if there remains a poor response, is referral to a specialist.[16]

Medication and/or Psychotherapy

The literature is mixed regarding the relative efficacy of psychopharmacological vs. psychotherapeutic treatments in GAD; level of functional impairment, factors such as age and comorbidities, and methodological variations of relevant studies complicate drawing firm conclusions from meta-analysis.[9-11,13]

Multiple studies show that psychotherapy — specifically CBT — and medication — specifically SSRIs or serotonin-norepinephrine reuptake inhibitors (SNRIs) — are more effective than placebo in the treatment of GAD.[17,18] Recent investigations suggest a combination of these modalities is more efficacious than either intervention alone, with a larger effect size and better overall outcomes.[9-11,13]

Psychotherapy

CBT is a type of talk therapy that generally involves specific mental exercises (introduced during sessions and practiced at home) designed to recognize and change dysfunctional thinking patterns and unhelpful behaviors. CBT is based on moving forward and emphasizes developing effective coping skills. Access to high-quality CBT is a major stumbling block to the use of this treatment.

Medication

First-line medications used in the treatment of GAD are SSRIs, followed by SNRIs. Large clinical trials point to the effectiveness of

the SSRIs paroxetine, escitalopram, and sertraline, and the SNRIs venlafaxine and duloxetine. Table 2 displays typical dose ranges.[13,17]

When these agents are used for the treatment of anxiety, they are started at a low dose to avoid jitteriness. The dose is slowly increased and the full clinical response may take four to six weeks.[13,17]

Typically, SSRIs and SNRIs are well tolerated. However, serious side effects include emergence of suicidal thinking (especially in teens and young adults); inform patients to monitor thoughts and report any unusual thought patterns. Other adverse effects are syndrome of inappropriate antidiuretic hormone secretion, decreased libido, and sexual side effects.[13,17]

A 2010 Cochrane review of the antihistamine hydroxyzine found this agent (dosed from 50 mg to 200 mg daily) is more effective in reducing anxiety than placebo, but a lack of robust studies and bias in studies are barriers to recommending first-line use of hydroxyzine for GAD.[19]

Quetiapine is a sedating atypical antipsychotic that may be used alone or in combination with a first-line medication for GAD. Side effects include sedation, significant weight gain, and the potential for metabolic syndrome.[17,20]

Tricyclic antidepressants (TCAs) may be used as an alternative treatment when other options fail or there are specific medical contraindications to first-line agents. TCAs are antidepressants burdened with anticholinergic and antihistaminic side effects and potential for lethality in overdose.[20]

Gamma aminobutyric acid agonists (GABA-A) include benzodiazepines and some anticonvulsants with GABAergic properties, such as pregabalin and gabapentin.[17,20] Pregabalin is approved in Europe (but not in the United States) for treatment of GAD. Pregabalin is administered in divided doses from up to 600 mg per day, and seems to have a one- to two-week lag period before evidence of clinical response. Pregabalin is a Schedule V (controlled substance with low potential for abuse) drug in the United States.[21] Gabapentin also is used off-label for anxiety, but research evidence supporting this indication is extremely limited.[21]

Benzodiazepines are commonly prescribed sedative-hypnotic agents and are acutely effective in reducing the somatic symptoms associated with GAD. However, the potential of abuse, dependence, and withdrawal, and the lack of long-term efficacy, make benzodiazepines a poor choice for most patients with GAD. It is recommended to use this class of medication only for patients presenting with severe, disabling anxiety and/or insomnia, to monitor use carefully, and to overlap with a first-line treatment (such as an SSRI) and/or buspirone.

Clinical Pearls for Generalized Anxiety Disorder

- GAD is the most common of the anxiety disorders.
- It has chronic and persistent symptoms.
- It often presents with somatic symptoms.
- The highest prevalence in middle-aged females (widowed or divorced).
- Treatment is aimed toward areas of functional impairment.
- CBT has established evidence of efficacy.
- SSRIs or SNRIs are used for first-line medication starting at low doses.
- There is a limited role for benzodiazepines.

Panic Disorder

A 22-year-old graduate student presents to the emergency room with acute onset severe chest pain, palpitations, dizziness, and a choking sensation. "I thought I was dying," he says. An electrocardiogram is without abnormalities, his blood work (including a toxicology screen) is unremarkable, and his symptoms responded to 1 mg intravenous lorazepam within minutes. He tells you this was his most severe episode, but that he has had similar experiences about weekly since moving to begin graduate school about one year ago. "I like it here," he notes, "but I do not like being so far from my family."

PD is characterized by unexpected panic attacks, associated with at least four of the following symptoms:

- palpitations, pounding heart, or rapid heart rate;
- sweating;
- trembling/shaking;
- feeling of choking;
- chest pain or discomfort;
- nausea or abdominal distress;
- feeling dizzy/unsteady/lightheaded;
- sensations of chills or heat flashes;
- numbness or tingling;
- feelings of unreality (derealization) or feeling detached (depersonalization);
- fear of losing control or "going crazy."

In addition, panic attacks are usually followed by one month or more of persistent fear of a recurrent panic episode and/or a maladaptive change in behavior related to the panic episodes.[22]

Often, a first panic episode will occur in response to an acute stressor, but subsequent events are spontaneous and without clear precipitants. The natural course of PD is episodic and relapsing, with recent studies indicating about one-third of patients will experience a recurrence within one year of remission.[23]

Epidemiology

The lifetime prevalence of PD is 5%, with occurrence in females about twice as often as in males.

The mean age of onset is younger than for GAD and typically occurs in early adulthood. Notably, PD tends to be comorbid with other disorders of mental health, including the other anxiety disorders, depressive disorders, and substance abuse.[23]

Genetic studies suggest that 30% to 40% of disease emergence is attributable to hereditary factors, while environment accounts for

the remainder. Research suggests that early experiences with abuse, medical illness, or other factors that affect attachment may cause a psychologic vulnerability that can be triggered by events later in life. The theory is that full expression of PD occurs in those individuals with both psychologic and biologic or genetic vulnerability.[23,24]

Differential Diagnosis and Screening Tools

The key feature of PD is unexpected, recurrent panic episodes. Although panic attacks may occur in the setting of other disorders of mental health, if the episodes are predictable and/or in response to an identified stressor, the diagnosis is unlikely to be PD.[23,25]

Note that 80% to 90% of patients with PD have comorbidities, and that the majority of these involve another mental illness. In other words, a patient may have symptoms of both GAD and PD or PD and major depression. Understanding how to differentiate these allows more precise targeting of treatment.[23,25]

Medical problems, such as thyroid dysfunction (hypo or hyper), pheochromocytoma, mitral valve prolapse, vestibular nerve disease, and substance-induced panic, all should be considered. Potential cardiac symptoms will need an appropriate cardiac workup.[23,25]

The GAD-7 does not measure PD, since there are no questions pertaining specifically to panic on this screen. A screen such as the Panic Disorder Severity Scale (PDSS) is a seven-item validated tool to measure and track the degree of impairment in individuals with PD. The maximum score is 28, with higher scores indicating more self-assessed impairment from symptoms related to PD.[26] When used for screening, a score of 9 or higher suggests the need for formal assessment.

Treatment

The initial treatment strategy for PD is aimed at interrupting the cycle of acute panic episodes. In this regard, and because of the highly episodic nature of panic attacks, treatment is very different than for the other disorders of anxiety, most of which are characterized by chronic and persistent symptoms.[23,25] As with the other disorders of anxiety, a combination of CBT and psychopharmacological interventions appears to have the largest effect on symptom reduction as compared to either intervention in isolation.

Acute Panic

A benzodiazepine is the agent of choice for acute panic and for stopping progression. These agents need to be used with caution and with proper patient education regarding dependence, tolerance, cognitive dulling, the potential for rebound anxiety, and withdrawal. In general, the use of benzodiazepines in PD is best reserved for the acute phase, with plans to phase out after allowing an SSRI or SNRI to gain full clinical strength. Ideally, a two- to four-week course of these agents while the SSRI or SNRI is initiated, followed by a gradual taper, is recommended.[27,28]

There are several choices of benzodiazepines. Often, clonazepam is chosen for PD because of a relatively long half-life and the low potential for rebound anxiety. In the elderly, alprazolam may be preferred because of a short half-life and the lack of active metabolites. In all patients, advise of the potential for sedation and cognitive impairment associated with this class of drugs. Warn that operating machinery and driving are not recommended after use.[27-29]

Although there is no evidence from clinical trials, hydroxyzine (typically 25 mg to 50 mg taken as needed for acute panic) is Food and Drug Administration-approved for anxiety in general and often is used in this population as an alternative to benzodiazepines. Other options are buspirone and risperidone.[27-29]

Long-Term Treatment

As noted earlier, starting an SSRI or SNRI in conjunction with a benzodiazepine often is an effective treatment strategy in PD. Large-scale efficacy studies confirming usefulness in PD are available for sertraline, paroxetine, and venlafaxine; there are suggestive positive results from studies of the other SSRIs as well. As with all anxiety disorders, starting any of these drugs at a low dose is essential to prevent the agitation and increased anxiety associated with starting at higher doses. A clinical response may be seen in a few weeks but may not be fully expressed until two to three months. Tracking symptoms and the frequency of panic episodes is useful to gauge clinical improvement or response over an extended time.[23,25]

Typically, these medications can be discontinued gradually after one to two years of treatment. However, building in strategies to recognize and control panic is central to maintaining remission.[23,25]

Psychotherapy

About 30% of patients with PD prefer nonpharmaceutical interventions to address symptoms. CBT shows efficacy in treatment of this disorder. Studies comparing CBT vs. pharmaceutical agents have yielded mixed results, but a large meta-analysis published in 2015 found a greater effect on symptom reduction from medication alone than from CBT.[30] However, there are limitations to this work and conclusions, making generalization difficult.

The goal of CBT in PD is to teach alternative ways of reacting to the feelings that accompany or presage a panic attack.[30,31] Given that there are physical sensations linked to anxiety during a panic episode, individuals can learn to use these sensations as cues and react in a new way.[30-32] Traditional CBT involves six to 12 weekly sessions. Recent studies evaluating intensive short-term therapy and exploring remote delivery of CBT show promise. However, it is notable that about 50% of patients are unable to obtain full remission with CBT alone.[31-33]

Current studies investigating several variants of CBT (panic-focused CBT and acceptance and commitment CBT) aim toward identifying patient populations most likely to respond to each distinct psychotherapeutic treatment modality.[32,33]

Clinical Pearls for Panic Disorder

- It is the second most common anxiety disorder presenting to PCP (after GAD).
- It typically presents during adolescence or early adulthood.
- Episodic and recurrent panic episodes are associated with somatic symptoms and often a sensation of being unable to breathe.
- Treatment is biphasic and initially aimed at acute relief.
- Benzodiazepines may be used with caution during acute treatment while waiting for clinical effect of first-line agents (SSRIs or SNRIs).
- Start low and go slow for SSRIs, SNRIs, or TCAs to avoid jitteriness and agitation seen with starting at higher doses.
- The efficacy of CBT is established; be familiar with options for CBT and variations of this therapeutic technique to provide patients with referral information.

Social Anxiety Disorder

You are talking a with a friend from college, a 35-year-old single professional. She tells you, "I know 2020 was a hard year for most people, but I have never felt better!" She explains that the reduced in-person expectations for work and social situations lessened her anxiety enough that she stopped her medication for anxiety. "I am more productive than ever. I exercise and read in my spare time, I stopped all alcohol and caffeine, and I finally am sleeping well," she notes. "However," she adds, "now I may have to return to in-person work and I am considering asking my doctor for a letter certifying that I should continue remote work because of my anxiety."

Social anxiety disorder (SAnD) is characterized by the manifestation of severe symptoms of anxiety when faced with a need for interaction or socialization. The DSM-5 criteria for SAnD include:

- "marked fear or anxiety" when an individual is exposed to possible scrutiny by others;
- fears that the individual will "act in a way or show anxiety symptoms" that others will evaluate negatively;
- most any situation where there is social anxiety provokes anxiety response — often socialization is avoided;
- anxiety that is out of proportion to any stimulus and has been occurring for more than six months;
- an anxiety response that causes dysfunction or significant distress;
- symptoms that are not better explained by the use of a substance, another disorder of mental health, or a medical condition.[34]

SAnD naturally runs a chronic and unremitting course. SAnD can be viewed on a continuum from shyness to seasonal affective disorder, with functional impairment as a critical distinguishing factor.[35]

Epidemiology

Social anxiety disorder is a common disorder with a worldwide overall lifetime prevalence of 4.0% and with higher prevalence in higher-income countries.[36] In the United States, the lifetime prevalence is 8% to 12%.

These numbers may underestimate the prevalence, since social anxiety per se typically is not the impetus for a visit to a medical provider. Often, the diagnosis is made after many years of progressive isolation, or when the status quo is unable to be maintained.[36,37]

Typically, signs and symptoms emerge in early adolescence (mean age of onset of 14.1 years). Girls are affected more commonly than boys. There is a high chance of comorbid mood and depressive disorders. In addition, substance abuse is high in those with untreated SAnD, with up to 48% of patients with SAnD developing alcohol abuse during a lifetime.[35-37]

Although there is no known inheritance pattern, parental depression or anxiety is a risk factor for the development of SAnD in offspring. Other risk factors include parental overprotection and child abuse.

Differential Diagnosis and Screening Tools

The differential involves mainly other disorders of mental health, including depressive disorder (with social withdrawal), avoidant personality disorder, schizoid personality disorder, and prodromal or early signs of schizophrenia with social avoidance or paranoia.[35,37]

There are screening tools to assess the degree of impairment from symptoms of SAnD. Perhaps the most widely used and well-validated screening tool is the Liebowitz Social Anxiety Scale (LSAS). This questionnaire asks the patient to rate both their degree of anxiety and practice of avoidance associated with 24 different social situations. Potential scores on the LSAS range from 0 to 144, with scores 50-65 indicative moderate social phobia, 65-80 indicative of marked social phobia, 80-95 indicative of severe social phobia, and > 95 indicating very severe social phobia.[38]

Treatment

As with the other disorders of anxiety discussed earlier, there is evidence for both psychopharmacologic and psychotherapeutic interventions to treat SAnD. The evidence is stronger toward CBT, with psychopharmacology reserved for those who refuse therapy.

CBT generally is conducted in 12 to 16 weekly hour-long sessions, with response often seen by week 6. The specific psychotherapeutic focus for SAnD includes a combination of social skills training, exposure therapy, and recognizing and correcting cognitive distortions.[39] There is strong evidence supporting CBT in the treatment of SAnD, in prevention of functional deterioration, and in supporting remission, with response rates hovering around 70%.

The FDA-approved medications for SAnD are paroxetine, sertraline, extended-release venlafaxine, and extended-release fluvoxamine. A

2017 Cochrane review points to low to moderate evidence suggesting that 50% to 75% of patients with SAnD will respond to medication alone, that initial response may be delayed until week 12, and that the risk of relapse is high if medication is discontinued within the first five months of treatment. Treatment should continue for at least one year from symptom remission and then the dose should be tapered gradually.[40-42]

Second-line agents include a limited role for benzodiazepines and the potential for propranolol. This beta-blocker may be useful for specific forms of SAnD, especially related to performance and especially if tremor is part of a target symptom. Typically, 10 mg taken one hour before an anticipated anxiety-provoking event aids with symptom control.[42]

There is limited evidence for a role for the atypical antipsychotics in SAnD, but some promising emerging studies are looking at gabapentin and pregabalin for use in this disorder when other options have failed.[42]

Clinical Pearls for Social Anxiety Disorder

- SAnD is a common disorder.
- It emerges in early adolescence and more often affects girls vs. boys.
- It is highly comorbid with depression, mood disorders, and/or substance abuse.
- The response rate is about 70% with either SSRIs/SNRIs or CBT focused on social skills and exposure training.

Cannabinoids in the Treatment of Anxiety Disorders

Cannabinoids include at least 66 compounds found in the cannabis plant. Perhaps the two most well-known of these compounds are tetrahydrocannabinol (THC) — the main psychoactive compound — and cannabidiol (CBD) — a nonpsychoactive agent. Although popular sentiment may lean toward using these substances for relief of anxiety, high-quality medical studies regarding the treatment of anxiety with cannabinoids are lacking. There is some limited evidence for efficacy of CBD in the treatment of GAD, PD, and SAnD and no indication that CBD increases anxiety. However, there is evidence that THC may worsen anxiety, especially as the dose is increased.[42,43]

Kava

Kava, an extract derived from the roots of a South Pacific plant, is perhaps the most studied herbal preparation for anxiety and currently is used for anxiety relief in many parts of the world. This compound appears to modulate GABA-A receptors in a manner similar to benzodiazepines. A 2003 Cochrane meta-analysis noted beneficial effects of kava on anxiety, while more recent investigations are less positive and note insufficient evidence to recommend kava in the treatment of anxiety. Kava is linked to a potential for liver toxicity; this serious side effect is noted in all of the studies.[42]

Physical Activity

A recent meta-analysis found that high-intensity exercise may have a beneficial role in alleviating symptoms of anxiety, particularly in patients with symptoms below the threshold of a DSM-5 diagnosis. In addition, there appears to be an inverse association between the level of physical activity and anxiety disorder symptoms, but a causative relationship is not established. However, there is no evidence of a negative effect on anxiety from this health-promoting intervention.[44,45]

A Note About Suicide

Patients with anxiety and comorbid substance abuse and/or major depression are at higher risk for suicide attempts. Patients may not express thoughts about suicide directly, but often will respond to open-ended queries. Asking patients with anxiety, especially patients with comorbid substance abuse or affective illness, about suicidal thoughts, plans, or intentions can open a discussion.[46]

Take-Home Points

1. Anxiety disorders are highly comorbid.
2. Consider anxiety when patients present with insomnia, headache, atypical chest pain, nonspecific gastrointestinal complaints, or cognitive concerns.
3. Conduct a careful history and physical examination; consider and rule out medical etiologies.
4. Determine if anxiety disorder is chronic or episodic.
5. Assess for suicide risk (especially if comorbid with depression or substance abuse).
6. Assess for key symptoms of panic and for avoidant behaviors.
7. Offer patients referral to psychotherapeutic interventions

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Upon completion of this educational activity, participants should be able to:

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CME/CE Questions

1. Which of the following is true of patients with generalized anxiety disorder (GAD)?
   a. They often present with panic and socially avoidant behavior.
   b. They often present with vague somatic symptoms and functional deterioration.
   c. They often present with numbness, tingling, and falls in older adults.
   d. They often present as high achievers with fear of failure.
2. Which of the following is true of patients with panic disorder (PD)?
   a. They often present with episodic panic attacks and fear of dying.
   b. They often present with hallucinations and agitation.
   c. They often present with episodic panic attacks associated with electrocardiogram abnormalities.
   d. They often present without comorbidities.
3. Which of the following is true of patients with social anxiety disorder (SAnD)?
   a. They often present as older adults with new onset socially avoidant behavior.
   b. They often present with episodic panic, insomnia, and poor appetite.
   c. They often present with multiple, vague somatic complaints.
   d. They often present with socially avoidant behavior for years.
4. Which of the following is correct regarding initial treatment for GAD?
   a. It includes benzodiazepines or atypical antipsychotics.
   b. It includes cognitive behavioral psychotherapy (CBT).
   c. It includes SSRIs or SNRIs starting at a high dose to obtain rapid relief.
   d. It includes a moderate-dose SSRI, counseling, and exercise.
5. Which of the following is correct regarding the initial treatment for PD?
   a. It often includes benzodiazepines, counseling, and buspirone.
   b. It often includes exposure therapy, reassurance, and propranolol.
   c. It includes CBT and/or benzodiazepines.
   d. It often includes hospitalization and intravenous benzodiazepines, then starting an SSRI/SNRI after the acute phase.
6. Which of the following is correct regarding the initial treatment for SAnD?
   a. It includes benzodiazepines, CBT, and a high-dose SSRI/SNRI.
   b. It includes CBT with social skills training and/or a low-dose SSRI/SNRI.
   c. It includes pregabalin, CBT, and a high-dose SSRI/SNRI.
   d. It includes benzodiazepines and the avoidance of situations causing anxiety.
7. Which of the following are common comorbidities with anxiety disorders?
   a. Mood and affective illness, substance use disorders, and other anxiety disorders
   b. Cardiovascular disease, diabetes, and mood disorder
   c. Schizophrenia, affective illness, and substance use disorder
   d. Cardiovascular disease, diabetes, and substance use disorder.

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Issues Relevant to Treating Patients with Anxiety Disorders in the Emergency Department

GAD-7 Anxiety

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3
Column totals	___ +	___+	___ +	___ =
			Total score	_____

Source: Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

Scoring GAD-7 Anxiety Severity
This is calculated by assigning scores of 0,1,2, and 3 to the response categories, respectively, of "not at all," "several days," "more than half the days," and "nearly every day." GAD-7 total score for the seven items ranges from 0 to 21.
0-4: minimal anxiety
5-9: mild anxiety
10-14: moderate anxiety
15-21: severe anxiety

SSRI/SNRI Recommended Doses for GAD, PD, and SAnD[4,13,25]

Medication	Drug Class	Dose Range	First-Line?	FDA-Approved for GAD?	FDA-Approved for PD?	FDA-Approved for SAnD?
Paroxetine (Paxil, Pexeva)	SSRI	10 mg to 50 mg (start low; advise against sudden discontinuation)	Yes	Yes	Yes	Yes
Sertraline (Zoloft)	SSRI	50 mg to 200 mg (start as low as 25 mg)	Yes	No*	Yes	Yes
Escitalopram (Lexapro)	SSRI	5 mg to 20 mg (start low)	Yes	Yes	No	No
Citalopram (Celexa)	SSRI	10 mg to 40 mg (start at 10 mg)	Yes	No	No	No
Fluoxetine (Prozac)	SSRI	10 mg to 60 mg (start low; long half-life: low potential for withdrawal)	Yes	No	Yes	No
Fluvoxamine CR (Luvox CR)	SSRI	100 mg to 300 mg per day, divided doses	Yes	No	No	Yes
Duloxetine (Cymbalta, Drizalma)	SNRI	60 mg to 120 mg (start at 30 mg)	Yes	Yes	No	No
Venlafaxine XR (Effexor XR)	SNRI	75 mg to 225 mg (start at 37.5 mg)	Yes	Yes	Yes	Yes

SSRI: selective serotonin reuptake inhibitor; SNRI: serotonin-norepinephrine reuptake inhibitor; GAD: generalized anxiety disorder; PD: panic disorder; SAnD: social anxiety disorder; FDA: Food and Drug Administration

*Supported by large clinical trials

Supplement to *Emergency Medicine Reports*, July 1, 2021: "Issues Relevant to Treating Patients with Anxiety Disorders in the Emergency Department." Author: Ellen Feldman, MD, Altru Health System, Grand Forks, ND.