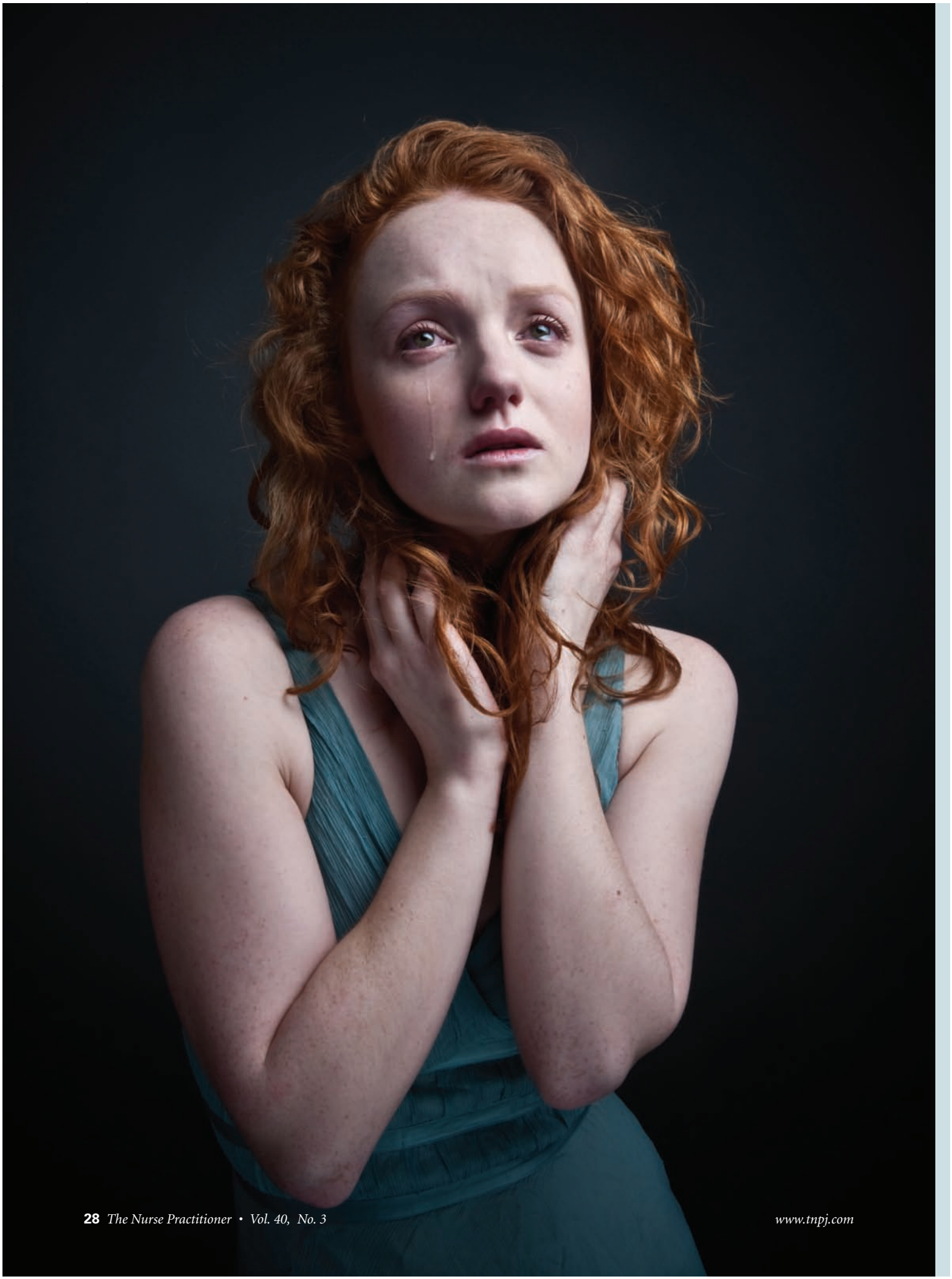

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Beyond butterflies:
Generalized anxiety disorder in adolescents

Abstract: A generalized anxiety disorder diagnosis must include thorough history-taking, the use of age-appropriate screening tools, and physical assessment. Research and development into the use of screening tools and effectiveness of treatment strategies for generalized anxiety disorder is needed to better manage adolescents with the disorder.

By Michon Elizabeth McBride, RN, MS, PNP

DL is a 17-year-old female presenting to her primary care provider for her annual exam. She reports "not feeling well" recently, complaining of almost daily debilitating headaches and moderate abdominal pain before school. She is very concerned about her health and is worried she has cancer or "some other horrible disease." She is concerned about school, as her grades have been dropping. She states she is having difficulty sleeping and concentrating in class and is almost constantly worrying about things such as her health, what she wants her major to be in college, and if her parents will have enough money to keep their home. DL reports not being able to stop thinking about her worries.

Overview

Anxiety disorders account for a major portion of common childhood behavioral and mental health concerns. Lifetime prevalence of anxiety disorders ranges from 8.3% to 27% depending on the level of impairment that is measured.[1] Within the pediatric population, generalized anxiety disorder (GAD) has a prevalence of approximately 15%, making it the second most common pediatric anxiety diagnosis.[1] GAD symptoms tend to appear infrequently in young children and become more prevalent in adolescent populations.[2] Despite their high prevalence, anxiety disorders are underrecognized and undertreated in adolescents.[1] In 2011, anxiety disorders were diagnosed in only 22% of adolescent patients who fit the diagnosis criteria in primary care settings.[3]

GAD presents as multiple, excessive, age-inappropriate worries about a variety of issues that occur for an extended period of time. Associated symptoms include feeling on edge or restless, being easily fatigued, muscle tension, difficulty sleeping, and problems with concentration.[4] The symptoms of GAD cause distress in the affected person's daily life, disrupt his or her ability to have normal peer relationships, negatively impact family functioning, and cause clinically significant impairment and distress in social, occupational, and other important areas.[1,4]

Adolescents with GAD and other anxiety disorders are more likely to report suicidal ideation as well as past threats/attempts of self-harm.[5] GAD is a risk factor for alcohol and cigarette abuse during adolescence, as those with GAD may self-medicate their symptoms of physiologic tension and psychological stress.[6] Adolescents with GAD will also likely experience academic difficulties, conflicts at home, struggles in social situations, and a negative self-image.[7] Difficulties in interpersonal relationships lead to fewer friendships and cause adolescents with GAD to be less liked by their peers.[8]

Keywords: adolescence, generalized anxiety disorder, pediatrics, screening tools

This article seeks to explore the various etiologies and risk factors of GAD, reviews the available screening tools for GAD, describes the clinical presentations of an adolescent with GAD, identifies conditions that may present similarly to GAD, reviews the evidence-based treatment guidelines for GAD, and discusses the role that the provider will play in caring for an adolescent patient with GAD.

Imaging studies have shown increased amygdala volume and activation in response to emotional stimuli in adolescents with GAD.

Etiology

The rates of anxiety disorders in children and adolescents who have parents with a diagnosed anxiety disorder range from 21% to 68% as compared to 0% to 26% in control groups.[9] There have been several hypothesized biological etiologies for GAD. Specific investigations of the genetics of GAD have focused on variations in serotonin receptors and enzymes that are involved in serotonin metabolism.[10]

Risk factors associated with GAD development[7,9,16-18]

Level	Risk factors
Child	• Female gender • Behavioral inhibition • High negative affect • Inability to self-regulate • Low self-esteem • Neuroticism
Family	• Overly negative/critical parenting style • Overly protective parenting style • Parental stress • Severe illness within the family • Unpredictable caregiver responsiveness • Ambivalent family attachment • Extreme sibling conflict
Environmental	• Being the victim of bullying • Being rejected by peers • Low socioeconomic status • Living in a neighborhood with few community resources • Past or current severe life stressors

Recent data suggest that GAD arises from dysregulation in the neural networks that are responsible for emotional processing, specifically the anterior limbic network (ALN).[11] Consistent with the hypothesized genetic link, this network contains serotonin receptors and is involved in regulating neurotransmitter levels.[9]

Behavioral inhibition (the temperamental tendency to exhibit restraint and withdrawal when faced with novel or unfamiliar stimuli) is highly linked to the development of GAD and is rooted in a lower threshold for limbic arousal, particularly in the amygdala.[9] Several brain imaging studies have shown both increased amygdala volume and activation in response to emotional stimuli in adolescents with GAD.[11] Adolescents with GAD will show abnormalities in putamen hyperactivation in response to valence decisions (gains versus losses), particularly with anticipated loss.[12] The previously mentioned studies suggest that the brain structures regulating emotion in adolescents with GAD are highly reactive to fear-provoking and emotional stimuli as well as to decision making that involves a potential loss or gain.

Certain cognitive and temperamental traits have been shown to contribute to the development of GAD. The two central temperaments that are highly associated with GAD are a withdrawn/inhibited temperament and lack of effortful control (the ability to self-regulate) temperament.[13] The anxiety from this dysfunction is maintained through negative reinforcement behaviors (primarily avoidance and escape) when the patient does not have the opportunity to learn new coping techniques.[14] Adolescents with GAD also display several cognitive biases, such as increased attention to threat-related stimuli and overestimation of personal risk in various situations, both of which enable anxious feelings and symptoms.[13,14]

Parental factors have been identified as an important part of the etiology of GAD. The two most common parenting styles that have been associated with a GAD diagnosis in adolescents are overprotective or overcontrolling and negative or highly critical.[13] A common finding in reviews of family systems for adolescents with GAD is perceived insecure parent-child relationships that are marked by lower levels of trust, greater feelings of alienation, and poor communication.[15]

Risk factors

The most consistent risk factor identified in GAD development is the patient's gender. (See *Risk factors associated with GAD development.*) Females have a higher rate of GAD

than males, with several studies showing a ratio of 2:1 that emerges by age six.[16] Personality characteristics that are risk factors for GAD are behavioral inhibition, highly negative affect, low self-esteem, decreased adaptability, and poor self-regulation.[17]

Familial risk factors for the development of GAD are both genetic and environmental. Children with an anxiety disorder are more likely to have a parent with an anxiety disorder than those who do not, regardless of parenting style.[13] Family factors that put a preadolescent at higher risk for GAD are family interactions that include high amounts of rejection or are highly enmeshed; both very high and very low levels of family adaptability are also associated with GAD. High levels of interparental and sibling conflict as well as interparental violence, separation, and divorce increase the risk of GAD development.[7,9,17]

The most important factor influenced by peer groups regarding GAD development is being a victim of bullying.[17] Being regularly left out of activities and rejected by peers also puts adolescents at high risk for GAD.[9] The effect that adverse life events have on the development of GAD has produced mixed results.[17]

Studies investigating the relationship between socioeconomic status and the risk of GAD in adolescents have produced mixed results. Vine and colleagues found that adolescents had a higher likelihood of developing GAD if their parents had a lower occupational status, income, and educational level.[18] The National Health and Nutrition Examination Survey, in contrast, found that adolescents from lower socioeconomic backgrounds had lower rates of GAD than their wealthier counterparts.[18]

Diagnosis

The recent publication of the updated *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) brought about no changes to the definition and criteria for GAD diagnosis.[19] The typical clinical presentation of an adolescent with GAD includes complaints of excessive age-inappropriate worry, difficulty controlling worries, at least one somatic symptom, and a perfectionist personality type.[20] The physical complaints reported by patients with GAD are often confusing and ill-defined, indicating a somatic nature, and also may disappear on the weekends or during vacations.[21] Adolescents with GAD often present with complaints that include headaches, gastrointestinal problems, and decreased ability to concentrate.[22] Cutting behaviors, substances abuse, and suicidal ideation or threats may also be indicators of GAD as the underlying disorder.[22]

Common red flags for GAD found on NEEDS* assessment[1,14,16,20,21,23,24]

Nutrition
- Unexplained weight loss or weight gain
- Nausea, swallowing or gagging concerns without organic cause

Elimination
- Long history of constipation or diarrhea without organic cause
- Chronic, functional abdominal pain without organic cause

Education
- Difficulty in or refusal to attend school
- Difficulty reading aloud or answering questions in class
- Inability to concentrate in school due to worries
- Reports of worry about schoolwork and grades with or without warrant

Development
- Inappropriateness of excessive distress when separating from major attachment figures at home
- Reports of worries that are developmentally immature or advanced for age
- Increased incidence of temper tantrums in older children and adolescents

Sleep, Social, Sexuality
- Refusal to sleep alone at appropriate age
- Experiencing repeated nightmares with themes of separation
- Difficulty falling or staying asleep despite complaints of chronic fatigue
- Reports of chronic worry about social events
- Inability to participate in after-school activities, attend parties, eat at restaurants, or engage in other social activities

*Nutrition, Elimination, Education, Development, Sexuality, Sleep, and Social (NEEDS)

In diagnosing GAD, a thorough history is necessary, including patient and family medical and mental health history as well as social and environmental history. (See *Common red flags for GAD found on NEEDS assessment.*)

High levels of interparental violence, separation, or divorce increase the risk of GAD development.

History-taking should focus on the onset and development of anxiety symptoms, rating their severity, associated stressors, and the impact that anxiety has on the patient's functioning.[20] Common themes in what the patient worries

Screening tools for assessing GAD[35]

Approved for ages	Completed by	Number of items	Time to complete	Specific to GAD	How to access	Cost
Tool/Spence Children's Anxiety Scale (SCAS)						
8-12 years	Patient and caregiver	45	5-10 mins.	Yes	http://www.scaswebsite.com	Free to download from website
Tool/Screen for Child Anxiety Related Disorders (SCARED)						
> 8 years	Patient and caregiver	41	5 mins.	Yes	http://www.psychiatry.pitt.edu/node/8209	Free to download from website
Tool/Multidimensional Anxiety Scale for Children – 2nd Edition (MASC-2)						
8-19 years	Patient	50	15 mins.	Yes	http://www.mhs.com/product.aspx?gr=cli&prod=masc2&id=overview	$189
Tool/Beck Youth Inventory (BYI) for Anxiety						
7-14 years	Patient	20	15 mins.	No	http://www.pearsonassessments.com/HAIWEB/Cultures/en-us/Productdetail.htm?Pid=015-8014-197	$189
Tool/Revised Children's Manifest Anxiety Scale – 2nd Edition (RCMAS-2)						
6-19 years	Patient	49	10-15 mins.	No	http://www.mhs.com/product.aspx?gr=edu&prod=rcmas2&id=overview	$119

about should be explored to determine whether they are age-normative (such as grades, friends, homework) or inappropriate.[23] The provider should note the number of worries the patient reports, as GAD is associated with worrying about an increased number of things.[24] If the clinical situation warrants such, the provider should question the patient about any past or present sexual abuse. The provider must also inquire about the use of any prescription, over-the-counter, or illicit drugs, specifically caffeine, diet pills, and cold medications, as these may trigger or exacerbate GAD as well as mimic its symptoms.[22]

Several screening tools have been developed to detect and diagnose GAD (see *Screening tools for assessing GAD*).

The most commonly utilized instruments that are specific for the screening of GAD include Screen for Child Anxiety Related Emotional Disorders (SCARED), the second edition of the Multidimensional Anxiety Scale for Children (MASC2), and the Fear Survey Schedule for Children.[14] The screening tools available have been shown to be effective in distinguishing anxious from nonanxious adolescents; yet additional development of screening tools that are developmentally appropriate for adolescent populations and are specific to each subtype of anxiety disorder is necessary to improve screening and diagnosis of GAD.[25,26]

The most common general findings on physical exam of an adolescent with GAD are weight loss and pallor.[14] There are also specific systems that should be closely examined to note any findings common in GAD presentation such as head, eyes, ears, nose, and throat (HEENT) (pupillary dilatation), respiratory (tachypnea), cardiovascular (tachycardia, hypertension), gastrointestinal (increased bowel sounds, bloating, diffuse tenderness), neurologic (numbness not following a dermatome, weakness, hyperreflexia), musculoskeletal (tremors), and the skin (flushing, blotchiness, excessive perspiration).[14]

Several differential diagnoses should be ruled out when considering a diagnosis of GAD (see *Differential diagnoses for GAD*).

Treatment

The two mainstay treatments for GAD are cognitive behavioral therapy (CBT) and, in particularly severe cases, pharmacotherapy. Both of these treatment modalities have been shown to be effective in the treatment of GAD and produce similar remission rates.[27] Treating an adolescent with CBT

and pharmacotherapy concurrently produces the best results.[1] The combination of CBT and pharmacotherapy can elicit a response in as high as 81% of GAD patients, compared with a response rate of 60% with CBT alone and a response rate of 55% using only pharmacotherapy.[24] When initiating treatment for GAD, the provider should provide the patient with the option of starting CBT concurrently with pharmacotherapy.[28]

Cognitive behavioral therapy

There is a strong cognitive component to GAD in that patients are often preoccupied with a variety of distorted thought processes. It is thought that using CBT to highlight these distortions will help patients challenge their maladaptive thoughts.[29] The vast majority of studies have focused on the effects of CBT on anxiety in general, not within a specific disorder.[13,30] Clinical studies have consistently shown that structured CBT programs produce significant reduction in anxiety symptoms and increase the quality of life for patients.[13] This is especially true in adolescent populations where the effects of CBT are seen on a larger scale than for younger populations.[31] There are different types of CBT programs, and among the most commonly used, the rates of effectiveness, and long-term outcomes are not significantly different.[32] CBT is a long-term therapy with the best treatment effects seen when a patient completes nine or more sessions.[31] When referrals to CBT are necessary, the provider should refer to programs that are pediatric-specific with on-staff providers properly trained in pediatric CBT. Providers with an interest in treating adolescents with GAD should receive training in CBT. (See *Online cognitive behavioral training*.) Although CBT has been shown to be an effective treatment for GAD, it is important for providers to closely monitor patients and educate patients and families to contact the provider or return to treatment with the recurrence of or increase in GAD symptoms.

Pharmacologic therapy

Pharmacologic interventions are helpful in decreasing anxious reactivity in the brain, which increases the opportunity for patients to learn and practice more adaptive responses to stressful stimuli. Pharmacotherapy is safe to start concurrently with CBT or may be started before or after therapy initiation. Selective serotonin reuptake inhibitors (SSRIs) are the first-line (off-label use for GAD) medications used to treat GAD (see *Medications used in GAD treatment*).[20] Numerous studies have shown that SSRIs and serotonin norepinephrine reuptake inhibitors (SNRIs) have a clear benefit in relieving symptoms of anxiety disorders in adolescent populations, specifically in GAD.

Differential diagnoses for GAD[14,16]

Category	Diagnosis
Endocrine disorders	• Hyperthyroidism • Hypoglycemia • Hyperglycemia
Neurologic disorders	• Seizure disorder • Encephalopathies • Intracranial mass lesion • Migraines • Postconcussive states
Psychiatric disorders	• Attention deficit hyperactivity disorder • Major depressive disorder • Bipolar disorder • Asperger disorder • Substance abuse disorder
Cardiovascular disorders	• Dysrhythmias
Medication use	• Antipsychotics • Antidepressants • Stimulants • Anticholinergics • Bronchodilators • Antihistamines
Illicit drug use	• Marijuana • Hallucinogens • Stimulants • Cocaine • Amphetamines
Miscellaneous	• Excessive caffeine use (caffeine pills, diet pills) • Alcohol • Withdrawal from illicit drug use • Normal developmental anxiety

Online cognitive behavioral training[36]

Beck Institute for Cognitive Behavioral Therapy
http://www.beckinstitute.org

Behavioral Health Associates Inc.
http://www.behavioralhealthassoc.com/educationalPrograms.php

Massachusetts General Hospital
http://mghcme.org/page/cognitive_behavioral_therapy

The Reach Institute
http://www.thereachinstitute.org/guidelines-for-adolescent-depression-primary-care/2-uncategorised/118-cognitive-behavioral-therapy-training-courses

Medications used in GAD treatment[33,37]

Listed below are examples of drugs that may be used to treat GAD in children and adolescents. Consult the manufacturer's full prescribing information including recommended dosages, contraindications, and precautions.

Drug Class	Example	Indication	Common adverse reactions	Special warnings
SSRI	Sertraline (FDA off-label use in GAD)	First-line therapy	Agitation, nausea, vomiting, increased appetite, weakness, sedation	Increased suicidal ideations and behaviors
SNRI	Venlafaxine (FDA off-label use in GAD in children and adolescents)	Two failed SSRI trials	Headache, agitation, abdominal pain, diarrhea, weakness, flu-like syndrome	Increased suicidal ideations and behaviors
SNRI	Duloxetine (FDA-approved for GAD in children and adolescents ages 7 to 17 years)	indicated for GAD; consider if SSRI is ineffective	Nausea, dry mouth,constipation, insomnia, dizziness	Increased suicidal ideations and behaviors
TCA	Clomipramine (FDA off-label use in GAD)	Two failed SSRI trials	Chest pain, tachycardia, insomnia, dry skin, tremor, myalgia, abdominal pain	Increased suicidal ideation and behaviors, cardiac dysrhythmias
Tetracyclic	Mirtazapine (FDA off-label use in GAD)	No response to SSRI, SNRI, or TCA, or patient/family preference	Sedation, nightmares, dizziness, increased appetite	Increased suicidal ideations and behaviors, and high potential for weight gain
Benzodiazepine	Clonazepam (FDA off-label use in GAD)	Acute relief of symptoms	Emotional lability, confusion, constipation, urine retention, weakness, sedation	Leads to physical dependence and tolerance, cannot be used for long-term therapy

Tricyclic antidepressants (TCAs) have been less studied in GAD treatment (off-label use for GAD), but may be an option for patients who are intolerant to SSRIs.[33] Benzodiazepines have been shown to be effective as short-term treatments but should be used with extreme caution in adolescent populations because of the adverse reaction profile and the high risk of physical and psychological dependence.[20] The healthcare provider should closely monitor the use of any antidepressant medication in pediatric populations. The FDA has issued a black box warning for the increased risk of suicide with the use of these medications.[20] When initiating medication use, the provider should see the patient for follow-up visits every 2 to 4 weeks to monitor effectiveness, tolerance, and to identify any issues with adverse reactions of medication use. The provider should educate the parents/caregivers on the possible adverse reactions of the medications, as they play a major role in monitoring the everyday health status of the patient. Medications should be maintained for 1 year after the resolution of symptoms followed by gradual tapering of the dosage.[33]

Role of the advanced practice registered nurse

The advanced practice registered nurse (APRN) must be aware of the prevalence and severity of anxiety disorders. Adolescents with GAD are more likely to regularly see a primary care provider rather than a mental health specialist.[1] A major component of the care of an adolescent with GAD is helping the patient and family understand the diagnosis of GAD. The APRN must be able to provide appropriate and sensitive education for both the family and

patient regarding the disorder, management options, and what they can expect in terms of treatment outcomes. The APRN must be aware of when a referral to a mental health specialist is warranted and will serve as a patient advocate. If the APRN recognizes that further help is necessary, he or she should consult with a pediatric psychiatric specialist who has more extensive experience in dealing with and treating GAD.

GAD and other anxiety disorders are often missed or not screened for by an adolescent's primary care provider. Within their practices, APRNs should address why providers miss this diagnosis and develop protocols and systems for the regular screening and diagnosing of GAD. APRNs with a specific interest in diagnosing and managing mental and behavioral health problems in children and adolescents should take advantage of continuing education and certification options. The Pediatric Nursing Certification Board (PNCB) offers the Pediatric Primary Care Mental Health Specialist Certification Exam for nurse practitioners and clinical nurse specialists. The role of the Pediatric Primary Care Mental Health Specialist (PMHS), as determined by the PNCB, is to provide advanced assessment, evaluation, diagnosis, and treatment of common behavioral or mental health problems in children or adolescents, including anxiety disorders.

Therapeutic services provided by the PMHS may include early recognition, intervention, active monitoring, appropriate referrals, use of evidence-based screening tools, psychotherapeutic interventions, and psychopharmacotherapy. Practitioners who are eligible to take the PMHS certification exam must have graduated from an accredited college or university offering an Accreditation Commission for Education in Nursing or the American Association of Colleges of Nursing, hold an active license, and demonstrate current certification as a pediatric nurse practitioner, family nurse practitioner, or psychiatric nurse practitioner. Additionally it is recommended that those taking the certification exam have a minimum of 1,000 clinical hours in primary care or mental health practice, have earned continuing-education credit in mental or behavioral health, and have experience in pediatric psychopharmacology.[34]

Effective management

GAD is a debilitating disorder fairly common in adolescent populations. Despite its prevalence, GAD is underdiagnosed and undertreated, causing major emotional and physical distress to the patient, and leads to a variety of disorders and comorbidities in adulthood. The etiology of GAD is often complex, involving a variety of genetic, biologic, cognitive, and environmental components. Healthcare providers must assess for the presence of risk factors for GAD, both in the patient and in his or her environment. APRNs must be diligent in using approved screening tools when assessing and diagnosing GAD as well as measuring treatment outcomes.

The two mainstay treatments for GAD are CBT and pharmacotherapy. CBT should be included in all GAD treatment plans, with a focus on relapse-prevention strategies once the patient is stable. Patients being treated for GAD should be closely followed and monitored for symptom improvement, adverse reactions of treatment, worsening symptoms, and comorbidities. In order to more effectively manage adolescent patients with GAD, additional research must be done assessing the usefulness of the available screening tools and current treatment strategies within this specific population. NP

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