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Dr. Diane McIntosh is a widely respected psychiatrist, author, educator, mental health advocate, and authority on the diagnosis and treatment of mood and anxiety disorders. In addition to over 20 years of direct experience providing psychiatric care to patients, Dr. McIntosh's career-long focus has been on improving access to mental health knowledge and expertise through technology and education. She co-founded SwitchRx, an online psychotropic switching tool used by over 75,000 healthcare professionals worldwide, and PsychedUp, a continuing medical education program developed to encourage appropriate and rational prescribing of psychiatric medications. She is the author of bestseller *This is Depression*, a comprehensive and evidence-based guide to one of the most common and debilitating disorders.

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PRINCIPLES OF ANXIETY MANAGEMENT FOR FAMILY PHYSICIANS

Introduction

Family practitioners (FPs) play an essential role in mental healthcare delivery, providing triage, diagnosis, patient referral, and treatment. They are usually are patient's first—and often their only—contact with mental healthcare services, due to the lack of access to psychiatric care. As such, FPs are commonly tasked with collecting and evaluating a broad range of symptoms that can be categorized as anxiety. The symptoms of anxiety have become increasingly ubiquitous, particularly due to the impact of the COVID-19 pandemic, leading many front-line providers to understandably feel anxious concerning optimal methods to assess and support these patients.

This article provides clinical pearls, supported by current empirical research, for assessing, diagnosing and treating patients presenting with anxiety.

Understanding the medical pathology of anxiety

While terms such as anxiety and depression are commonly employed, their meaning often varies between individuals. When a patient reports they are experiencing anxiety, their clinicians should ask, "What does anxiety mean for you?" Clinicians should then determine whether the anxiety symptoms are impairing the individual's ability to function in their usual roles—at work, home, and school—and whether they are severe enough to require treatment.

It can be challenging, particularly in the age of social media, where clinical terms have been integrated into everyday language, to differentiate between normal worries and anxiety symptoms that require medical intervention. Parents, in particular, are struggling with the term anxiety, because it has become a catch-all phrase for every unpleasant sensation their child may be experiencing.

An example of normal worry is captured in the statement, "My school exams make me anxious"; examinations are designed to prompt individuals to master new material in a limited amount of time. Some young people, however, exhibit symptoms of anxiety that are extremely severe, impacting their ability to attend school, seek employment, or develop relationships. Anxiety symptoms might also be a harbinger of another serious mental illness, such as clinical depression, bipolar disorder or schizophrenia.

The Fear Response versus Pathological Anxiety

Fear is a normal response to a concrete threat, and it is critical for individuals' safety. When confronted by a threat, the brain transmits sensory information via neuronal pathways from the thalamus to the amygdala, which orchestrates an appropriate response to the perceived threat, known as the fight, flight, or freeze response. The amygdala provokes an increase in norepinephrine, leading to heightened arousal, sharpened attention, and greater sensory acuity. This surge of norepinephrine

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increases the heart rate and blood pressure via the lateral hypothalamus. When a threat is perceived, blood is rapidly directed away from less vital organs, toward body sites necessary to adopt evasive coping measures.

The sensation of fear provokes the hypothalamic-pituitary-adrenal axis (HPAA) to increase the release of corticotropin-releasing hormone (CRH), subsequently provoking the pituitary glad to release adenocorticotropic hormone (ACTH), which ultimately triggers the release of cortisol. Cortisol is a critical stress-response hormone that protects the body from stress-related tissue and nerve damage and, in the context of normal functioning, returns an individual's body to homeostasis. If, however, the level of cortisol remains excessively high for a prolonged period of time, as sometimes occurs with chronic depression or anxiety, it can provoke an inflammatory cascade, increasing pro-inflammatory cytokines and altering brain structure and functioning. This can ultimately lead to greater symptom severity and chronicity, treatment resistance, and functional impairment.

Individuals with pathological anxiety experience fear that is excessive, unwarranted, inappropriate, and impairing. Rather than reacting to an obvious threat such as an aggressive, barking dog, pathological anxiety is a response to a threat that is vague, unclear, and at times of unknown origin.

Anxious Distress versus Anxiety Disorders

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) has added the "anxious distress specifier" to the major depressive disorder (MDD) and bipolar disorder diagnoses to highlight the important clinical impact of anxiety associated with mood disorders.[1] Approximately three-quarters of patients with MDD meet the criteria for the anxious distress specifier.[1] Anxious distress typically resolves with the appropriate management of the primary disorder. The presence of anxiety commonly implies that the disorder is more severe,[2] more challenging to treat,[3] and will take longer to resolve.[4,5] In cases where medication is required, the patient may require higher doses and more medications than those required to treat the mood disorder in the absence of anxious distress. In addition, anxiety is associated with poor functioning and reduced quality of life.[6] Anxiety significantly heightens the risk of suicidal ideation and suicide attempts associated with mood disorders.[7–10] Furthermore, anxiety may provoke self-medication, including the excessive use of alcohol or cannabis.[11]

Anxiety disorders are distinct psychiatric disorders, each with a unique constellation of symptoms. As with all DSM-5 diagnoses, to meet the criteria for an anxiety disorder the symptoms must impair social, occupational or other important areas of functioning, and cause clinically significant distress. DSM-5 anxiety disorders include separation anxiety, social anxiety disorder (SAD), generalized anxiety disorder (GAD), panic disorder (PD), and specific phobia.

While previously considered anxiety disorders, post-traumatic stress disorder (PTSD) and obsessive-compulsive disorder (OCD) have been reclassified under separate categories in the DSM-5, together with other similar diagnoses. The purpose of grouping similar disorders into two new categories, Trauma- and Stressor-Related Disorders, and Obsessive-Compulsive and Related Disorders, was to reflect the current clinical evidence that these diagnostic groups are related through their unique neurobiology and treatment response patterns.[12]

Anxiety Screening

Any patient presenting with a mood disorder should be screened for anxiety, due to the heightened morbidity and mortality associated with anxious distress. Likewise, because anxiety can worsen the outcome of any psychiatric disorder, it is important to screen all patients with a psychiatric diagnosis, including ADHD, psychotic disorders, eating disorders, and dementia.

For those patients who have chronic anxiety or a suspected anxiety disorder, a few targeted questions can help to hone in on a specific anxiety disorder diagnosis, which can then be confirmed using DSM-5 criteria.

Individuals with GAD frequently ask themselves, "What if." Commonly, their worries are focused on everyday issues like health, relationships, or finances. Someone with GAD might repeatedly worry "What if my partner gets sick and we can't pay the mortgage?" even though their partner is in good health and their family is financially stable. Occasional worries of this nature are not unusual, particularly if they rooted in legitimate concerns, but they rarely cause a significant impact on functioning. However, those living with GAD are unable to cease worrying about everyday matters. In fact, they worry about their worry. Their worry consumes their entire life, their relationships, and their ability to function in their usual roles. GAD commonly presents co-morbidly with MDD, so both should be considered for screening.

Patients with SAD experience intense discomfort when they are the centre of attention, particularly in social settings with people they do not know well. Additionally, they often feel that they have missed out on important life experiences as a result of their anxiety.

The diagnosis of panic disorder is usually straightforward, although patients sometimes complain of days-long panic attacks. While they have clearly experienced extremely unpleasant and intense anxiety, they are not experiencing a true panic attack. A panic attack is a discrete episode of intense fear or discomfort that emerges very suddenly, peaks over several minutes (usually within 10 minutes), and then slowly resolves. A panic disorder diagnosis requires repeated *unexpected* panic attacks and a pattern of post-panic concern about having a subsequent attack and/or maladaptive behaviour as a result of the panic attack, including functional impairments such as being

unable to venture to the grocery store. Panic attacks are not necessarily associated with a psychiatric disorder; approximately 30% of panic attacks occur in individuals who do not have a psychiatric diagnosis.

Diagnosing Anxiety

The anxious distress specifier cited in the DSM-5 includes:

1. Feeling keyed up or tense
2. Feeling unusually restless
3. Difficulty concentrating because of worry
4. Fear that something awful may happen
5. Feeling like one might lose control

Severity-based symptom number and type:

1. Mild: Two symptoms
2. Moderate: Three symptoms
3. Moderate-to-Severe: Four or five symptoms
4. Severe: 4 or 5 symptoms accompanied by motor agitation

The Generalized Anxiety Disorder Scale-7 (GAD-7) is a critical self-reporting tool for evaluating the presence and severity of generalized anxiety disorder. Additionally, it has been shown to have moderate sensitivity and specificity for screening PD, SAD, and PTSD. Patients can complete the GAD-7 as part of an initial evaluation and at follow-up appointments to assess treatment response (**Figure 1**).[13]

Validated self-report scales have been developed for the majority of mental health disorders. Patients can be assessed for SAD by using the Liebowitz Social Anxiety Scale.[14] A rapid screening tool for OCD, the Obsessive-Compulsive Inventory-Revised (OCI-R) scale, has now been validated as a four-item version self-report tool (OCI-4).[15] This concise version can identify OCD in settings where it is not possible to access an in-depth assessment. There were three version of the PTSD Checklist (PCL) for the DSM-4: PCL-M (military), PCL-C (civilian) and PCL-S (specific). The PCL-5 is a 20-item self-report questionnaire corresponding to the updated DSM-5 criteria for PTSD. There are no longer military or civilian versions.[16]

The impact of a patient's symptoms on their functioning is a critical aspect of any DSM-5 diagnosis. The Sheehan Disability Scale (SDS) was developed to assess functioning in three domains: work/school, social life, and family life (**Figure 2**). This self-report, concise scale requires patients to rate the extent to which their functioning is impaired as it relates to their psychiatric symptoms, on a 10-point visual analog scale. The SDS can be employed at the time of diagnosis and with each follow-up appointment to assess the patient's response to treatment in terms of functional recovery. It has been validated for use in several mood and anxiety disorders, including MDD, GAD, OCD, and PD.[17]

It is important to note that a positive result on a clinical screening tool should be considered in combination with a clinical interview to confirm the diagnosis.

Treatment of Anxiety Disorders

Anxiety disorders tend to be chronic as well as highly recurrent. One clinical study of 643 women with no history of depression found that during the three-year study period, 35% experienced a new onset of an anxiety disorder, and 65% reported a recurrence of anxiety.[18]

Generalized Anxiety Disorder 7-item (GAD-7) Scale

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over 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's 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
Add the score for each column	+	+	+	
Total Score (*add your column score*) =				

If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all _____

Somewhat difficult _____

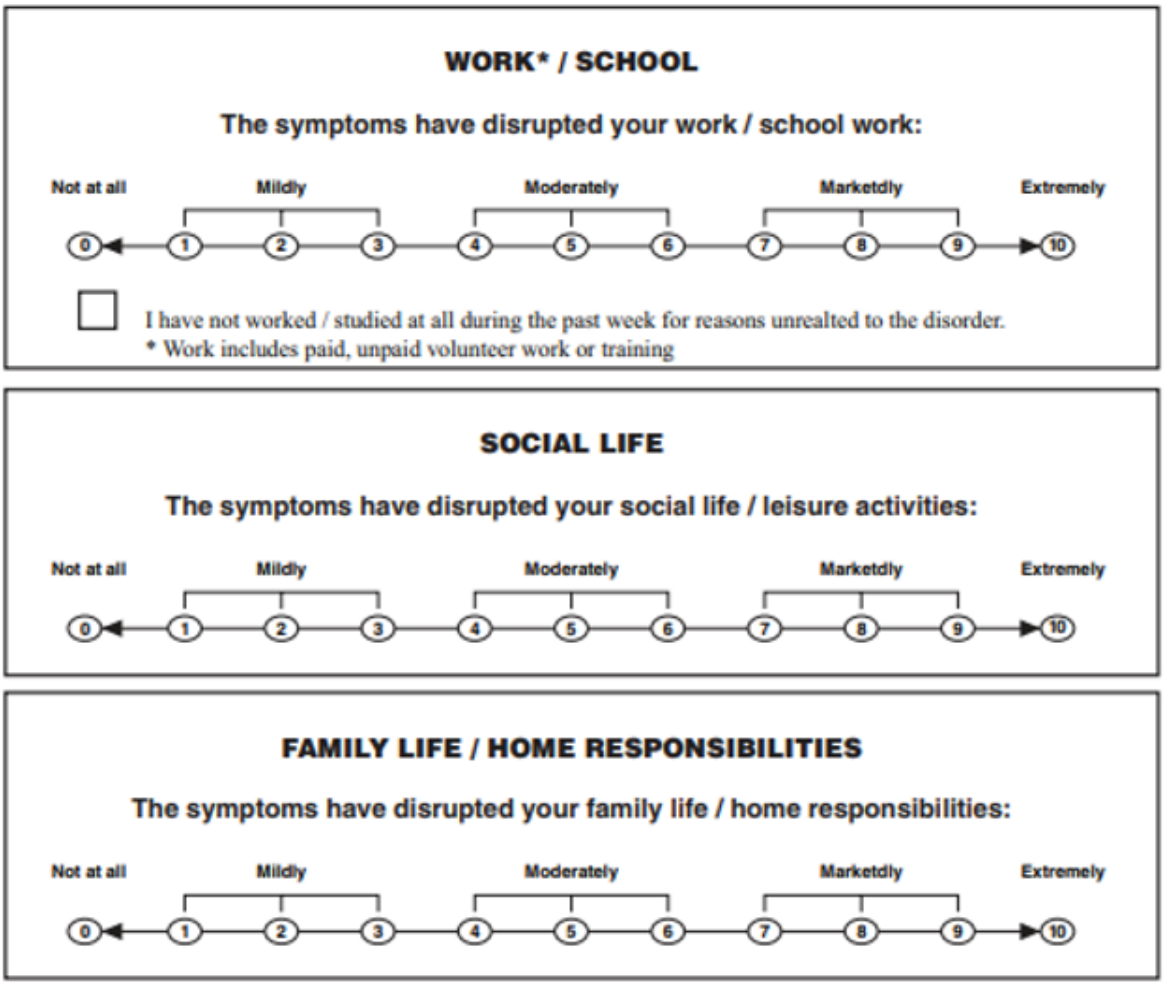
Very difficult _____

Extremely difficult _____

Figure 1: GAD-7 Scale. Adapted from Kroenke et al, 2007.

A brief, patient rated, measure of disability and impairment.

Please mark ONE circle for each scale.



Days Lost

On how many days in the last week did your symptoms cause you to miss school or work or leave you unable to carry out your normal daily responsibilities? _____

Days Unproductive

On how many days in the last week did you feel so impaired by your symptoms, that even though you went to school or work, your productivity was reduced? _____

Figure 2: Sheehan Disability Scale. Adpated from Sheehan DV et al, 1996.

When anxiety disorders are recurrent, approximately 33% of patients will present with a different anxiety disorder.[19] For this reason, the goals of anxiety treatment should include complete symptom remission and full functional recovery.

A biopsychosocial approach to anxiety management is most likely to provide enduring benefits to the patient. The psychological therapy with the greatest empirical evidence demonstrating its value for treating anxiety and anxiety disorders is cognitive-behavioural therapy (CBT).[20] While CBT can be expensive and difficult to access, clinical evidence supports its value when it is delivered from multiple modalities: bibliotherapy, group therapy, virtual CBT, and one-on-one therapy are all known to provide therapeutic value.

Prior to suggesting CBT, it is critical to consider whether the patient is cognitively able to benefit. If short-term memory or concentration are severely impaired, it will be very difficult for them to focus and practice to learn new skills, which are the cornerstones of CBT. In such cases, it may be necessary to initiate medication prior to initiating formal CBT. While the medication is helping to manage cognitive symptoms, patients generally benefit from supportive therapy and a compassionate approach.

Mindfulness meditation, yoga, and regular mild-to-moderate exercise are complimentary therapies that support anxiety management, which has been confirmed by clinical research.

Pharmacotherapy for Anxiety Disorders

The pharmacotherapy guidance provided herein is based on treatment guidelines, as well as a long history of clinical experience.[21] As the Canadian guidelines[22] are outdated, and it is exceedingly rare for pharmaceutical companies to pursue formal regulatory indications for anxiety disorders, the guidance offered below is largely based on off-label use.

The effectiveness of pharmacotherapy is dependent on patient compliance. Identifying a treatment to which a patient is willing to adhere depends on its effectiveness and tolerability. Critical side effects with the greatest impact on adherence include weight gain, sexual dysfunction, excessive daytime sedation, and "zombification". This term refers to the unpleasant experience of feeling emotionally blunted, apathetic or unmotivated, and occurs in approximately 30% of patients prescribed a selective serotonin reuptake inhibitor (SSRI) or low-dose serotonin and norepinephrine reuptake inhibitor (SNRI).

Patient education regarding psychopharmacology is imperative. Patients commonly under-value the importance of treating their anxiety symptoms fully. They may benefit from gentle reminders regarding the value of full symptom remission and functional recovery. Engaging their primary support person—for example, a close friend or family member—can have a significant impact on treatment adherence and helping the patient remain patient during the treatment process.

Fortunately, numerous antidepressants are available and most have been proven helpful in managing moderate-to-severe anxiety. Managing anxiety disorders typically requires augmenting serotonin levels, which involves employing an SSRI, SNRI or multimodal antidepressant.

It is critical to remember that while all antidepressants are effective, not all of them are effective for every patient. Treatment of psychiatric illness requires a trial-and-error approach, and it is important to inform patients about what to expect at treatment initiation.

Patients struggling with anxiety may be highly sensitive to side effects and the initial weeks of treatment are often the most challenging. The majority of early side effects, such as headache and nausea, resolve completely within the first two weeks of treatment. Minor changes, such as dose timing and administration with food, can have a significant impact on tolerability. Sensitivity to side effects makes it even more imperative to initiate an antidepressant at a low dose, titrate slowly and only when the initial side effects have resolved, and continue to optimize the dosage until full remission is achieved.

In some cases, a short-term benzodiazepine, such as low-dose lorazepam or clonazepam, can make a significant difference in tolerability at treatment initiation. Alprazolam should be avoided because it is difficult to taper. Likewise, avoid diazepam, which has active metabolites that accumulate, heightening or prolonging side effects.

Recommended choices for the treatment of anxiety disorders:

SSRIs: escitalopram, sertraline

SNRIs: duloxetine, desvenlafaxine, levomilnacipran

Multimodal agents: vortioxetine, vilazodone

While bupropion XL is very well-tolerated, with clinical data supporting its value in treating anxious distress and GAD, there is a paucity of favourable data supporting its use in other anxiety disorders. Mirtazapine can be helpful for some anxiety disorders, but consistent weight gain and excessive sedation make it a less desirable first-line choice of treatment.

Antidepressants previously considered mainstays for the treatment of depression and anxiety are not cited above due to their considerable side effect burden. For example, paroxetine and venlafaxine XR are effective, but both carry the risk of severe discontinuation syndrome. Paroxetine is known to cause significant weight gain and both agents carry a high risk of sexual dysfunction. In general, SNRIs and multimodal agents have more favourable side effect profiles, particularly concerning weight gain and sexual dysfunction, compared to SSRIs.

Treatment augmentation for severe anxiety may include combining two antidepressants with distinct mechanisms

of action, such as combining an SSRI, SNRI or multimodal agent with bupropion XL or mirtazapine. However, adding an atypical antipsychotic with empirically validated antidepressant benefits, as well as a Health Canada/FDA indication, is more likely to be beneficial than an antidepressant combination. These medications include brexpiprazole, aripiprazole, cariprazine and quetiapine. The first three of these are D2 partial agonists and are less likely to promote weight gain or metabolic syndrome, although every medication in this class carries some risk.

Alternatives to antidepressants and atypical antipsychotics include pregabalin and beta- blockers. Pregabalin is commonly used to treat anxiety, however, its benefits are inconsistent. It has been associated with unfavourable side effects, including weight gain and cognitive impairment. Beta-blockers treat only the physical manifestations of anxiety. They may be helpful for patients who have intense performance anxiety and can be used on a PRN basis for that purpose.

Conclusion

While anxiety is often viewed as less severe and less worthy of clinical concern than MDD, clinical research highlights its significant impact on patient functioning, suicide risk and quality of life. It is incumbent on mental health care providers to assess the presence and severity of the patient's anxiety, measure it using validated clinical scales, treat it to complete remission, and monitor the patient's treatment progress.

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