

Anxiety in the emergency medical practice – its psychiatric and somatic origin, comorbidities, behavior and treatment

Silvia Sarakostova¹, Diyana Pantileeva¹, Dancho Dilkov², Niya Semerdzhieva³, Mariya Chaneva³, Stefka Ivanova⁴, Ventseslava Atanasova⁵, Petar Atanasov², Diana Rangelova⁶

¹ Multidisciplinary Emergency Department, University Hospital “N. I. Pirogov”, Sofia, Bulgaria

² Clinic of psychiatry and military psychology, Sofia, Bulgaria

³ Clinic of Internal Medicine, University Hospital “N. I. Pirogov”, Sofia, Bulgaria

⁴ Bulgarian Pharmaceutical Science Society, Sofia, Bulgaria

⁵ Bulgarian Pharmaceutical Union, Sofia, Bulgaria

⁶ Department of Educational and Scientific Activity, UMHATEM “N.I. Pirogov”, Sofia 1606, Bulgaria

Corresponding author: Stefka Ivanova (ivanovastefka_pharm@yahoo.com)

Received 4 April 2024 ♦ Accepted 4 April 2024 ♦ Published 16 May 2024

Citation: Sarakostova S, Pantileeva D, Dilkov D, Semerdzhieva N, Chaneva M, Ivanova S, Atanasova V, Atanasov P, Rangelova D (2024) Anxiety in the emergency medical practice – its psychiatric and somatic origin, comorbidities, behavior and treatment. *Pharmacia* 71: 1–7. <https://doi.org/10.3897/pharmacia.71.e124695>

Abstract

Anxiety conditions and disorders are common in the general population, and patients suffering from them often seek the services of emergency departments. Anxiety is a psychopathological symptom that accompanies not only psychiatric conditions, but a wide range of somatic diseases, and a combination of both. The biochemical and pathophysiological mechanisms of psychosomatic interrelationship and comorbidity are complex and multi-layered. Thus, diagnosing the root cause of anxiety is a clinical challenge. Early, and on time, recognition of an anxiety disorder helps to avoid unnecessary investigations, ensures correct treatment and saves hospital resources. Careful use of medications, psychoeducation and referral to a specialist improves patient outcome with this potentially debilitating disease.

In this article, the authors aim to present in a synthesized form the main epidemiological data on the prevalence of anxiety symptoms and disorders, anatomical localization and biochemical mechanisms and relationships in the pathogenesis of anxiety symptoms, as well as to derive the main guidelines for recognizing and differentiating clinicopathological constellations in somatic conditions in emergency medical practice.

Materials and methods. Existing published studies from an international database, related to the subject of the article, have been thoroughly studied.

Results. Anxiety symptoms, in particular panic attacks and disorders, are widespread in primary care and occupy a significant part of the work process, especially at times of peak loads, natural disasters and situations of mass traumatism.

Conclusions. Timely training and good preparation for recognition and adequate assessment of anxiety conditions in primary and emergency medical care significantly shorten the therapeutic route of patients. They receive competent help on time, and the cost of their treatment is significantly reduced.

Discussion. Modern medical science, including psychiatric, offers advanced drug and non-drug methods for the treatment and prevention of anxiety conditions and disorders.

Keywords

Anxiety, panic attack, symptoms, stages, pharmacotherapy

Introduction

In recent years, 'anxiety' that does not meet the full criteria for some type of anxiety disorder (e.g. panic disorder) but is characterized by a variety of somatic complaints and resembles a panic attack has become increasingly common in emergency medical care (including psychiatric settings). The diagnostic work-up of such an 'anxious state' usually evokes a series of tests conducted on the patient, and various consultations with physicians of different specialties. The latter reinforce the patient's conviction of the presence of an 'undetected physical problem'. The latter is iatrogenic in nature and can become a source of hypochondria and depression for the patient. Although these 'anxiety states' cannot be certainly categorized under the diagnosis of 'anxiety disorder', their presence requires timely psychiatric intervention and treatment. Anxiety

is an emotional state causing serious discomfort. It is associated with psychophysiological changes and results in an intrapsychic conflict. Anxiety is more intense and 'exaggerated', if pathologic and, in such cases, anxiety occurs without an actual threat.

Pathophysiology of anxiety and its systemic effects

Experimental evidence supports the hypothesis that fear encoding occurs in the amygdala, and the prefrontal cortex exerts controls fear to suppress anxiety. Prolonged stress leads to high levels of glucocorticosteroids, damaging the prefrontal cortex and the control mechanisms of amygdala. The stimulated amygdala becomes overactive: each subsequent signal from the cortex is coded as stronger and more threatening, and as a result the suppression of fear becomes increasingly difficult. Thus, through its central nucleus, the amygdala is involved in triggering panic attacks. If it is also connected to centers in the brainstem that control breathing and heart activity, mechanisms are unlocked for the formation of physical symptoms during a panic attack (Dilkov et al. 2011). A state of distress induces the secretion of norepinephrine, and a state of tension induces the secretion of cortisol, adrenaline and norepinephrine. Cardiovascular centers in the central nervous system (CNS) regulate circulatory response to emotional stress and the impact of psychological processes. Experiencing high-intensity negative emotions is associated with increased blood pressure and heart rate, and increased cardiovascular reactivity to emotional stress could trigger pathologic cardiovascular and brain reactions (Nikolova 2007). As far as the digestive system is involved, the vasoconstriction of vessels in the gastric and duodenal mucosa reduces its protective ability, which becomes a prerequisite for the development of gastritis, ulcers (e.g. stress ulcers), etc. Increased release of catecholamines during stress leads to local ischemia and decreased tissue resistance. Chronic emotional stress also disrupts the motor activity of the stomach. The peristal-

tic, rhythmic, and tonic muscle contractions by which the stomach evacuates food into the duodenum and small intestine are affected (Stoinov et al. 2016).

Anxiety disorders are very common in the general population (with an estimated frequency range between 20 and 30%) and a lifetime chance of developing an anxiety disorder of 16.6% (Bandelow and Michaelis 2015). In situations of natural disasters, severe industrial accidents, acts of terrorism and others, more than half of the visitors to emergency medical units have found themselves with such disorders (Dilkov et al. 2010). A major psychopathologic symptom is the anxiety, defined as the tension that occurs because the patient refuses to undertake an ordinary action, which is perceived as very unpleasant and potentially life-threatening (Sadock and Sadock 2008). In ICD-10, the set of anxiety disorders or 'Neurotic disorders related to stress and somatoform disorders (F40–F48)' is too large (ICD-10 Mental and behavioral disorders 2008). In emergency medicine, anxiety can be classified into four groups (Felder et al. 2013):

- A. Primary psychiatric illness, e.g. 'Generalized Anxiety Disorder'.
- B. Anxiety disorder and another mental illness – e.g. 'Depressive disorder'.
- C. A response to stress or a stressful event, e.g. 'Acute stress disorder'.
- D. Medical condition or substance abuse that mimics anxiety symptoms – e.g. hyperthyroidism.

Table 1 Medical conditions that may cause anxiety (Tan et al. 2007).

This large range of somatic diseases and their acute manifestations are the reason why patients often contact an emergency medical service on suspicion of a medical emergency – e.g. stroke or heart attack, accompanied by tension and anxiety. However, a significant number of patients with panic attacks only without any somatic disorder are admitted as emergency patients in multi-specialty hospitals, e.g. to the neurological clinic with diagnoses 'vertigo' or with 'atypical facial pain'; or to cardiology clinic for 'acute coronary syndrome' or suspicion of 'acute myocardial infarction', etc. It is important that the doctor in emergency care can distinguish between anxiety and somatic disease. Quite often, the psychiatric morbidity and the somatic morbidity are co-existing.

Comorbidities and anxiety

Many patients suffer anxiety disorder along with other psychiatric illness – such as personality disorders (most commonly borderline personality disorder), various types of addictions, major depression, bipolar affective disorder, schizophrenia, and schizoaffective disorders (Marinov and Angelova 2008). Some patients with anxiety disorders may use psychoactive substances (PASs) as a method of self-medication. On the contrary, if the pa-

Table 1. lists the somatic disorders that can lead to anxiety.

Organ/system involved	Disorder
Cardiovascular system	congestive heart failure, acute aortic syndrome, acute myocardial infarction, stable and unstable angina pectoris, anemia, hypotension, arterial hypertension, arrhythmias, hypovolemia
Respiratory system	asthma, acute and chronic bronchiolitis, chronic obstructive pulmonary disease, pneumonia, hyperventilation, sleep apnea
Metabolic syndrome	hypocalcemia, hypokalemia, porphyria, pellagra, uremia
Endocrine diseases	hyperadrenocorticism, pituitary dysfunction, hyperthyroidism, hypothyroidism, parathyroid dysfunction, pheochromocytoma, hypoglycemia, polycystic ovary syndrome, premenstrual syndrome
Neurological diseases	cerebrovascular disease, cerebral neoplasm, encephalitis, migraine, subarachnoid hemorrhage, closed brain injury, multiple sclerosis, Wilson's disease, vestibular disorders, dementia, delirium, Huntington's disease, temporal lobe disorders, epilepsy
Inflammatory diseases	systemic lupus erythematosus, rheumatoid arthritis, temporal arteritis, fibromyalgia, allergic reactions
Toxicity	caffeine intoxication, amphetamines, heavy metal intoxication, vasopressors and sympathomimetics, organophosphates, alcohol, opiates, phencyclidine, cocaine, ecstasy
Infectious	septicemia, carcinoid syndrome, infectious mononucleosis, AIDS ¹ , malignancies, subacute bacterial endocarditis, gastrointestinal hemorrhage
Various	irritable bowel syndrome, dyspepsia, gastro-oesophagic reflux disease, herpes zoster

Legend: ¹ AIDS – acquired immunodeficiency syndrome.

tient has an inherited predisposition, the chronic use of psychoactive substances can lead to the development of an anxiety disorder or other mental illness. Thus, one of the most difficult tasks in diagnosis turns out to be differentiating symptoms due to abuse with psychoactive substances from the symptoms of psychiatric by origin (Clark et al. 2021). Both acute PAS intoxication and PAS withdrawal syndrome can mimic anxiety disorder. Early screening of patients with similar comorbidity is of particular importance for timely diagnosis, treatment and good therapeutic effect (Ivanov et al. 2013). The comorbidity of chronic physical disease and anxiety disorder has also been proven, although research in the field is still insufficient. The relationship between panic disorder (PD) and cardiovascular disease (CVD) has been widely studied – the characteristics of an anxiety disorder along with cardiovascular disease in particular and whether anxiety disorders increase the risk of developing heart disease. The biological and pathophysiological mechanisms that mediate this relationship are discussed, including shared genes (so-called pleiotropic effect), various rhythm disorders, unhealthy lifestyles, atherosclerosis, psychological stress, and defects in myocardial nutrition (Machado et al. 2017). Recent research confirms the observed greater cardiac excitability in patients with PD and the risk of developing ventricular and supraventricular arrhythmias in untreated PD (Yilmaz et al. 2024). Pulmonary pathology has also been widely studied – for example, it is already known that in some chronic diseases such as chronic obstructive pulmonary disease (COPD) the frequency of PD is about 10 times greater than in the general population (1.5–3.5%). Furthermore, in patients with COPD, panic attacks are usually fully resolved (Livermore et al. 2010). There are also numerous reports of a relationship and comorbidity between PD with irritable bowel syndrome and diabetes (Meuret et al. 2017). Another comorbid relationship of recent interest is that of migraine and PD (Wang et al. 2010). Thus far, it has proven difficult to make a distinction between somatic and mental illness, and to diagnose both of them in one patient.

Table 2 attempts to give guidelines for anxiety that is likely to be purely somatically determined (Zun and Nathan 2009):

When the patient does not meet the conditions described in Table 2, and no current serious physical problem is found, the anxiety is probably a pathologic and is a purely psychiatric disease.

The patient presenting to the emergency department with a mental problem most often suffers from panic disorder or another anxiety disorder that occurs immediately after experiencing acute stress. Patients who meet the psychiatric criteria of the diagnosis of PD visit emergency departments quite often. Studies show that this frequency is much higher than previously thought (Zane et al. 2003). In this context, it is important for the emergency medicine specialist to be able to recognize a psychiatric condition so that proper treatment can be started (Lentz 2017). Commonly, the above refers to the patients with panic disorder. Its main distinguishing feature is the simultaneous presence of physical and cognitive symptoms. It is characterized by repeated attacks of intense fear – panic attacks, with a sudden onset, which become most intense within about 10 minutes, and the duration of the attack can last up to 1 hour. In typical cases, the frequency of attacks is 2 to 4 times per week, and in the time between attacks there is anxiety caused by waiting for the next one (anticipatory anxiety) (Manjunatha et al. 2022). Attacks are more frequent in the late afternoon hours, as well as during the

Table 2. Cases of anxiety due to an underlying physical illness.

Characteristic features
Onset of anxiety symptoms after age 35
No past or family history of anxiety disorder
Lack of childhood history of pathological anxiety, phobia, separation anxiety. There is a number of studies showing that pathologic anxiety in childhood tends to continue later in adulthood (Polnareva 2013)
Absence of behavior of avoidance
Lack of significant life events, the reason for the emergence of anxiety symptoms
Poor or insufficient response to anxiolytic drug treatment

summer season (hot weather). Up to 40% of patients also have nocturnal panic attacks (Hranov et al. 2013).

The panic attack is a brief episode of intense fear or discomfort with four or more of the following symptoms occurring suddenly and peaking within 10 min (American Psychiatric Association 2013):

- Palpitations, palpitations or rapid heart rate
- Sweating
- Trembling or shaking
- Feeling of shortness of breath or suffocation
- Chest pain and/or chest discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, faint
- Derealization (feeling of unreality) or depersonalization (feeling detached from oneself)
- Fear of losing control or fear of 'going crazy'
- Fear that 'you will die'
- Paresthesia (tingling sensations)
- Chills or hot flashes

The cases of recurrent and sudden panic attacks, related to continuous fear of having another panic attack with a duration of at least one month and also a significant change in seizure behavior is classified as panic disorder. Six stages have been identified in the development of panic disorder. The stages 1 and 2 are the most common at the time of diagnosis.

The stages are as follows: 1. Symptomatic attack, minor; 2. Extended attack; 3. Hypochondria; 4. Limited phobic avoidance/agoraphobia; 5. Extended phobic avoidance/agoraphobia; 6. Secondary depression.

As a rule, the advanced stages of the panic disorder in the respective patient impair seriously his/her daily life and the needed treatment is more difficult and prolonged (Merritt et al. 2000). The diagnosis made in the first two stages is compatible with lower likelihood of deterioration of the disorder (Noyes et al. 1980).

Table 4 describes the different stages in the development of PD.

Table 3. Lists the typical and atypical physical complaints seen in a panic attack (Pollard and Lewis 1989).

Typical symptoms	Atypical symptoms
tachycardia, palpitations / 'atypical' chest pain	chest tightness / pleural chest pain
Tingling	trembling 'freezing', numbness
Sweating	generalized sweating
Dyspnea	Stridor
subjective weakness in the limbs	objective muscle weakness
apparent lack of coordination	generalized erythema or rash dry mouth
redness or chills fever	
feeling of suffocation	mechanical block in swallowing reflex
dizziness true vertigo	Syncope
depersonalization and derealization	lack of all-round orientation
abdominal discomfort	nausea, vomiting
fear of 'loss of control' or other 'inappropriate' catastrophic event	strange behavior (not close to fear)

Table 4. Stages in the development of PD (Zun 1997).

Stage	Symptom complex
I Symptom-limited panic attack	Patients exhibit fewer than the 4 symptoms required for a diagnosis of PD
II Full-blown panic attack	Patients met the definition of PD in terms of frequency and duration, as well as the presence of 4 or more symptoms
III Hypochondria	Patients become preoccupied with worries about the presence of bodily disease, regardless of medical evidence to the contrary
IV Agoraphobia	Panic attacks are tied to certain environmental stimuli – the so-called phobic avoidance behavior
V Advanced phobic avoidance	Most common fears of driving, visiting shops and crowded places
VI Secondary depression	It occurs as a result of increasing dysfunction and demoralization

The research reports on behavior in PD

Patients with PD or anxiety usually present to the emergency department with somatic complaints such as shortness of breath, palpitations, chest pain, etc. Sometimes they are diagnosed with an acute respiratory or cardiac event or other physical illness. Although they have panic attacks, it is extremely important to rule out acute somatic illness. The first steps in the case work-up is to ensure a correct recording of the patient's history, careful physical examination, an assessment of basic

vital parameters (arterial pressure, pulse rate and characteristics, saturation, respiratory rate) and some laboratory tests – complete blood count, serum electrolytes, levels blood glucose, arterial blood gas analysis, thyroid function tests, and kidney function tests. Electrolyte abnormalities such as low levels of ionized calcium and serum phosphate are seen in patients with hyperventilation. An electrocardiogram should be performed, so as to rule out an acute cardiovascular event. A chest X-ray, ultrasound examination of the lungs, and spirometry are recommended if a respiratory problem is suspected. Toxicological analysis is required in case there is evidence of substance abuse. After excluding possible somatic illness, the patient may be diagnosed with PD or another anxiety disorder. Due to the lack of psychiatrists in the emergency departments, applying DSM-V or ICD-10 diagnostic criteria to such emergency situations can be difficult. This may be the reason for underdiagnosing or misdiagnosing of PD. The use of standardized screening tools can be helpful in such cases.

Table 5 lists some screening tools that can be used by the clinician in an emergency setting:

Treatment in the emergency department

After careful assessment, the patient may be diagnosed with a somatic illness or an anxiety or panic disorder. The treatment is immediately started by the emergency physi-

Table 5. Screening tools for anxiety disorder and panic disorder.

Screening tools for anxiety/PD	
For anxiety disorder in general	For panic disorder
Anxiety Disorder Diagnostic Questionnaire (Norton and Robinson 2010)	Panic Disorder Self-Report (Newman et al. 2006)
Generalized Anxiety Disorder 7 (Spitzer et al. 2006)	Panic Disorder Severity Scale (Shear et al. 2001)
Beck Anxiety Inventory (Beck et al. 1988)	Panic and Agoraphobia Scale (Bandelow 1999)
Hamilton Anxiety Rating Scale (Öst and Westling 1995)	NIMH Panic Questionnaire (Scupi et al. 1992)
	Panic associated symptoms scale (Argyle et al. 1991)

cian if there is a co-existing somatic illness, and later the patient is referred to a psychiatrist. If a current panic attack or other anxiety disorder is detected – the emergency physician initiates treatment to control the crisis, and then refers the patient to a psychiatrist. It is not uncommon for patients with a primary psychiatric disorder to have underlying somatic illnesses that must be taken into account while making a treatment plan. The treatment of PD/anxiety disorder is pharmacological and includes non-pharmacological methods as well.

Pharmacotherapy

The aim of the initial treatment is the control of the symptoms of the panic attack. Benzodiazepines are the drug of choice for this purpose, as they provide rapid results. These are diazepam, clonazepam, lorazepam and alprazolam. Diazepam 10 mg is administered on an emergency basis by muscular or intravenous route: aparenteral preparations of clonazepam (1 mg/1 ml) are already available in Bulgaria. The maximum daily dose of clonazepam in the treatment of anxiety states is 4 mg/day, and after the acute episode, it is taken as tablets or solution by mouth. Clonazepam exerts a weaker sedative effect in contrast to diazepam and is less likely to suppress breathing. Lorazepam is administered in doses of 1–4 mg/day, divided into 2 to 3 daily doses; and its maximum dose is no more than 10 mg/day (Vlastra et al. 2018). The initial dose of alprazolam is usually 0.25 mg three times a day, and the daily dose can reach 4 mg (Locke et al. 2015). The abrupt discontinuation of benzodiazepines is associated with a withdrawal effect. They should be tapered gradually. It is extremely important to mention that benzodiazepines are not a long-term treatment. Their long-term use leads to benzodiazepine dependence and worsening of anxiety complaints if the treatment does not include medications of new generation. The role of benzodiazepines is to relieve the patient's complaints in the first days to a week or two after the start of treatment until the other drugs develop their potential for action.

The molecular basis for anxiety disorders is the disturbance in the serotonergic, noradrenergic, GABAergic, and cholecystokinergic neurotransmitter systems (Nikolkova and Marinov 2007). The interactions between

brain structures and other organs have been recently found to be characterized by asynchronous excitatory and inhibitory processes, which set the ground for occurring psychopathological symptoms such as derealization and depersonalization (Northoff et al. 2021). Therefore, the medications that provide the actual healing effect and require long-term intake are selective serotonin reuptake inhibitors (SSRIs). They are the first-line drug of choice (a newer generation antidepressants). These are escitalopram, paroxetine, sertraline and fluoxetine. Although they are all equally effective, paroxetine is more commonly used (Du et al. 2021). These drugs are titrated slowly, and it takes about 2 weeks to reach the expected therapeutic effect. Their common side effects are nausea, diarrhea, constipation, headache, tremors, tension, dizziness, sweating, and sexual dysfunction. Initially, they may be administered together with a short course of alprazolam. Serotonin and norepinephrine reuptake Inhibitors (SNRIs) such as venlafaxine are also used. In rarer cases, the use of tricyclic antidepressants is resorted, e.g. clomipramine.

Table 6 summarizes the benzodiazepines and antidepressants that are used to treat PD and anxiety:

However, practice shows that the use of these medications is often not sufficient to control the symptoms of anxiety. In such cases, other drug classes – mood stabilizers (valproic acid, carbamazepine, lamotrigine, drugs with gamma-amino butyric acid (GABA), etc.) and antipsychotics (olanzapine, aripiprazole, sulpiride, etc.) should be added (Masdrakis and Baldwin 2021). Their application is particularly effective when it comes to a difficult to control PD or there is a concomitant psychiatric problem – addiction, personality disorder, etc. Non-pharmacological treatment of PD. Panic attacks or episodes of intense anxiety usually resolve themselves spontaneously within 30 minutes. Often, patients visit the emergency room after the panic attack has subsided or during a period of preparatory anxiety – anticipation of the next one. At this point, it is important for the patient to receive understanding, attention and support from the emergency physician, who is good at briefly explaining the nature of the condition and giving reassurance that a serious physical problem does not exist. Education of the patient and his relatives is ther-

Table 6. Medications to treat panic disorder/anxiety.

Medicine	Starting dose	Therapeutic dose
Benzodiazepines		
Alprazolam	0.25–0.5 mg, t.i.d	0.5–2 mg, t.i.d
Lorazepam	1–2 mg, b.d.	1–2 mg, t.i.d
Clonazepam	0.25–0.5 mg, b.d.	0.5–2 mg, b.d.
Selective Serotonin Reuptake Inhibitors		
Paroxetine	5–10 mg	20–60 mg b.d.
Fluoxetine	20 mg	20–60 mg b.d.
Escitalopram	5–10 mg	10–20 mg
Sertraline	25–50 mg	50–200 mg
Serotonin and Norepinephrine Reuptake Inhibitors		
Venlafaxine	75 mg	75–150 mg
Tricyclic antidepressants		
Clomipramine	5–12.5 mg	50–125 mg

apeutic in itself and relieves tension (Sarkhel et al. 2020). In the long term, Cognitive-Behavioral Psychotherapy (Otto and Deveney 2005), Interpersonal Psychotherapy or Mindfulness practices are recommended, but they take at least a few weeks to be effective. For this reason, emergency health workers, who are practically the first to encounter mental psychopathology, should lay the foundations of the correct approach to anxiety states and provide basic guidelines for a proper life-style – e.g. refusal to take stimulating foods, drinks and substances, adequate amount of quality sleep, physical activity, etc. Relaxation techniques (Öst and Westling 1995) and presentation of certain images (e.g. scenery) (Öst et al. 1993) can be very effective in quickly relieving anxiety symptoms, and are easily applicable even in emergency medical conditions. Another proven effective method is deep breathing exercises (Taylor 2001) – consciously slowing down breathing and focusing on even, slow and deep breaths. There are also online self-help programs that are based mainly on behavioral approaches and teaching the patient not to be afraid of their bodily sensations during a panic attack (Huppert 2022). In the long term, especially in more severe cases and in co-occurring anxiety disorder depression, repet-

itive Transcranial Magnetic Stimulation (rTMS) may be effective (Dilkov and Sarakostova 2019). Early referral to a specialist reduces the overall cost of research and treatment (Chen et al. 2009).

Conclusion

Anxiety symptoms are prevalent in primary care settings, especially emergency departments. Most of the patients suffering from them have accompanying cardiac, respiratory, gastrointestinal or neurological diseases. Emergency physicians have an important role in diagnosing worrisome psychiatric conditions because they are the first to encounter them. Their early recognition and treatment help reduce psychiatric morbidity and mortality. A holistic approach and clinical assessment, followed by emergency interventions to reduce anxiety and timely referral to a psychiatrist, are paramount for the emergency physician, especially if the patient is at suicidal risk or is severely uncritically aware of the condition, or has an inadequate response to initial interventions. Early referral to a specialist reduces the overall cost of research and treatment.

References

- American Psychiatric Association (2013) Diagnostic and Statistical Manual of Mental Disorders-5, Arlington, VA: American Psychiatric Publishing, 4th edn. <https://doi.org/10.1176/appi.books.9780890425596>
- Argyle N, Deltito J, Allerup P, Maier W, Albus M, Nutzinger D, Rasmussen S, Ayuso JL, Bech P (1991) The Panic-Associated Symptom Scale: Measuring the severity of panic disorder. *Acta Psychiatr Scand* 83(1): 20–26. <https://doi.org/10.1111/j.1600-0447.1991.tb05506.x>
- Bandelow B, Michaelis S (2015) Epidemiology of anxiety disorders in the 21st century. *Dialogues Clin Neurosci*. 17(3): 327–335. <https://doi.org/10.31887/DCNS.2015.17.3/bbandelow>
- Bandelow B (1999) Panic and Agoraphobia Scale (PAS). Newbury port, Massachusetts: Hogrefe & Huber Publishers.
- Beck AT, Epstein N, Brown G, Steer RA (1988) An inventory for measuring clinical anxiety: psychometric properties. *Journal of Consulting and Clinical Psychology* 56(6): 893–897. <https://doi.org/10.1037/0022-006X.56.6.893>
- Chen YH, Chen SF, Lin HC (2009) Healthcare utilization patterns before and after contact with psychiatrist care for panic disorder. *Journal of Affective Disorders* 119(1–3): 172–176. <https://doi.org/10.1016/j.jad.2009.02.011>
- Clark AE, Goodwin SR, Marks RM, Belcher AM, Heinlein E, Bennett ME, Roche DJO (2021) A narrative literature review of the epidemiology, etiology, and treatment of co-occurring panic disorder and opioid use disorder. *Journal of Dual Diagnosis* 17(4): 313–332. <https://doi.org/10.1080/15504263.2021.1965407>
- Dilkov D, Kostadinov R, Dimitrov A (2010) Combating stress and anxiety disorders – a basic element of medical insurance for concussions. *Military Medicine* LXII(4): 46–49.
- Dilkov D, Kaludiev E (2011) Repetitive transcranial magnetic stimulation - principles, indications, contraindications and clinical application in mental illnesses. *Psychosomatic Medicine* 20(1/2): 30.
- Dilkov D, Sarakostova S (2019) Effect of repetitive Transcranial Magnetic Stimulation on anxiety symptoms in drug-resistant depression. *Military Medicine* 2: 13–14.
- Du Y, Du B, Diao Y, Yin Z, Li J, Yunfeng Shu Y, Zhang Z, Chen L (2021) Comparative efficacy and acceptability of antidepressants and benzodiazepines for the treatment of panic disorder: A systematic review and network meta-analysis. *Asian Journal of Psychiatry* 60: 102664. <https://doi.org/10.1016/j.ajp.2021.102664>
- Felder ML, Perry MA (2013) The patient with anxiety disorders in the emergency department. *Behavioral Emergencies for the Emergency Physician*. Cambridge, Cambridge University Press 76–82. <https://doi.org/10.1017/CBO9781139088077.015>
- Hranov L, Natsov I (2013) Anxiety, somatoform, conversion and dissociative disorders. *Psychiatry under the editorship of Prof. Dr. Vihra Milanova, dmn. Medicine and Physical Education*. Sofia, 267.
- Huppert JD (2022) Panic Disorder. *Comprehensive Clinical Psychology* (2nd edn.) 6: 320–335. <https://doi.org/10.1016/B978-0-12-818697-8.00226-0>
- ICD-10 Mental and behavioral disorders (2008) *Bulgarian Psychiatric Association*. Sofia. 2008; 114–147.
- Ivanov K, Chumpalova P, Stoychev K et al. (2013) Comorbidity of affective, anxiety, and substance use disorders. *Medinfo* 12: 56–57.
- Lentz C (2017) Anxiety and mood disorders in an emergency context. *Big Book of Emergency Department Psychiatry*. New York, Productivity Press. 147–176. <https://doi.org/10.1201/b21955-10>
- Livermore N, Sharpe L, McKenzie D (2010) Panic attacks and panic disorder in chronic obstructive pulmonary disease: A cognitive behavioral perspective. *Respiratory Medicine* 104(9): 1246–1253. <https://doi.org/10.1016/j.rmed.2010.04.011>
- Locke AB, Kirst N, Shultz CG (2015) Diagnosis and management of generalized anxiety disorder and panic disorder in adults. *American Family Physician* 91(9): 617–624. [PMID: 25955736]

- Machado S, Sancassiani F, Paes F, Rocha N, Murillo-Rodriguez E, Nardi AE (2017) Panic disorder and cardiovascular diseases: an overview. *International Review of Psychiatry* 29(5): 436–444. <https://doi.org/10.1080/09540261.2017.1357540>
- Manjunatha N, Ram D (2022) Panic disorder in general medical practice – A narrative review. *Journal of Family Medicine and Primary Care* 11(3): 861–869. https://doi.org/10.4103/jfmpc.jfmpc_888_21
- Marinov P, Angelova A (2008) Anxiety. Aspects of classification, comorbidity and clinical case presentation. *Medinfo* 6: 9–10.
- Masdrakis VG, Baldwin DS (2021) Anticonvulsant and antipsychotic medications in the pharmacotherapy of panic disorder: a structured review. *Therapeutic Advances in Psychopharmacology* 11: 20451253211002320. <https://doi.org/10.1177/20451253211002320> [PMID: 33815761; PMCID: PMC7989133]
- Merritt TC (2000) Recognition and acute management of patients with panic attacks in the emergency department. *Emergency Medicine Clinics of North America* 18(2): 289–300. [https://doi.org/10.1016/s0733-8627\(05\)70125-5](https://doi.org/10.1016/s0733-8627(05)70125-5)
- Meuret AE, Kroll J, Ritz T (2017) Panic disorder comorbidity with medical conditions and treatment implications. *Annual Review of Clinical Psychology* 13: 209–240. <https://doi.org/10.1146/annurev-clinpsy-021815-093044>
- Newman MG, Holmes M, Zuellig AR, Kachin KE, Behar E (2006) The reliability and validity of the panic disorder self-report: A new diagnostic screening measure of panic disorder. *Psychological Assessment* 18(1): 49–61. <https://doi.org/10.1037/1040-3590.18.1.49>
- Nikolkova S, Marinov P (2007) Psychiatry, psychology and psychotherapy for general practitioners. Gorex Press, Sofia. 136.
- Nikolova R (2007) Impact of emotions on cardiovascular status (psychophysiological approach). *Receptor* 4: 21.
- Northoff G (2020) Anxiety Disorders and the Brain's Resting State Networks: From Altered Spatiotemporal Synchronization to Psychopathological Symptoms. *Advances in Experimental Medicine and Biology* 1191: 71–90. https://doi.org/10.1007/978-981-32-9705-0_5
- Norton PJ, Robinson CM (2010) Development and evaluation of the anxiety disorder diagnostic questionnaire. *Cognitive Behavioral Therapy* 39(2): 137–149. <https://doi.org/10.1080/16506070903140430>
- Noyes R, Clancy J, Hoehn PR, Slymen DJ (1980) The prognosis of anxiety neurosis. *Archives of General Psychiatry* 37(2): 173–178. <https://doi.org/10.1001/archpsyc.1980.01780150063006>
- Öst LG, Westling BE, Hellström K (1993) Applied relaxation, exposure in vivo and cognitive methods in the treatment of panic disorder with agoraphobia. *Behaviour Research and Therapy* 31(4): 383–394. [https://doi.org/10.1016/0005-7967\(93\)90095-C](https://doi.org/10.1016/0005-7967(93)90095-C)
- Öst LG, Westling BE (1995) Applied relaxation vs cognitive behavior therapy in the treatment of panic disorder. *Behaviour Research and Therapy* 33(2): 145–158. [https://doi.org/10.1016/0005-7967\(94\)E0026-F](https://doi.org/10.1016/0005-7967(94)E0026-F)
- Otto MW, Deveney C (2005) Cognitive-behavioral therapy and the treatment of panic disorder: Efficacy and strategies. *Journal of Clinical Psychiatry* 66(4): 28–32. [PMID: 15842185]
- Pollard CA, Lewis LM (1989) Managing panic attacks in emergency patients. *Journal of Emergency Medicine* 7(5): 547–552. [https://doi.org/10.1016/0736-4679\(89\)90164-9](https://doi.org/10.1016/0736-4679(89)90164-9)
- Polnareva N (2013) Internalized mental disorders in children and adolescents. *Clinical and Behavioral Perspectives*. Gorex Press, 33–69.
- Sadock BJ, Sadock VA (2008) Kaplan and Sadock's Concise Textbook of Clinical Psychiatry. 3rd edn. Philadelphia, PA: Lippincott Williams and Wilkins.
- Sarkhel S, Singh OP, Arora M (2020) Clinical practice guidelines for psychoeducation in psychiatric disorders general principles of psychoeducation. *Indian Journal of Psychiatry* 62(2): 319–323. https://doi.org/10.4103/psychiatry.IndianJPsychiatry_780_19
- Scupi BS, Maser JD, Uhde TW (1992) The national institute of mental health panic questionnaire: An instrument for assessing clinical characteristics of panic disorder. *The Journal of Nervous and Mental Disease* 180(9): 566–572. <https://doi.org/10.1097/00005053-199209000-00004>
- Shear MK, Rucci P, Williams J E Frank, Grochocinski V, Vander Bilt J, Houck P, Wang T (2001) Reliability and validity of the Panic Disorder Severity Scale: Replication and extension. *Journal of Psychiatric Research* 35(5): 293–296. [https://doi.org/10.1016/S0022-3956\(01\)00028-0](https://doi.org/10.1016/S0022-3956(01)00028-0)
- Spitzer RL, Kroenke K, Williams JB, Löwe B (2006) A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine* 166(10): 1092–1097. <https://doi.org/10.1001/archinte.166.10.1092>
- Stoinov K, Donchev T, Dilkov D (2016) Conceptual features of stress and pathophysiological aspects of emotional stress. *Bulgarian Journal of Psychiatry* 1(1): 22.
- Tan DT, Khouzam H, Gill T (2007) Handbook of Emergency Psychiatry. 1st edn. Philadelphia. Mosby. The Acutely Anxious Patient, 214–233.
- Taylor S (2001) Breathing retraining in the treatment of panic disorder: Efficacy, caveats and indications. *Scanning Journal Behavior in Hemianopia* 30: 49–56.
- Vlastra W, Delewi R, Rohling WJ, Wagenaar TC, Hirsch A, Meesterma MG, Vis MM, Wykrzykowska JJ, Koch KT, de Winter RJ, Baan Jr J, Piek JJ, Sprangers MAG, Henriques JPS (2018) Premedication to reduce anxiety in patients undergoing coronary angiography and percutaneous coronary intervention. *Open Heart* 5(2): e000833. <https://doi.org/10.1136/openhrt-2018-000833> [PMID: 30275956; PMCID: PMC6157563]
- Wang SJ, Chen PK, Fuh JL (2010) Comorbidities of migraine. *Front Neurol* 1: 16. <https://doi.org/10.3389/fneur.2010.00016> [PMID: 21188255; PMCID: PMC3008936]
- Yilmaz M, Yilmaz S (2024) Electrocardiographic frontal QRS-T angle is independently associated with panic disorder. *The International Journal of Psychiatry in Medicine* 59(2): 167–181. <https://doi.org/10.1177/00912174231184759> [Epub 2023 Jun 21. PMID: 37342881]
- Zane RD, McAfee AT, Sherburne S, Billeter G, Barsky A (2003) Panic disorder and emergency services utilization. *Academic Emergency Medicine* 10(10): 1065–1069. [https://doi.org/10.1197/S1069-6563\(03\)00349-X](https://doi.org/10.1197/S1069-6563(03)00349-X)
- Zun LS, Nathan JB (2009) Rosen's Emergency Medicine: Concepts and Clinical Practice, 7th edn. Philadelphia, PA: Mosby Elsevier, Anxiety disorders.
- Zun LS (1997) Panic disorder: Diagnosis and treatment in emergency medicine. *Ann Emerg Med* 30(1): 92–96. [https://doi.org/10.1016/s0196-0644\(97\)70117-3](https://doi.org/10.1016/s0196-0644(97)70117-3)