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# Anxiety Disorders

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## 1. Introduction

Modern man spends a lot of time, money and energy on alleviating his anxiety. In the Unites States the number of people who see clinicians because of anxiety complaints exceeds by far that the patients who see help for their colds. Tranquilizers prescribed either by psychiatrists or by general physicians, are among the top sellers both in Europe and in US. There hardly seems to be anyone who has not used tranquilizers at least once in his life in order to relieve stress.

What do we know about anxiety? Anxiety, fright, fear, worry, dread, anguish, terror-this is a long list of approximate synonyms! The very fine differences separating this notions may often generate confusion: it is normal to feel worried or scared, but is it all right to be anxious? If it is , then there is normal anxiety. What about anguish? On the other hand, could we live without anxiety? Quite a number of philosophers, psychologists and psychiatrists think that the answer is negative. Anxiety, like love, joy, hope, anger, disgust or hatred, is an integral part of life. It may act as a creative impulse or a muse, friend or foe, destroyer or advisor. Just think how many hasty decisions, how many mistakes we have all made because we felt anxious. The reverse is also true: there have been quite a few times in our lives when we passed a difficult exam, wrote a good paper or created a work of art because of anxiety.

Anxiety is one of the most frequent nosologic entities encountered not only in psychiatric but in general practice too. It was defined by Janet as "fear without object".

Anxiety is characterized by a diffuse, unpleasant, vague sensation of fear or anguish accompanied by autonomic symptoms such as head ache, sweating, palpitations, tachycardia, gastric discomfort, etc. Therefore it includes both a physiological and a psychological component, anxious individuals being usually aware of both. Anxiety may affect thinking, perception and learning, it can generate distortion of perception, impairment in concentration, recall and associations. Another important aspect is the effect it may have on selective attention, anxious individuals select certain things or events around them and exaggerate the importance of others, in an attempt to justify their anxiety as reaction to a fearful situation.

(Feraru R, Podea D, 1998, *Panic Disorder*, MAIKO, ISBN 973-95649-6-8, Bucharest)

The perception of an event as stressful depends both on the nature of the event and on the subject's resources. Individuals with an adequate ego are in a state of adaptive balance between the outer world and their inner world. The upsetting of this balance generates anxiety. The anxiety plays the role of an alarm signal that warns the person about

impending danger and helps him to prepare to face it. Fear, another signal alerting the body, appear as a response to a familiar, external, well-defined threat or nonconflictual at origin, while anxiety is a response to an unfamiliar, internal, vague threat or may be conflictual at origin. The two notions came to be differentiated absolutely by chance, as the first translators of Freud into English chose to translate German concept "angst" by "anxiety" rather than "fear". Anxiety and fear have in common lots subjective and physiological aspects, that's why the difference between the two terms is still debated. ( Marinescu M, Udristoiu T, Podea D., Ciucu A, 2008, *Tulburarea depresiva si anxioasa- actualitati*, AIUS, ISBN 978-973-1780-97-9, Craiova)

## 2. Comparative nosology DSM-IV to ICD-10

DSM (Diagnostical and Statistical Manual of Mental Disorders) is the official classification system of mental disorders used in the United States, while ICD (International Classification of Diseases and Related Health Problems) in the counterpart of that system in Europe. Each of them sets clear and accurate diagnostic criteria; the system are correlated in order to provide a common language to mental health professional all over the world.

The first edition of DSM was published in 1952 and the second in 1968. The third one came out in 1980 and brought along five important innovations. First there was a heavy emphasis on operational criteria for each disorder, with rules for inclusion and exclusion.

The second important feature was a multiaxial system including five axes:

- clinical syndromes and other conditions that require follow-up and treatment
- developmental and personality disorders
- physical disorders
- severity of psychosocial stressors
- degree of adaptive functioning during the last year

The third innovation was a review of the terminology and regrouping of some syndromes (thus, for instance, the notions of neurosis and hysteria were abandoned, while all affective disorders were grouped together)

The fourth change was a restricted use of psychodynamic concepts in the substantiation of classifications, while the fifth was the inclusion among the diagnostic criteria of the duration of the disorder in some categories.

DSM-III-R released in 1987 was a intermediary scheme, before a comprehensive review was operated in DSM-IV in 1994. It coded pervasive development disorders on axis I, while axis II was limited only to personality disorders and mental retardation. DSM-IV includes an appendix that reflects the cultural and ethnic influences that may be relevant in evaluation and diagnosis.

In the same interval, the World Health Organization collaborated with psychiatric organizations of several countries in order to construct the 10<sup>th</sup> edition of Chapter V of the international classification (ICD-10) published in 1992.

ICD-10 reproduces many of the conceptual and taxonomic achievements of DSM-III.

ICD-10 is in many ways similar to DSM-II-R and DSM-IV, but contains clinical descriptions and diagnostic orientations that are less detailed and less restrictive. They are some important differences, such as those regarding terminology, the grouping of disorders and the definitions of some basic concepts. (see Table 1) (Feraru R, Podea D, 1998, *Panic Disorder*, MAIKO, ISBN 973-95649-6-8, Bucharest; Marinescu M, Udristoiu T, Podea D., Ciucu A, 2008, *Tulburarea depresiva si anxioasa- actualitati*, AIUS, ISBN 978-973-1780-97-9, Craiova)

DSM-IV	ICD-10 CHAPTERV
Panic disorder -without agoraphobia -with agoraphobia	Panic disorder (episodic paroxysmal anxiety) Agoraphobia with panic disorder
Agoraphobia without history of panic disorder	Agoraphobia ( without panic disorder)
Specific phobia	Specific (isolated) phobia
Social phobia	Social phobia
Generalized anxiety disorder	Generalized anxiety disorder
Anxiety disorder NOS	1. Mixed anxiety and depressive disorder 2. Other mixed anxiety disorders 3. Other specified anxiety disorders 4. Anxiety disorder, unspecified

Table 1. Comparative nosology between DSM-IV-TR and ICD-10 (American Psychiatric Association, 1994, *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition , American Psychiatric Association, ISBN 0-89042-064-5, Washington, DC; WHO, 1998, ICD-10 *Clasificarea tulburarilor mentale si de comportament*, ALL, ISBN 973-9392-73-3, Romania)

3. Epidemiology

Epidemiological data about anxiety disorders in general are varied and controversial due to differences on the screening method and instruments used.

The overall lifetime prevalence of anxiety disorders was 14,6% and annually was 12,6 % in the Epidemiological Catchement Area compared with national Comorbidity Survey where the prevalence of anxiety disorders was 25% (19% at men and 31% at women)

The prevalence is ranged around 3.8% for panic disorders and 5.6% for panic attacks. For agoraphobia the prevalence ranges between 0.6-6 %; the higher prevalence rate in the last decade does not seem to reflect a true increase: it is more indicative of a higher level of education and the uniformity of diagnostic criteria. At any rate , one of the most fascinating mysteries of agoraphobia remains its distribution by sexes: approximately 75% of agoraphobics are women.

The prevalence of OCD is around 2% in general population.

Social anxiety is the most frequent of the anxiety disorders with lifetime prevalence of approximately 13%.

When examining prevalence of PTSD, two conditional probabilities are important: the probability of PTSD in the general population and the probability of PTSD within specific trauma populations. General population prevalence estimates range from 1% to 9 %. Among individuals who have traumatic events higher rates of PTSD where found (24%). (Marinescu M, Udristoiu T, Podea D., Ciucu A,2008, *Tulburarea depresiva si anxioasa- actualitati*, AIUS, ISBN 978-973-1780-97-9, Craiova)

4. Etiopathogeny

Three theoretical schools, three different trends intersect, contradict and complete one another in an attempt to explain the etiology of anxiety disorders: psychoanalytic, cognitive behavioral and biological theories.

#### 4.1 Psychoanalytic theories

One of Freud's major contributions to psychoanalytic thinking was the conceptualization of anxiety, a concern that stayed with him throughout his career. A careful analysis of Freud's neurophysiological model of anxiety, one of the first models created by him towards the end of the 19th century, reveals that anxiety neurosis described at the time is easily comparable to panic disorder as it is described today in DSM-IV. In the early period, Freud grouped neuroses into two major classes: actual neuroses and psychoneuroses.

##### 4.1.1 Actual neuroses

Actual neuroses include neurasthenia, anxiety neurosis and hypochondriasis. They were considered somatic in origin, anxiety being attributed to a sexual disorder; in other words, direct transformation of sexual energy into anxiety was thought to be responsible for actual neurosis. The premise upon which this theory was based was that an increase in sexual tension which is a physiological phenomenon, leads to a correspondent increase of the libido, namely of its mental representation. The normal release of sexual tension and implicitly of the libido is the sexual intercourse. In Freud's view, abnormal practices, sexual dissatisfaction or frustration resulting from abstinence, or "coitus interruptus" prevent this release of tension thus triggering actual neurosis.

##### 4.1.2 Psychoneuroses

Psychoneuroses were represented by hysteria, fobias and obsession neurosis. Unlike actual neurosis which were somatically determined, psychoneuroses were psychological in nature, tension being generated by an unacceptable sexual impulse, there for by an intrapsychic conflict. According to Freud this anxiety was less intense than that occurring in actual neurosis.

Subsequently Freud abandoned the concept in favor of a psychological one. With the replacement of the topographic model by the tripartite structural model of the mind, which divides the psychic apparatus into the id, the ego and the super ego, a second theory of anxiety was born: "signal anxiety". The hypothesis was subsequently expanded by classifying this signals into:

- internal or neurotic, coming from the id or the ego, and
  - external or real threats. Finally, Freud generalized this concept by identifying two types of anxiety: traumatic and signal anxiety.
- a. traumatic anxiety appears in response to actual traumatic situations. More frequently encountered in childhood, when the ego is insufficiently developed, it may also appear in adults in panic or in psychotic states when the ego has suffered massive disorganization.
  - b. Signal anxiety, which is more common, appears in anticipation of danger, not as a result thereof. Produced at a subconscious or an unconscious level, it plays a protective role warning the ego about impending internal or external dangers. It appears in adults whose defense mechanisms are mature. It may be useful to repeat here that defense mechanisms are psychological mechanisms designed to mediate between individual wishes, impulses, needs and emotions, on one hand, and internalized interdictions and external reality, on the other.

Departing from Freud's early theory, where anxiety neurosis was seen as somatically conditioned, subsequent psychoanalytic theories have conceptualized panic disorder as a result of failed defense, a partial failure of the ego to face the stimuli endangering it. Although in the later part of his career Freud devoted more attention to anticipatory



anxiety, he always maintained the distinction between the two forms of anxiety, one mediated mainly biologically and the other psychologically.

Recent biological research has also confirmed the existence of two forms of anxiety one predominantly psychological in nature, appearing as anticipatory anxiety or signal anxiety, and the other predominantly neurophysiological, assuming the form of panic disorder.

## **4.2 Cognitive-behavioral theories**

Like psychoanalysts, the supporters of cognitive-behavioral theories considered that biological hypotheses are insufficient to explain all the clinical manifestations of panic disorder. Starting from the premise that anxiety is a learned response, with learning occurring either as a result of classical conditioning or by following parental behavioral models (social learning theory), they have proposed a variety of etiologic explanations for panic disorder. In a similar way to Freud's theories, cognitive-behavioral theories have undergone numerous modifications and improvements over time. Some of these are:

### **4.2.1 Classical conditioning**

Systematic exposure to anxiogenic situations has been observed to reduce avoidance behavior in agoraphobic patients and to alleviate panic attacks. In their attempts to explain the phenomenon, researchers have invoked classical conditioning as the etiology of panic disorder.

Let us remember that the first stage of conditioning is the association of a noxious stimulus, such as an electric shock (unconditioned stimulus) to an event perceived as neutral, such as entering a crowded shop or crossing a bridge (conditioned stimulus). Concomitant and repeated association of the two event induces fear (conditioned response). Which subsequently appears even in the absence of the unconditioned stimulus.

The second stage involves the subject's attempts to avoid the fear produced by dangerous and unpleasant situations by escape or by avoidance.

Although interesting, the theory of classical conditioning has numerous limitations, the most significant being that the most panic disorder patients external noxious elements (unconditioned stimuli) cannot be identified.

### **4.2.2 The "fear of fear" principle and interoceptive conditioning**

As unconditioned external stimuli were hard to detect, subsequent cognitive-behavioral theories focused on more indepth research on internal stimuli, starting from the observation that the symptoms of panic disorder patients were in fact produced by internal and not external stimuli.

In panic disorder patients the interoceptive stimuli represented by harmless somatic sensations, such as dizziness or palpitations, become conditioned stimuli following association with panic attacks, generating fear or future attacks. After the first panic attack, patients frightened by the experience they experience, become hypervigilant concerning their own body. They may thus observe sensations they would have ignored or would have failed to notice otherwise; once this was observed they increase their anxiety. This closes the vicious cycle and may trigger new attacks.

The theory has its limitations too, the most serious objection being the overlap between conditioned stimuli and conditioned responses.

### **4.2.3 Catastrophic misinterpretation**

The interpretation of harmless sensations as evidence for imminent catastrophe lies at the foundation of cognitive theories. According to these theories, panic attacks are caused by the

individual's tendency to interpret somatic sensations in a catastrophic manner; palpitations for example are perceived as a symptom of imminent myocardial infarction, dizziness as a symptom of imminent fainting. The perception of imminent disaster triggers panic attacks. The theory, although interesting it fails to offer a full satisfactory explanation for panic attacks.

#### 4.2.4 Anxiety sensitivity

This theory claims that panic disorder patients develop or maintain a mistaken interpretation of their harmless somatic sensations because of high anxiety sensitivity. Anxiety sensitivity reflects a pathological belief connected to anxiety symptoms; it appears before the onset of the disease and is a predisposing factor of panic disorder.

#### 4.3 Neurobiological factors

The biology of anxiety and panic represents one of the biggest and most interesting fields of current research. Biological theories are based on experimental studies performed on animals and on comparative clinical research. The unprecedented accumulation of knowledge in neurochemistry, pharmacology, genetics and neuroendocrinology has helped researchers clarify many aspects of anxiety.

The stimulation of the Autonomic Nervous System (ANS) produces cardiovascular, respiratory, muscular and gastrointestinal symptoms such as dizziness, tremor, diarrhea, hypertension, palpitations, tachycardia, mydriasis and gastric discomfort. These are in fact the peripheral manifestations of anxiety.

It is generally accepted that central nervous system anxiety precedes its peripheral manifestation.

Some panic disorder patients exhibit increased sympathetic tone, adapt slowly and with difficulty to repeated stimuli, and respond excessively to moderate stimuli.

Epinephrine and norepinephrine were among the first panic-inducing agents known. Both are secreted in response to stress. Epinephrine stimulates beta-adrenergic receptors, while norepinephrine is an alpha-adrenergic agonist producing peripheral vasoconstriction, increased blood pressure and decreased heart rate. Epinephrine and norepinephrine do not cross the blood-brain barrier.

Isoproterenol, an agonist of beta-adrenergic receptors, has a more specific action than epinephrine. It induces attacks in panic disorder patients but not in normal subjects. It does not cross the blood-brain barrier.

The major neurotransmitters involved in anxiety are nor-epinephrine, serotonin and gamma-aminobutyric acid (GABA).

The noradrenergic hypothesis stresses the role of hyperactivity of the central noradrenergic system in the occurrence of panic disorder. The noradrenergic hyperactivity in the locus ceruleus produces both psychic and somatic symptoms of anxiety. The theory stipulates that patients with panic disorder have a dysfunction of the noradrenergic system manifested by occasional hyperactivity of the system. It is known that most noradrenergic neurons are located in locus ceruleus of the pons. They establish multiple connections with the cerebral cortex, the limbic system, the thalamus, the hypothalamus, the brainstem and the spinal cord. The locus ceruleus receives information on potential dangers and activates the cerebral areas.

The serotonergic hypothesis focuses on the role of this system in the etiology of panic disorder. Most of serotonergic neurons are found in the raphe nucleus, in the caudal locus ceruleus, in the area postrema and in the interpeduncular area. The raphe nucleus is situated in the brainstem; it sends impulses to the cerebral cortex, the limbic system, the thalamus,

the hypothalamus, the locus ceruleus, the cerebellum and the spinal cord. Initially, serotonergic drugs may aggravate anxiety, as the anxiolytic effect appears only three to six weeks later; their therapeutic action is supposed to be biphasic.

The GABA-ergic hypothesis of panic disorder is based on the observation that benzodiazepines increase the activity of GABA-A receptors. Benzodiazepines have proven their efficacy in the treatment of anxiety, and high-potency benzodiazepines are used successfully in panic disorder.

In the etiology of anxiety disorders are involved also other neurotransmitters (histamine, acetylcholine, adenosine, cholecystokinin) psycho-neuroendocrinological aspects, genetic ones. The neuroanatomical basis of anxiety disorders is still a topic of considerable interest.

The locus ceruleus, the raphe nucleus, the limbic system and cerebral cortex (the frontal cortex) are all involved in the etiology of anxiety disorders.

Anatomical images of the human brain can be produced by the use of X-ray computed tomography (CT) or of magnetic resonance imaging (MRI). For exploring neuroanatomical aspects can be utilized positron emission tomography (PET), single photon emission computed tomography (SPECT), functional MRI, magnetic resonance spectroscopy (MRS).

Studies have shown that persons with an asymmetric increase of regional cerebral flow (more on the right side) in the parahippocampal area of the temporal lobe and in the inferior prefrontal areas are more susceptible to sodium lactate-induced panic attacks. MRIs performed in panic disorder patients indicate abnormalities of the right temporal lobe, especially cortical atrophy.

(Marinescu M, Udristoiu T, Podea D., Ciucu A, 2008, *Tulburarea depresiva si anxioasa-actualitati*, AIUS, ISBN 978-973-1780-97-9, Craiova)

## 5. Symptoms

The anxiety can take different aspects. It can be perceived as an inexplicable feeling of eminent death, as an unfounded and exaggerated worry from daily life (health of children, professional or financial problems, etc.) or an unjustified fear of certain situations (traveling by bus) of an activity (driving the car) or of an object (fear of sharp objects, of animals). Usually patients describe the following physical or psychical signs:

- excessive and unrealistic worries
- fear without a cause
- unreal fear about an unknown danger
- flash-backs of some past trauma
- compulsive behavior (rituals) as a way of minimize the anxiety
- shaking, muscular pain, sweating, nausea, tension, fatigue, palpitations, dry mouth, digestive discomfort, feeling of choking, heart pounding
- losing the ability to relax
- insomnia

Into the anxiety disorders are specified disorders that have anxiety as a principal symptom (panic disorder and generalized anxiety disorder) and disorders in which anxiety is secondary to cognitive routes and inadequate conduits (obsessive-compulsive disorder and phobic disorder). Also in anxiety disorders are described anxiety feelings as an abnormal response to different stress factors (adaptive disorders), psychological reactions to traumatic events (acute stress disorder and posttraumatic stress disorder).



In classic psychiatry, after the symptomatology was recognized, before a diagnose was established, the grouping of the symptoms in syndromes was mandatory. In this way, was defined the anxious syndrome that is encountered not only in different forms of anxiety disorders but also in others psychic and somatic illnesses.

Nowadays is considered that exists a clear separation of anxious syndromes in different anxious disorders. This can be exactly diagnosed but there are vary comorbidities between them and each one can complicate with depression and abuse or substance dependence.

In general medicine, in classic acception, the anxious syndrome can be encountered an a compound of clinic image of an organic illness, function of organic and toxicological causes. In actual acception according to DSM-IV-TR, secondary anxious symptoms to an organic illness corresponds to anxious disorder due to a general medical condition and anxious disorder substance induced ( see table 2). The correspondent in ICD-10 for this disorders if Organic anxious disorder (F06.4). (Marinescu M, Udristoiu T, Podea D., Ciucu A,2008, *Tulburarea depresiva si anxioasa- actualitati*, AIUS, ISBN 978-973-1780-97-9, Craiova)

Endocrinologic and metabolic disorders	dysfunction of the pituitary gland, thyroid, adrenals and parathyroid glands, changes in serum calcium, serum sodium and potassium, premenstrual syndrome, hypoglycemia
Cardiac diseases	Angina pectoris, arrhythmias, heart failure, arterial hypertension, hypovolemia, myocardial infarction, valvular heart disease
Respiratory diseases	asthma, respiratory failure, chronic obstructive pulmonary disease, pneumonia, pneumothorax, pulmonary edema, acute pulmonary embolism
Neurological disorders	brain neoplasms, brain injury, postcontuzionale syndromes, cerebrovascular disease, intracranial hemorrhage, migraine, encephalitis, cerebral syphilis, multiple sclerosis, epilepsy temporal, Wilson disease, Hungtington disease
Inflammatory and immune system diseases	systemic erythematosus lupus, rheumatoid arthritis, polyarthritis nodosa, temporal arteritis, anaphylactic shock
Carential states	pellagra, iron deficiency anemia, vitamin B12 deficiency
Secreting tumors	carcinoid syndrome, pheochromocytoma, insulinom
Intoxications	amphetamines and other sympathomimetics, anticholinergics, caffeine, theophylline, Yohimbine, cocaine, cannabis, hallucinogens
different substance withdrawal syndromes	alcohol withdrawal, hypertensive, caffeine, opioids, sedative / hypnotics

Table 2. Organic and toxic etiologies of anxiety syndrome

To recognize pathologic anxiety is necessary to establish if there is an organic, toxicological cause or is a psychic disorder. The differentiation is sometimes hard to be done, because the organism can react to anxiety through a somatic participation. (see table 3), the anxiety can be primary in psychic disorder or secondary ( organic, drug induced or toxic)

RESPIRATORY sensation of breathlessness or suffocation chest tightness tachypnea choking	CARDIOVASCULAR tachycardia palpitations precordial pain "sine materia" syncopate	MUSCULAR tremor muscle contractures muscle weakness startles muscle back pain
VEGETATIVE dry mouth pale face redness on skin "in cleavage" sweating Hot flashes	NEUROLOGICAL headache vertigo paresthesia visual illusions blurred vision hyperesthesia	GASTROINTESTINAL acceleration of intestinal transit cramps nausea vomiting abdominal pains

Table 3. Somatic symptoms of anxiety

6. Diagnostic criteria according to DSM-IV-TR

6.1 Panic attacks

is a discrete period of intense fear, anxiety, discomfort or apprehension during which at least four of the following 13 symptoms develop abruptly are exacerbated and reach a peak within 10 minutes of onset:

- Palpitations or tachychardia
- Sweating
- Tremor
- Sensation of dyspnea or smothering
- Feeling of choking
- Thoracic pain, constriction or discomfort
- Nausea or abdominal distress
- Sensation of dizziness, instability or fainting
- Derealization (feeling of unreality), or depersonalization (self-detachment)
- Fear of losing control or going crazy
- Fear of dying
- Paresthesias (numbness or tingling)
- Hot or cold flushes

6.2 Panic disorder without agoraphobia

- a. Both (1) and (2) have to be met:
  - 1. Unexpected recurrent panic attacks
  - 2. At least one of the attacks should be followed for a month (or several) by:
    - a) persistent concern for the recurrence of the panic attacks
    - b) worry about the implications or consequences of the panic attack (such as fear of losing control, of being seized by a heart attack or of going crazy)
    - c) significant modification in behavior related to panic attack
- b. Absence of agoraphobia

- c. Panic attacks are not a result of the direct physiological effects of a substance (as in the case of drug abuse, medication) or of a general medical condition (such as hyperthyroidism)
- d. Panic attacks are not caused by another mental disorder, such as social phobia (for instance occurring on exposure to social circumstances the patient is afraid of), specific phobia (caused by exposure to a specific phobic situation), obsessive-compulsive disorder (occurring for instance on exposure to dirt of an individual with an obsession about contamination), post-traumatic stress disorder (occurring in a response to a stimuli associated with a severe stressor) or separation anxiety disorder (in response to being separated from home or close relatives)

### 6.3 Panic disorder with agoraphobia

- a. Both (1) and (2) have to be met:
  - 1. Unexpected recurrent panic attacks
  - 2. At least one of the attacks should be followed for a month (or several) by:
    - a) persistent concern for the recurrence of the panic attacks
    - b) worry about the implications or consequence of the panic attack (such as fear of losing control, of being seized by a heart attack or of going crazy)
    - c) significant modification in behavior related to panic attack
- b. presence of agoraphobia
- c. Panic attacks are not a result of the direct physiological effects of a substance (as in the case of drug abuse, medication) or of a general medical condition (such as hyperthyroidism)
- d. Panic attacks are not caused by another mental disorder, such as social phobia (for instance occurring on exposure to social circumstances the patient is afraid of), specific phobia (caused by exposure to a specific phobic situation), obsessive-compulsive disorder (occurring for instance on exposure to dirt of an individual with an obsession about contamination), post-traumatic stress disorder (occurring in a response to a stimuli associated with a severe stressor) or separation anxiety disorder (in response to being separated from home or close relatives)

### 6.4 Agoraphobia

NOTE: Agoraphobia is not coded separately. The code is specific to disorders in which it occurs.

- a. The anxiety about being in places from which the escape might be difficult (or embarrassing) or where help would be inaccessible in the case of having an unexpected or situationally predisposed panic attack or panic-like symptoms. Agoraphobics are afraid of a set of characteristic situations such as being outside the home alone, being in a crowd or standing in a line, on a bridge, traveling in a bus, train or automobile.

NOTE: If the avoidance is limited to only one or a few specific situations the diagnoses considered will be specific phobia, while if the avoidance is limited to social situations, the diagnosis will be social phobia.

- b. The situation are avoided or endured with severe distress or with anxiety about recurrent panic attacks or panic-like symptoms, or else the presence of a companion is required.
- c. Anxiety or avoidance behavior are not caused by another mental disorder such as: social phobia, specific phobia, obsessive-compulsive disorders or separation anxiety disorder.

### 6.5 Agoraphobia without history of panic disorder

- a. The presence of agoraphobia related to fear of developing panic-like symptoms (e.g., dizziness or diarrhea).
- b. Criteria have never been met for Panic Disorder.
- c. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.
- d. If an associated general medical condition is present, the fear described in Criterion A is clearly in excess of that usually associated with the condition.

### 6.6 Specific phobia

- a. Marked and persistent fear that is excessive or unreasonable, cued by the presence or anticipation of a specific object or situation (e.g., flying, heights, animals, receiving an injection, seeing blood).
- b. Exposure to the phobic stimulus almost invariably provokes an immediate anxiety response, which may take the form of a situationally bound or situationally predisposed Panic Attack. Note: In children, the anxiety may be expressed by crying, tantrums, freezing, or clinging.
- c. The person recognizes that the fear is excessive or unreasonable. Note: In children, this feature may be absent.
- d. The phobic situation(s) is avoided or else is endured with intense anxiety or distress.
- e. The avoidance, anxious anticipation, or distress in the feared situation(s) interferes significantly with the person's normal routine, occupational (or academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.
- f. In individuals under age 18 years, the duration is at least 6 months.
- g. The anxiety, Panic Attacks, or phobic avoidance associated with the specific object or situation are not better accounted for by another mental disorder, such as Obsessive Compulsive Disorder (e.g., fear of dirt in someone with an obsession about contamination), Posttraumatic Stress Disorder (e.g., avoidance of stimuli associated with a severe stressor), Separation Anxiety Disorder (e.g., avoidance of school), Social Phobia (e.g., avoidance of social situations because of fear of embarrassment), Panic Disorder With Agoraphobia, or Agoraphobia Without History of Panic Disorder.

Specify type:

Animal Type

Natural Environment Type (e.g., heights, storms, water)

Blood-Injection-Injury Type

Situational Type (e.g., airplanes, elevators, enclosed places)

Other Type (e.g., fear of choking, vomiting, or contracting an illness; in children, fear of loud sounds or costumed characters)

### 6.7 Social phobia

- a. A marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others.

The individual fears that he or she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing.

Note: In children, there must be evidence of the capacity for age-appropriate social relationships with familiar people and the anxiety must occur in peer settings, not just in interactions with adults.

- b. Exposure to the feared social situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally predisposed Panic Attack.

Note: In children, the anxiety may be expressed by crying, tantrums, freezing, or shrinking from social situations with unfamiliar people.

- c. The person recognizes that the fear is excessive or unreasonable.

Note: In children, this feature may be absent.

- d. The feared social or performance situations are avoided or else are endured with intense anxiety or distress.
- e. The avoidance, anxious anticipation, or distress in the feared social or performance situation(s) interferes significantly with the person's normal routine, occupational (academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.
- f. In individuals under age 18 years, the duration is at least 6 months.
- g. The fear or avoidance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition and is not better accounted for by another mental disorder (e.g., Panic Disorder With or Without Agoraphobia, Separation Anxiety Disorder, Body Dysmorphic Disorder, a Pervasive Developmental Disorder, or Schizoid Personality Disorder).
- h. If a general medical condition or another mental disorder is present, the fear in Criterion A is unrelated to it, e.g., the fear is not of Stuttering, trembling in Parkinson's disease, or exhibiting abnormal eating behavior in Anorexia Nervosa or Bulimia Nervosa.

Specify if:

Generalized: if the fears include most social situations (also consider the additional diagnosis of Avoidant Personality Disorder)

## 6.8 Obsessive compulsive disorder

- a. Either obsessions or compulsions:

Obsessions as defined by (1), (2), (3), and (4):

1. recurrent and persistent thoughts, impulses, or images that are experienced, at some time during the disturbance, as intrusive and inappropriate and that cause marked anxiety or distress
2. the thoughts, impulses, or images are not simply excessive worries about real life problems
3. the person attempts to ignore or suppress such thoughts, impulses, or images, or to neutralize them with some other thought or action
4. the person recognizes that the obsessional thoughts, impulses, or images are a product of his or her own mind (not imposed from without as in thought insertion)

Compulsions as defined by (1) and (2):

1. repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the person feels driven to perform in response to an obsession, or according to rules that must be applied rigidly
2. the behaviors or mental acts are aimed at preventing or reducing distress or preventing some dreaded event or situation; however, these behaviors or mental acts either are not connected in a realistic way with what they are designed to neutralize or prevent or are clearly excessive



At some point during the course of the disorder, the person has recognized that the obsessions or compulsions are excessive or unreasonable. Note: This does not apply to children.

- b. The obsessions or compulsions cause marked distress, are time consuming (take more than 1 hour a day), or significantly interfere with the person's normal routine, occupational (or academic) functioning, or usual social activities or relationships.
- c. If another Axis I disorder is present, the content of the obsessions or compulsions is not restricted to it (e.g. preoccupation with food in the presence of an Eating Disorder; hair pulling in the presence of Trichotillomania; concern with appearance in the presence of Body Dysmorphic Disorder; preoccupation with drugs in the presence of a Substance Use Disorder; preoccupation with having a serious illness in the presence of Hypochondriasis; preoccupation with sexual urges or fantasies in the presence of a Paraphilia; or guilty ruminations in the presence of Major Depressive Disorder).
- d. The disturbance is not due to the direct physiological effects of a substance (e.g. a drug abuse or medication abuse) or a general medical condition.

Specify if:

With Poor Insight: if, for most of the time during the current episode, the person does not recognize that the obsessions and compulsions are excessive or unreasonable

## 6.9 Posttraumatic stress disorder

- a. The person has been exposed to a traumatic event in which both of the following were present:
  1. the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
  2. the person's response involved intense fear, helplessness, or horror.

Note: In children, this may be expressed instead by disorganized or agitated behavior

- b. The traumatic event is persistently reexperienced in one (or more) of the following ways:
  1. recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. Note: In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.
  2. recurrent distressing dreams of the event.

Note: In children, there may be frightening dreams without recognizable content.

3. acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated).

Note: In young children, trauma-specific reenactment may occur.

4. intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
  5. physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
- c. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:
    1. efforts to avoid thoughts, feelings, or conversations associated with the trauma
    2. efforts to avoid activities, places, or people that arouse recollections of the trauma

3. inability to recall an important aspect of the trauma
4. markedly diminished interest or participation in significant activities
5. feeling of detachment from others
6. restricted range of affect (e.g., unable to have loving feelings)
7. sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life)
- d. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:
  1. difficulty falling or staying asleep
  2. irritability or outbursts of anger
  3. difficulty concentrating
  4. hypervigilance
  5. exaggerated startle response
- e. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than 1 month.
- f. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

Acute: if duration of symptoms is less than 3 months

Chronic: if duration of symptoms is 3 months or more

Specify if:

With Delayed Onset: if onset of symptoms is at least 6 months after the stressor

#### 6.10 Acute stress disorder

- a. The person has been exposed to a traumatic event in which both of the following were present:
  - (1) the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
  - (2) the person's response involved intense fear, helplessness, or horror
- b. B. Either while experiencing or after experiencing the distressing event, the individual has three (or more) of the following dissociative symptoms:
  1. a subjective sense of numbing, detachment, or absence of emotional responsiveness
  2. a reduction in awareness of his or her surroundings (e.g., "being in a daze")
  3. derealization
  4. depersonalization
  5. dissociative amnesia (i.e., inability to recall an important aspect of the trauma)

The traumatic event is persistently reexperienced in at least one of the following ways: recurrent images, thoughts, dreams, illusions, flashback episodes, or a sense of reliving the experience; or distress on exposure to reminders of the traumatic event.
- c. Marked avoidance of stimuli that arouse recollections of the trauma (e.g., thoughts, feelings, conversations, activities, places, people).
- d. Marked symptoms of anxiety or increased arousal (e.g., difficulty sleeping, irritability, poor concentration, hypervigilance, exaggerated startle response, motor restlessness).
- e. The disturbance causes clinically significant distress or impairment in social, occupational or other important areas of functioning or impairs the individual's ability to pursue some necessary task, such as obtaining necessary assistance or mobilizing personal resources by telling family members about the traumatic experience.

- f. The disturbance lasts for a minimum of 2 days and a maximum of 4 weeks and occurs within 4 weeks of the traumatic event.
- g. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition, is not better accounted for by Brief Psychotic Disorder, and is not merely an exacerbation of a preexisting Axis I or Axis II disorder.

### 6.11 Generalized anxiety disorder

- a. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
- b. The person finds it difficult to control the worry.
- c. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past 6 months), Note: Only one item is required in children.
  - 1. restlessness or feeling keyed up or on edge
  - 2. being easily fatigued
  - 3. difficulty concentrating or mind going blank
  - 4. irritability
  - 5. muscle tension
  - 6. sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)
- d. The focus of the anxiety and worry is not confined to features of an Axis I disorder, e.g., the anxiety or worry is not about having a Panic Attack (as in Panic Disorder), being embarrassed in public (as in Social Phobia), being contaminated (as in Obsessive Compulsive Disorder), being away from home or close relatives (as in Separation Anxiety Disorder), gaining weight (as in Anorexia Nervosa), having multiple physical complaints (as in Somatization Disorder), or having a serious illness (as in Hypochondriasis), and the anxiety and worry do not occur exclusively during Posttraumatic Stress Disorder.
- e. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- f. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism) and does not occur exclusively during a Mood Disorder, a Psychotic Disorder, or a Pervasive Developmental Disorder.

### 6.12 Anxiety disorder due to

*[Indicate the General Medical Condition]*

- a. Prominent anxiety, Panic Attacks, or obsessions or compulsions predominate in the clinical picture.
- b. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct physiological consequence of a general medical condition.
- c. The disturbance is not better accounted for by another mental disorder (e.g., Adjustment Disorder With Anxiety in which the stressor is a serious general medical condition).
- d. The disturbance does not occur exclusively during the course of a delirium.

- e. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

With Generalized Anxiety: if excessive anxiety or worry about a number of events or activities predominates in the clinical presentation

With Panic Attacks: if Panic Attacks predominate in the clinical presentation

With Obsessive-Compulsive Symptoms: if obsessions or compulsions predominate in the clinical presentation

Coding note: Include the name of the general medical condition on Axis I

Anxiety Disorder Due to Pheochromocytoma, With Generalized Anxiety

Diagnostic criteria for Substance-Induced Anxiety Disorder

- a. Prominent anxiety, Panic Attacks, or obsessions or compulsions predominate in the clinical picture.
- b. There is evidence from the history, physical examination, or laboratory findings of either (1) or (2):
  - 1 the symptoms in Criterion A developed during, or within 1 month of, Substance Intoxication or Withdrawal
  - 2 medication use is etiologically related to the disturbance
- c. The disturbance is not better accounted for by an Anxiety Disorder that is not substance induced. Evidence that the symptoms are better accounted for by an Anxiety Disorder that is not substance induced might include the following: the symptoms precede the onset of the substance use (or medication use); the symptoms persist for a substantial period of time (e.g., about a month) after the cessation of acute withdrawal or severe intoxication or are substantially in excess of what would be expected given the type or amount of the substance used or the duration of use; or there is other evidence suggesting the existence of an independent non-substance-induced Anxiety Disorder (e.g., a history of recurrent non-substance-related episodes).
- d. The disturbance does not occur exclusively during the course of a delirium.
- e. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: This diagnosis should be made instead of a diagnosis of Substance Intoxication or Substance Withdrawal only when the anxiety symptoms are in excess of those usually associated with the intoxication or withdrawal syndrome and when the anxiety symptoms are sufficiently severe to warrant independent clinical attention.

Specify if:

With Generalized Anxiety: if excessive anxiety or worry about a number of events or activities predominates in the clinical presentation

With Panic Attacks: if Panic Attacks predominate in the clinical presentation With Obsessive-Compulsive Symptoms: if obsessions or compulsions predominate in the clinical presentation

With Phobic Symptoms: if phobic symptoms predominate in the clinical presentation

Specify if :

With Onset During Intoxication: if the criteria are met for Intoxication with the substance and the symptoms develop during the intoxication syndrome

With Onset During Withdrawal: if criteria are met for Withdrawal from the substance and the symptoms develop during, or shortly after, a withdrawal syndrome

(American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, American Psychiatric Association, 2000, ISBN 0-890-12-025-4, Washington, DC)

## 7. Evaluation

A special sub-chapter is dedicated to the psychological assessment of anxiety disorders (structured or semi-structured interviews, psychometric tests).

The diagnosis of anxiety disorders is established mainly through clinical interviews. We will therefore review some aspects related to interviews, without however going into the specifics of technique, methods, time influencing factors circumstances or setting.

The interview usually is structured or semi-structured. The interview may be free or standardized. Some of the best standardized interviews are: SCID, SADS, DIS, PSE.

Generally, in evaluation of anxiety disorders is used psychometric assessment having a diagnostic role, helping the clinician to establish a positive or differential diagnosis and it evaluates progress during therapy.

The tests used in anxiety may be objective and projective. Objective tests are: MMPI, MCMI, ADIS-R, HAM-A, STAI, SADS-LA, API, Cognitive Questionnaire for Agoraphobia, Daily Activity Form, Zung, Beck and Sheehan anxiety scales and so on.

Projective tests evaluate the individual's personality in its complexity assessing so the level of current anxiety. Some of this tests are the Rorschach, TAT, SCT, Draw-a-Person.

## 8. Treatment

Treatment of anxiety disorder is carried out in several stages:

- Acute phase. The goal of treatment in this phase is a rapidly reduce symptoms and allow better control, if not a complete remission of panic attacks. It has a duration of 4 to 6 weeks with benzodiazepines, but usually takes 2 to 3 months of treatment with tricyclic antidepressants, SSRIs or monoamine oxidase inhibitors (MAOIs), time in which the appropriate dose is reached. If improvement does not occur within 8 to 10 weeks after starting pharmacotherapy, requires a reassessment of drug therapy.
- Stabilization phase. Its purpose is to maintain and expand the response obtained in the acute phase; and extend is focused specifically on improving the avoidant behavior. Stabilization phase is between the second and sixth months of treatment, dosage of medication is adjusted to obtain maximum clinical response with minimal side effects.
- Maintenance phase. Includes 6-24 months of treatment, the main purpose being to maintain and improve the socio-professional rehabilitation. In this phase, the patient returns to a normal life, both professionally and socially. Drug doses can be reduced, taking care not won away in the early symptomatic phase.
- The discontinuation phase. In general, most authors agree that 12 to 24 months after drug therapy can be stopped. Stopping will be a gradual decline, particularly slow, which will stretch over two to four months. So gradual reduction aims at preventing the occurrence of benzodiazepine withdrawal symptoms, and also enables temporary readjustment of dosage for panic recurrence of complaints.

A great number of therapeutic agents have proved their efficacy in anxiety disorders. For didactic purposes, we shall attempt a systematic presentation in what follows:

Antidepressants:



- tricyclics
- serotonin specific reuptake inhibitors (SSRI)
- monoamine oxidase inhibitors (MAOI)
- recently introduced agents –venlafaxine
- nefazodone
- High-potency benzodiazepines:
  - alprazolam
  - Clonazepam

Other agents

None of this drug groups has been proven to be more efficient than the others in the treatment of anxiety disorders, each having both advantages and disadvantages. Tricyclics, for instance, can be described in a single dose to be taken in the evening before going to bed, but improvements can only appear 6 to 12 weeks later, and in the most cases side effects are difficult to tolerate. MAOIs also have several potential side effects and are accompanied by severe dietary restrictions. SSRIs develop fewer side effects and are safer than tricyclics, owing to their lower toxicity giving rise to a reduced mortality rate in overdose; as is the case for tricyclics, however, clinical improvement only becomes apparent after 6 to 12 weeks of treatment. Benzodiazepines act faster (one to two weeks), they have a significant effect on anticipatory anxiety, they are more easily tolerated by patients, but due to their short duration of acting the administration of several daily doses is required, and they produce dependence and withdrawal syndromes(see Table 4).

Advantages	Disadvantages
<ul style="list-style-type: none"><li>• rapid effect</li><li>• safety in overdosing</li><li>• improvment in sleep quality</li></ul>	<ul style="list-style-type: none"><li>• sedative effect</li><li>• balance disorders</li><li>• memory disorders<ul style="list-style-type: none"><li>• potentiating of alcohol effects</li><li>• depresogen effect</li><li>• addictive potential</li><li>• Paradoxical reactions</li></ul></li></ul>

Table 4. Advantajes and disadvantages of benzodiazepine use in anxiety therapy

Nowadays, the most widely used drugs are SSRIs. In the tables below we present the efficacy of SSRIs in different types of anxiety disorders, their side effects, the dosage and the advantages and disadvantages of SSRI versus Venlafaxine (see table 5, 6, 7).

8.1 Panic disorder

Pharmacological and psychotherapeutic treatment in most cases leads to a dramatic improvement of agoraphobic and panic disorder symptoms. Goals of treatment are:

- reducing the number and intensity of panic attacks
- reduction of anticipatory anxiety
- treatment of comorbid disorders
- identification and treatment of agoraphobia

ISRS		Anxiety disorders				
Generic name	Trade name	PD	OCD	SAD	GAD	PTSD
Paroxetină	ALS-Paroxetin, Arketis, Paroxat, Paroxetin Stada, Paroxetin Teva, Paxetin, Rexetin, Seroxat	X	X	X	X	X
Fluvoxamină	Fevarin, Fluvoxamin Stada, Fluvoxamine Teva	X	X	X		
Fluoxetină	Fluohexal, Fluoxetine, Fluoxin, Fluran, Magrilan, Prozac	X	X			
Sertralina	Asentra, Serlift, Sertralin, Sertralin Sandoz, Sertralina Dr. Reddy's, Stimuloton, Zoloft	X	X	X		X
Citalopram	Citalec, Citalomerk, Citalopram Stada, Citaloran, Dalsan, Linisan	X	X	X	X	
Escitalopram	Cipralex	X	X	X	X	

Table 5. ISRS efficacy in anxiety disorders.

Advantages	Disadvantages
<ul style="list-style-type: none"><li>effectiveness in all anxiety disorders</li><li>antidepressant effect</li><li>safety in overdose</li><li>reduced weight gain</li></ul>	<ul style="list-style-type: none"><li>delayed onset of therapeutic effect</li><li>early treatment may increase anxiety</li><li>Gastrointestinal side effects especially at the beginning of treatment</li><li>Sexual dysfunction is maintained throughout treatment</li></ul>

Table 6. Advantages and disadvantages of Venlafaxine and ISRS use in anxiety disorders.

Citalopram	Fluoxetine	Fluvoxamine	Paroxetine	Sertraline
Headache	Nausea	Nausea	Nausea	Nausea
Nausea	Headache	Insomnia	Sedation	Headache
Dry mouth	Nervousness	Headache	Headache	Diarrhea
Insomnia	Insomnia	Dry mouth	Dry mouth	Sexual dysfunction
somnolence	Anxiety	somnolence	fatigue	insomnia

Table 7. The most common side effects of SSRIs

8.1.1 Pharmacological treatment

Tricyclic antidepressants

The first study demonstrated the efficacy of imipramine in TP therapy was developed by Klein and was published in 1964. This finding was confirmed by a further 15 controlled

studies. Given the equivalence of tricyclic antidepressants is very likely, although there are few controlled studies, that other than tricyclic imipramine have similar effectiveness. In most trials, tricyclic antidepressant average dose was approximately 150 mg / day and maximum dose of 300 mg per day. Selective serotonin reuptake inhibitors (SSRIs). The main goals of therapy with an SSRI is to reduce the intensity and frequency of panic attacks, reduce anticipatory anxiety and to treat depression associated. Also, appropriate therapy leads to reduction of phobic avoidance. For all SSRIs are currently available randomized controlled trials demonstrating efficacy of this class compared with placebo. TP patients who are prescribed an SSRI, may appear during the first two weeks of treatment an increase in anxiety, which is why it is recommended that therapy with low doses: 5-10 mg for fluoxetine, 25 mg for sertraline, 10 mg 50 mg paroxetine and fluvoxamine. It is generally accepted that the effect of therapy with an SSRI does not occur until after about four weeks, 8-12 weeks is needed to install full effect.

**Benzodiazepines**

Alprazolam was the first treatment approved by the FDA for the treatment of PD and although effective in relieving symptoms quickly, it is difficult to cut the majority of patients. Alprazolam dose for PD therapy is 5-6 mg / day. Studies have been published suggesting that other benzodiazepines (especially diazepam, clonazepam and lorazepam), administered in doses equivalent, may be as effective as alprazolam in the treatment of TP(Table\*). Due to the risk of dependence and tolerance that it involves therapy with benzodiazepines, benzodiazepines are currently recommended only as short-term therapy. (see table 8, 9)

Generic name	Trade name	Equivalent dose	Daily usual dose for adults and regimen
clonazepam	Rivotril	0,5	1-6mg/day, 2 times/day
diazepam	Diazepam	5	4 - 40 mg/day 2-4 times/day
alprazolam	Xanax, Alprazolam LPH, Frontin, Prazolex, Neurol SR (preparat retard)	0,25	0,5 - 10 mg/day 2-4 times/day
lorazepam	Anxiar	1	1 - 6 mg/day 3 times/day
oxazepam		15	30 - 120 mg/day 3 - 4 times/day
clordiazepoxid		10	10 - 150 mg/day 3-4 times/day
clorazepat	Tranxene	7,5	15 - 60 mg/day 2- 4 times/day
prazepam		10	20 - 60 mg/day 3- 4 times/day
halazepam		20	60 - 160 mg/day 3- 4 times/day

Table 8. Benzodiazepine used in anxiety treatment (Ballenger J,2005, Benzodiazepine receptor agonist and antagonist, Kaplan and Sadock’s Comprehensive Textbook of Psychiatry, Eight edition, Lippincott Williams & Wilkins,ISBN 0-7817-3434-7, Philadelphia,Baltimore, New-York, London, Buenosaires, Hong-Kong, Sydney, Tokyo).

anxiety irritability insomnia fatigue headache spasms or muscular pain vertigo tremors sweating concentrating difficulty nausea sau loss of appetite * depression * depersonalization, derealisation * high senzorial perception (smell, light, taste, feel) * abnormal perception sensation of movement *
<ul style="list-style-type: none"><li>• symptoms that represent more likely a withdrawal syndrom rather than exacerbation or reaparance of initial anxiety symptoms</li></ul>

Table 9. Symptoms frequently observed during benzodiazepine withdrawal.

Also proved useful venlafaxine (mean dose 150 mg / day), nefazodone (300-500 mg / day), mirtazapine, gabapentin and pregabalin. In cases resistant to SSRIs or augmentation therapy have proven useful and MAOIs.

8.1.2 Psychotherapy

Should be encouraged in all patients participating in cognitive-behavioral psychotherapy sessions, which is recognized as the most effective psychotherapeutic techniques for patients with PD with or without agoraphobia. Can be used in combination with pharmacotherapy.

8.2 Generalized anxiety disorder

Currently we have a wide choice of treatment of GAD, both psychopharmacology and psychotherapy. However, although patients with GAD are frequent users of medical services, only about 25% of people who actually suffer from this disorder are treated.

8.2.1 Pharmacological treatment

Benzodiazepines

A long period of time, GAD has been treated with benzodiazepines. Several double-blind placebo controlled clinical trials have demonstrated the efficacy of certain benzodiazepines (diazepam, clorazepat, alprazolam, lorazepam) in the acute treatment (3-6 months) of GAD, but long-term efficacy (6 months - 1 year) is less robust. Primary anxiolytic effect of benzodiazepines is mainly aimed at somatic symptoms of GAD, leaving cognitive symptoms, such as concern, partly unresolved. Moreover, benzodiazepines do not reduce depressive symptoms, while often present in these individuals. Main advantages of benzodiazepines in the treatment of GAD are fast effect, safety in overdose and rapid improvement of the quality of sleep.

In general, different benzodiazepines have equivalent efficacy in the treatment of GAD. Approximately 35% of patients obtain a marked benefit, and 40% achieved a moderate improvement. The response is rapid, usually within the first week. Equivalent to 15-25 mg daily doses of diazepam produced an adequate therapeutic effect (see Table 10).

Benzodiazepine	Recommended daily dose (mg)
Alprazolam	0,75 - 10
Clordiazepoxid	5 - 100
Clorazepat	15 - 60
Diazepam	4 - 40
Halazepam	60 - 160
Lorazepam	1 - 10
Oxazepam	30 - 120
Prazepam	20 - 60

Table 10. Recommended daily dose

Patients treated with benzodiazepines have a recurrence rate of symptoms two times higher than patients treated with medication nonbenzodiazepinic. Although benzodiazepines have a faster onset of action 3-6 weeks of treatment efficacy is similar to that of antidepressants or buspirone.

Due to the risk of physical dependence, rebound anxiety upon discontinuation of treatment and adverse effects, benzodiazepines are now considered as second choice treatment or as adjuvant agents in short-term treatment with other compounds.

**Buspirone**

Initial studies on the efficacy of buspirone in the treatment of GAD have suggested that buspirone would be an alternative to benzodiazepines in treating anxiety, with some specificity for psychiatric symptoms of the disorder. However, more recent studies questioning its effectiveness in the treatment of GAD. Some authors believe that patients often discontinue treatment with buspirone than patients treated with benzodiazepines. Not sure if this is due to decreased efficacy of this compound over time.

Buspirone effect occurs in about 2-3 weeks. Doses useful are between 30 mg and 60 mg, although sometimes they even used a dose of 90 mg. At doses below 30 mg, buspirone is not superior to placebo. The effect is weaker on patients previously treated with benzodiazepines.

**Selective serotonin reuptake inhibitors (SSRIs)**

Currently, data from the literature on the effectiveness of SSRIs is increasing. Most studies have focused on paroxetine (20-50 mg / day), which is currently approved by the FDA for the treatment of GAD. Positive results have been published and fluvoxamine, sertraline (50-150 mg/day) and escitalopram (10-20 mg/day). So far, three randomized placebo controlled



studies have demonstrated the efficacy of escitalopram in the treatment of GAD, which is why escitalopram is approved by the FDA for the treatment of GAD.

It was suggested that the effectiveness of SSRIs in the treatment of GAD was due, as in depression or other anxiety disorders, normalizing dysfunctional activity in certain neuroanatomic circuits involved in the pathophysiology of GAD.

### **Venlafaxine**

Several studies have demonstrated venlafaxine (extended-release form) efficacy compared with placebo, in reducing somatic and psychological symptoms specific to TAG, both in acute treatment and long term, venlafaxine was approved by the FDA for the treatment of GAD. Doses up to 150 mg/day are needed for symptom control.

Antidepressants in the treatment of GAD have shown improvement in joint symptoms in about 2-4 weeks and, unlike benzodiazepines, mainly improves psychiatric symptoms of anxiety. Because anxious patients are particularly sensitive to the activating effects of some antidepressants, it is generally recommended that treatment be started with half the dose recommended for treatment of depression, with dose titration in 1-2 weeks. The optimal dose of antidepressant for the treatment of GAD is similar to that used in the treatment of depression.

Beta blockers can be used with high efficacy in anxious patients with cardio vascular symptoms; atenolol is preferred because it has less bronchoconstrictor effect. It is used for short periods of time associated with benzodiazepines.

Limited efficacy has riluzole also, a antiglutamatergic compound and pregabalin and tiagabine. In patients refractory to treatment with SSRIs, can be augmented with olanzapine, ziprasidone or risperidone.

### **Psychopharmacological treatment guide**

- Antidepressants (SSRIs and venlafaxine), are now considered first-line therapy in the GAD treatment because of their proven efficacy, the possibility of concomitant comorbid depression often, lack of dependence, potential and favorable profile of adverse effects.
- buspirone is currently indicated for patients with a history of substance abuse that have not responded or have not tolerated treatment with antidepressants.
- The use of benzodiazepines should be limited to short-term administration due to the potential development of dependency.
- In case of lack of response to treatment given in appropriate dose and for a sufficient length of time, a rational approach would be a therapy change from another class. When this event does not get an adequate response could be given a combination of two drugs from different classes.
- Currently there is insufficient data on treatment duration for GAD after getting a favorable response. Relapse rates are significant if medication is discontinued in the early months after obtaining a response and it is not known at what point the risk of relapse is low enough to try stopping the medication. Since GAD tends to be chronic and often complicated by depression, the psychiatrist must be careful discontinuing of treatment. Some authors have suggested that patients should be treated with the lowest effective dose and for stopping medication reviewed every six months. At present, it is

considered that treatment should be continued for another 6 months to a year after remission of symptoms.

### 8.2.2 Psychotherapy

The most intensively studied modality of psychotherapy for GAD is cognitive-behavioral psychotherapy addressed to intolerance of uncertainty and danger, associated with concerns perceived by this patients as uncontrollable. Cognitive-behavioral psychotherapy has demonstrated efficacy in controlling symptoms, in both short and long term, associated with a low rate of relapse.

### 8.3 Specific phobias

Phobia, as the central symptom of phobic disorder, is defined as a persistent and irrational fear to specific stimuli. Exposure to these stimuli triggers an intense anxiety response (suggesting the panic attack) and the development of avoidance behavior. Phobias are classified as:

- Specific phobias
- agoraphobia
- social phobia.

We present only the specific phobias; agoraphobia and social phobia being presented separately.

While behavioral therapy is the main method of treatment for specific phobias that affect quality of life and interferes with daily functioning, studies have shown the efficacy of SSRIs in the treatment of phobias. Recent studies have demonstrated the efficacy of combining pharmacological treatment (especially the D-cycloserine dose of 50 mg/day) with psychotherapy.

### 8.4 Obsessive compulsive disorder (OCD)

Obsessive Compulsive Disorder (OCD) is an anxiety disorder characterized by the appearance of obsessive ideas and compulsive behaviors, and significantly affects quality of life. It is a chronic disorder with a typical evolution, with periods of improvement which alternate with periods of rebound symptoms.

OCD is likely psychological disorder for which the last 20 years of psychopharmacological and psychotherapeutic treatment have been most progressive. OCD anxiety disorder is probably the most difficult to treat, while having the highest rate of resistance to treatment. Modern treatment of OCD consists of pharmacotherapy combined with cognitive-behavioral therapy.

The goal of treatment is to reduce symptoms and improve patients functioning in society, so that the patient have a normal life. A modest proportion of patients will achieve a complete release of symptoms.

Before prescribing drug therapy must take into account the following steps:

- assess the awareness that obsessions and compulsions are excessive and unjustified
- Assessment of comorbid conditions: affective disorders, other anxiety disorders, substance abuse, personality disorder
- identifying and exploring the patient's symptoms
- measurement of severity at baseline using the Yale-Brown scale

- patient and family education on OCD and its treatment

#### 8.4.1 Pharmacological treatment

Of all the classes of drugs used in psychiatry, serotonin reuptake inhibitors are by far the most effective in treating OCD, as first line therapy in the treatment of this disorder. Of this group of drugs are clomipramine - tricyclic antidepressant (TCA) - and selective serotonin reuptake inhibitors (SSRIs) - fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram and escitalopram. Although the response to treatment does not necessarily imply remission of symptoms, one can obtain a substantial improvement in quality of life. Among patients treated with SSRIs, 40 - 60% will have a good response and very good.

The therapeutic effect of SSRIs are of particular interest because, from a therapeutic perspective, OCD appears to be a single disorder. From numerous studies on the treatment of OCD is clear that only antidepressants with a specific action on the serotonin system have demonstrated efficacy. The efficacy of SSRIs in treating OCD does confirm that serotonin may be a specific condition. Unlike other mental disorders, the placebo response rate is typically low.

Clomipramine was the first effective treatment for OCD treatment. Its beneficial effect was seen in 60 years, but its effectiveness has been clearly demonstrated in studies compared with placebo in 80 years. Was also shown to have a beneficial effect in both adults and children. The consistency with which its effect was confirmed in studies anti-obsessive even small scale is a measure of the robustness of the effect. Positive results are in contrast to clomipramine with results for other tricyclic antidepressants have been tested for a possible positive effect, but without success. The dose used is: clomipramine 200-250 mg/day, which provides a clear antiobsessional effect in 4-6 weeks. Starting dose (25 mg/day given vesperal) will be increased gradually by 25 mg every four days or 50 mg weekly until reach maximum dose. If patients can not tolerate adverse effects (dry mouth, sedation, tremor, nausea and abnormal ejaculation), the administered dose will be 150-200 mg/day (Clomipramine Collaborative Study Group, 1991). For nonresponsive or multiple adverse effects cases can be used clomipramine i.v., a equivalent dose, with antiobsessional effect obtained in 4-5 days.

Given that there are currently no studies that compare the effectiveness of SSRIs in treating OCD, the choice of a particular SSRI should take into account the adverse effect profile, potential interactions with other drugs, pharmacokinetic properties and personal experience of each physician. In most cases the use of higher doses than those needed to treat depression were more likely to produce better therapeutic effect. If one starts with a lower dose patients should be reassessed and the dose should be increased if the response is not satisfactory. With higher doses, we can expect more side effects. The problem of adverse effects is extremely important because the negative influence on adherence to treatment, and efficacy also. Clomipramine usefulness is limited by side effects typical of tricyclic antidepressants.

Long-term studies conclusion is that SSRI efficacy is maintained. If treatment is interrupted, a considerable number of patients will relapse. For this reason, treatment should be followed for long periods of time. It was very clear that the antiobsessive efficacy of clomipramine and SSRIs is independent of their antidepressant activity. In this regard, OCD resembles other non-affective disorders such as panic disorder, bulimia, enuresis, migraine, chronic neuropathic pain, the tricyclic antidepressants are effective in the absence of depression.

A significant proportion of patients with OCD and depressive symptoms have been marked. From a therapeutic standpoint it is important to note that depressive symptoms associated with OCD have the same therapeutic specificity and OCD symptoms. Depressive symptoms do not respond to antidepressants that have a strong activity on the serotonin system. Symptoms improve in the same time with OCD symptoms only with anti-obsessive treatment. It is considered that depressive symptoms in people in which it appears, is a part of the TOC and not a secondary disorder.

The most important predictor of a possible negative response is early onset. The presence of a borderline type of personality disorder, schizotypal or avoided also have a negative predictive role. Also it was found that the severity, duration of disorder, gender, age and type of symptoms have no predictive value in this respect.

Recent studies (Denys et al., 2004, Grossman and Hollander, 1996) recommends the use of venlafaxine (a selective inhibitor of serotonin and norepinephrine reuptake) at a dose of 37.5 to 225 mg/day, maximum dose is 375 mg/day (March et al., 1997).

### Treatment guide

1. Treatment of choice is represented by an SSRI. Principles of treatment:
  - effective doses to treat OCD are generally higher than those used to treat depression;
  - Many patients notice a clear benefit after about six weeks of treatment, lack of efficacy during this period should not be viewed as a discouraging sign;
  - it takes several months, half a year, even more to achieve maximum response;
  - patients not responding to low doses of SSRIs may respond to higher doses;
  - treatment with an SSRI should be followed at least 10-12 weeks, including at least 6 weeks at maximum tolerated dose, before being replaced with another SSRI if the ineffectiveness of the former;
  - patients who have never received treatment with SSRIs have a greater likelihood of response to treatment than patients who have received treatment with SSRIs, without obtaining a significant improvement in symptoms;
  - SSRIs are better tolerated than clomipramine, all SSRIs are well tolerated by most patients, side effects are usually mild
  - Because we can not predict which of the SSRIs to be effective in a given patient often requires a number of attempts to find the right medicine;

If a patient treated with an SSRI does not tolerate appropriate dose or does not achieve a clinical response to a dose at the upper limit of the recommended therapeutic dose, the change of treatment with another SSRI is recommended, since there is evidence that patients that do not respond to a particular SSRI, often respond to another SSRI. Also to be considered clomipramine administration after trying unsuccessfully of one or more SSRIs. As with SSRIs, to determine the efficacy, increased doses should be administered, if tolerated, for 10-12 weeks.
2. In case of obtaining only a partial response to the second SSRI or no response to a third SSRI, augmentation is useful to test the therapeutic effect by combining SSRIs with other drugs.
3. Even if other compounds were tried to be used for this purpose - buspirone (20-60 mg/day), lithium (300-600 mg/day), gabapentin (300-2400 mg/day), inositol (16-18 mg/day), L-tryptophan (4-6 g/day), fenfluramine (20-60 mg/day), topiramate (250

mg/day) - only small doses of risperidone (1-2 mg 2 times/day) and pindolol ( 2.5 mg three times daily) have proved effective in double-blind comparative studies (Jenike and Rauch, 1994; Rasmussen, Eisen and Pato, 1993; Piccinelli et al., 1995, Saxena et al., 1996).

4. Clonazepam that has serotonergic action too, has proved to be effective as monotherapy in a double blind study. However, there were presented cases in which clonazepam augmentation was beneficial in cases resistant to treatment. For this reason, clonazepam can be a useful option that can be taken into account in some cases requiring augmentation.
5. There is evidence that the beneficial effects of treatment with clomipramine and SSRIs are maintained throughout treatment. Patients should be encouraged to continue treatment with the same dose with clinical response was obtained for periods of at least one year after they get this response. Discontinuation should be achieved by very slow gradual decrease in dosage (e.g, lowering the dose by 20-30% every 6-8 weeks).

#### **8.4.2 Psychotherapy**

For a long time it was considered that psychoanalysis would be effective in treating OCD. However, there are insufficient data to support the usefulness of the techniques of psychotherapy. Cognitive behavioral psychotherapy is the most frequently used psychological treatment for OCD.

Research in recent years have shown that behavioral therapy technique of exposure and response prevention (exposure and response prevention, to - ERP) is an extremely effective therapy for OCD in adults and children.

#### **8.5 Social anxiety disorder (social phobia)**

The initial problem in the treatment of SAD is to identify the disorder. Many patients affected by the SAD does not realize that they have a condition that is treatable. They consider their symptoms as extreme shyness or as an unpleasant feature of their personality, so they have to be convinced that a long-term treatment may be useful.

##### **8.5.1 Partial form treatment**

Partial form presents an unsatisfactory response to drug therapy, most appropriate treatment being behavioral psychotherapy in vivo exposure. Specific social phobias such as fear of speaking in public, respond quite well to  $\beta$  blockers drug administration, although most data come from isolated cases. They must be administered several hours before the performance. It is used a dose of 20 mg propranolol, atenolol dose of 50 mg.

##### **8.5.2 Generalized form treatment**

###### **Pharmacological treatment**

Only in recent years psychopharmacological treatment has been accepted by clinicians as a therapeutic option for SAD. In the 80s, when they began studying for the medical treatment of SAD, many clinicians regarded SAD as a personality disorder, which is why it was not considered appropriate psychopharmacological treatment.

Selective serotonin reuptake inhibitors (SSRIs) are effective antidepressants, widely used, which have a positive effect on depression and anxiety in the different anxiety disorders.



The class of drugs that has been the most extensively studied for TAS. Paroxetine, fluvoxamine, sertraline and escitalopram were studied in double-blind placebo for generalized form of SBP, demonstrating their effectiveness in treating this disorder.

Among SSRIs, paroxetine is the most studied, the first SSRI approved for the treatment of social phobia by the FDA. Preferred dose of paroxetine seems to be 20-40 mg / day. Today and sertraline has received approval from the FDA for the same indication. Because efficacy and safety of SSRIs are considered first-line treatment for SBP. Since about 60-70% respond to treatment with an SSRI, it is clear the need to expand and diversify ways of treatment.

Oxidase inhibitors (MAOIs) were the first drugs with proven efficacy in the treatment of TAS. Dietary restrictions and the many troublesome side effects is a significant disadvantage compared to SSRIs, which are much better tolerated. However, MAOIs can be used in case of resistance to other safer ways of treatment. Moclobemide, a reversible inhibitor of monoamine oxidase A, has proven effective in the treatment of SBP in most studies.

Among benzodiazepines, clonazepam alone is demonstrated efficacy in a double-blind study. Clonazepam has the advantage of twice daily administration and a lower potential than other benzodiazepines to be misused. However, clonazepam as monotherapy because of adverse reactions is not considered first-line treatment. Therapeutic effects appear quite quickly, with greater efficacy in less severe cases. It may be useful as an adjunctive therapy in patients with a high level of anxiety, but its use should be limited to initial clonazepam period of treatment. Used as adjunctive therapy could be an alternative in refractory cases.

Venlafaxine, a selective inhibitor of serotonin and norepinephrine reuptake, is approved by the FDA for the treatment of TAS.

Have been tested, obtaining encouraging results: mirtazapine, pregabalin (600 mg / day), topiramate, buspirone (30 mg / day), bupropion, gabapentin, citalopram, olanzapine, valproate and D-cycloserine (antagonist of NMDA receptor glutamate, and has proven effective in combination with behavioral therapy graduated exposure).

Most studies on the efficacy of pharmacotherapy in the treatment of SBP were of short duration. However, TAS is a chronic condition. It was shown that patients who discontinue paroxetine or phenelzine have a significantly increased risk of relapse than those who continued treatment for longer periods.

Most patients who responded to treatment achieved a reduction of anxiety and avoidance behavior, leading to improved social and occupational functioning. However, most patients do not obtain a complete and permanent disappearance of symptoms.

### **Treatment guide**

1. Treatment of first choice is an SSRI. Treatment should be started at doses used to treat depression - such as paroxetine 20 mg/day, sertraline 50 mg/day. For SAD, as in OCD, there is a period of latency in onset of response to treatment and are often required higher doses than those used to treat depression. Control disorder is usually found after 6 to 8 weeks. To determine the effectiveness of SSRI administration is required for a period of 10-12 weeks.
2. Currently there are insufficient data to guide treatment choice if not get a satisfactory response after treatment with SSRIs first. You can try another SSRI. When this event does not get a response, is another option and then use of clonazepam, the gabapentin

or venlafaxine. Only if the latter inefficiency and treatment can try a MAOI (e.g phenelzine).

3. Having achieved a significant improvement of symptoms is recommended to continue treatment for at least a year. Interruption of treatment is achieved by gradually lowering the dose very slowly during several months (eg, lowering the dose by 20-30% every 6-8 weeks). During this period, physicians should be alert to symptoms of possible relapse.

### **Psychotherapy**

Psychotherapy is effective in the treatment of SAD, but most of them are safe and cognitive-behavioral therapy group. They are geared to strengthen and affirm the patient's self, and lead to different social skills, to produce a cognitive restructuring and exposure to find appropriate techniques in different social situations. In two recent meta-effectiveness of pharmacotherapy and psychotherapy should be similar, with a slight superiority in the short term pharmacotherapy

### **8.4 Post traumatic stress disorder (PTSD)**

An important component of treatment is to ensure psychoeducation, which should help the patient understand the nature of the condition of suffering and what is the process of recovery.

In addition to the choice of therapeutic modalities, the physician should take into account other factors that may influence the disorder: the stigma, ambivalence regarding treatment, shame, social support, attitudes and behaviors of family antitherapeutics possibility of legal action or the victim.

The psychopharmacological treatment, especially with SSRIs and psychotherapy have proven effective in relieving symptoms of PTSD, there are even studies showing superior efficacy of combining two therapeutic modalities, compared with each treatment method in part.

#### **8.4.1 Pharmacological treatment**

Psychopharmacological treatment of PTSD goals are: improvement of key symptoms, minimize disability and to comorbidities, quality of life and prevent recurrence.

Although the diagnosis of PTSD in DSM was introduced in 1980, the number of studies pharmacological treatment of this condition is surprisingly low. Have not yet developed pharmacological compounds that affect biological changes characteristic of PTSD, so that psychopharmacological treatment of this disease was limited to the administration of different compounds with proven efficacy in other anxiety disorders or depression.

SSRIs are the most studied antidepressants for the treatment of PTSD and are considered as first line therapy (Stein, 2006). The effectiveness of these compounds has been demonstrated in double blind studies for sertraline, paroxetine and fluoxetine in open studies for escitalopram (10-20 mg/day), citalopram (20-60 mg/day), fluvoxamine (100-300 mg/day) , nefazodone (200-600 mg/day), venlafaxine (150-225 mg/day) and mirtazapine (15-45 mg/day) .

SSRIs have proven efficacy clear cases of PTSD experienced by civilians, although there are conflicting data could be effective in cases arising after military conflicts. SSRIs results in an improvement in all PTSD symptoms, with the exception of sleep disorders. Improvement of symptoms seen in 2-4 weeks, but may improve irritability and dysphoria as the first week.

Paroxetine and sertraline are approved by the FDA for the treatment of PTSD. The doses used are higher than those commonly used, being 100-200 mg/day for sertraline and 30-50 mg/day for paroxetine (Ninan and Dunlop, 2006). Also, amitriptyline and imipramine (initial dose of 50-75 mg/day increased to 300 mg/day) have proven their efficacy in the treatment of this disorder.

It has been suggested that patients with comorbid mental illness and another might show a better response to antidepressant treatment than patients who do not have other comorbid mental disorder, since the differences between active drug and placebo would be higher if a comorbidities. This might explain the higher rate of response to placebo if no other comorbid condition.

Of the anticonvulsants, lamotrigine has demonstrated efficacy for the treatment of PTSD in a double blind, mainly improving the symptoms of reliving the traumatic event and avoidant behavior. Have been published and smaller studies have demonstrated that other anticonvulsants (sodium valproate and carbamazepine) could play a role in PTSD therapy. In the treatment of PTSD and have proven effectiveness and:

- MAOI - phenelzine at a dose of 45-75 mg/day in improving symptoms of intrusive (Davidson, 1994);
- $\alpha 1$  adrenergic blockers - prazosin vesperal administered at a dose of 1-4 mg in relieving nightmares, and intrusive symptoms
- benzodiazepines in improving sleep disorders

#### **Treatment guide**

- SSRIs are currently recommended as first choice therapy in the treatment of PTSD due to efficacy, safety and tolerability of this class of compounds.
- If a patient does not tolerate or respond to an SSRI, you can try another compound in this class. Nefazodone, amitriptyline, imipramine, lamotrigine are other options for these patients.
- Augmentation of drug treatment is necessary in cases where only get a partial answer to the second treatment tried (in this case you can try and replace it with another drug), or if no response is achieved or attempted in the third treatment. Thus, depending on each patient's specific symptoms, you can try taking lithium or an anticonvulsant in patients with fits of anger and an atypical neuroleptic (especially Olanzapine) in agitated patients. Quetiapine (100 mg/day) is recommended in the treatment of refractory severe insomnia (Robert et al., 2005; Ninan and Dunlop, 2006).
- Where the PTSD is a chronic evolution is continued treatment for at least a year after obtaining the response to treatment. Discontinuation of treatment, as with other anxiety disorders, it is recommended to achieve the slow decrease in dosage (eg 20-30% of the dose a few months). Currently there are no sufficient data on the maintenance of therapeutic effect compared with placebo or the long term development disorder after discontinuation of drug therapy.

#### **8.4.2 Psychotherapy**

Among the psychotherapeutic methods tested for PTSD treatment, the most effective is cognitive behavioral psychotherapy, which is indicated as first line therapy in the treatment of mild or moderate PTSD. Among the most effective techniques are used exposure therapy and cognitive restructuring.

### 8.5 Acute stress disorder

Acute stress disorder is a short transitional period - lasting less than a month - a significant severity characterized by intrusive memories that occurs shortly after a physically or emotionally stressful event exceptional. It is similar to post traumatic stress disorder, distinguishing evolutionarily. Occurs within 4 weeks after the traumatic event, lasting from 2 days to 4 weeks. Stresorul can be a traumatic experience involving a serious threat to the security or integrity of the subject or someone close (eg natural disasters, accidents, fights, criminal assault, rape, etc.), or an unusually sudden and threatening change social position and / or the subject's social network, for example: multiple losses of people close to the fire house, etc..

An important role in the occurrence and severity of side play individual vulnerability and capacity to cope with events.

Treatment of acute stress disorder include psychopharmacological and psychotherapeutic intervention, psychoeducation, and case management.

Currently there are few studies on the psychopharmacological intervention in acute stress disorder. However, it can be recommended selective serotonin reuptake inhibitors (SSRIs) and other antidepressants. Benzodiazepines are useful in cases where immediate cause persists (diazepam: 5-10 mg / day or i.m. lorazepam: 1-2 mg / day). In patients who are contraindicated benzodiazepines can be used low doses of neuroleptic sedatives

### 8.6 Adjustment disorder with anxiety

(ICD-10 Clasificarea tulburarilor mentale si de comportament, ALL, ISBN 973-9392-73-3, Romania)

Adjustment disorder is defined as a maladaptive response, a response to an identifiable stressor, namely: a significant life change or a stressful life event (presence or possibility of a serious physical illness).

#### Treatment

Adjustment disorder requires a psycho-therapeutic approach centered on stress, on its significance and how the patient perceives and controls the stress. It is recommended bio feedback, relaxation techniques and hypnosis. Medications (anxiolytics) has an auxiliary role by reducing the severity of symptoms.

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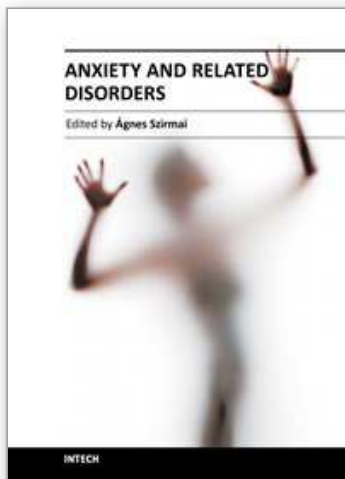
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## **Anxiety and Related Disorders**

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Anxiety disorders are one of the most common psychiatric disorders worldwide and many aspects of anxiety can be observed. Anxious patients often consult primary care physicians for their treatment, but in most cases they do not accept the diagnosis of anxiety disorder. Anxiety is a symptom that could be seen in many organic disorders and can accompany almost any psychiatric disorder. Anxiety disorders are frequent and are associated with significant distress and dysfunction. Stigmatization is an important factor in insufficient diagnosis. The problems of anxiety cover all fields of life. This book intends to describe the epidemiological aspects and the main co-morbidities and consecutive diseases of the anxiety disorders.

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