

COURSE OF

# GENERAL PSYCHIATRY

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**„Victor Babeș” Publishing  
Timișoara, 2017**





TEXTBOOK  
collection

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**CNCSIS code: 324**

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**ISBN 978-606-786-048-1**

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## Chapter I - NORMALITY – PSYCHOPATHOLOGICAL DISORDER

Psychiatry is a medical discipline, thus its psychopathological disorders require a medical way of thinking.

Circumscribing the notion of a disorder requires (especially in psychiatry), the understanding of the concept of normality and focusing on a person-based type of medicine.

There are 3 underlying norms regarding normality:

1. The norm of statistical medicine: the more a frequent a phenomenon is, the more normal it is considered. This type of norm is necessary, but insufficient, it needs to be correlated with the other two types of norms.
2. The ideal norm, which refers to the ideal of normality, both individually and in the community. The ideal norm is difficult to obtain, it varies widely and is linked to society and culture and mainly refers to the way the community thinks the person should be.
3. The functional norm reflects the way a person fulfills its functional “role” in the system where they live in.

Opposite to normality is abnormality. In the general anthropological perspective, a shift from the norm (in a positive way), defines exceptional individuals, geniuses. A shift from the norm in a negative way (deficit), represents a disorder (pathology).

A psychopathological disorder consists of a disorganization, a lack of psychological equilibrium and because of this deficit certain manifestations appear, which are not seen in normality.

A disorder is an abnormal state, which debuts at a certain point in time, with a certain clinical picture, a certain etiological substrate, a certain outcome and therapeutic responsiveness.

As happens most often in psychiatry, a disorder is defined longitudinally and is correlated with an endogenous predisposition.

A disorder episode is limited in time and correlated with circumstantial vulnerability. A disorder may consist of several episodes, with periods of complete or incomplete inter-episodic remission.

A psychopathological disorder influences the global functioning of the individual and may, in time, lead to various types of deterioration or disabilities.

The etiology of psychopathological disorders is complex, without it being subjected to the linear explicative model (“cause-effect” type); the causes are always multi-factorial, which intersect and interfere with one another, thus defining the “circular-systemic” explicative model.

Understanding psychopathological disorders should be done by considering other disciplines, which constitute explicative bases. The most important are:

1. Biological: neuroanatomy, neurophysiology (neurotransmitters: norepinephrine, dopamine, serotonin, acetylcholine, histamine, GABA, neuropeptides), genetics.
2. Psychological: genesis of the human psyche, genesis of the personality (including temperament, character)
3. Social: the existence of each individual (healthy or ill) occurs in a certain culture, by interacting with others. The most important here are: the social network and the social support network.

The social existence of a person articulates with certain life cycles. Transition periods (from one cycle to another) may be critical periods for the individual (in terms of vulnerability for developing psychopathological disorders).

## Chapter II – SEMIOLOGY. THE HUMAN PSYCHE

The human psyche represents the conscious and unconscious ensemble of vital, affective, cognitive and spiritual needs of an individual.

The term “psyche” originates in the Greek language, where it represents the personification of the human soul (in Greek mythology Princess Psyche fell in love with Eros). It’s Latin equivalent is “anima”. Initially, it referred to just the meaning of the word “soul”.

Afterwards, the meaning began to shift towards concepts like “spirit” and “mind”.

The term “psychiatry” was first introduced in the beginning of the 19th century by J.C. Reil and defined the branch of medicine that dealt with the study of psychopathological disorders.

Symptom = disturbance of a subjective psychological function and/or a behavioral aspect.

Syndrome = coherent and recognizable ensemble of signs and symptoms which occurs within several disorders. IT DOES NOT INVOLVE AN ATTRIBUTION OF A DISTINCT MORPHO-FUNCTIONAL SUBSTRATE!

A DISORDER encompasses an ensemble of specific signs and symptoms, that are attributable to a precise subjacent substrate and which has a specific treatment.

As examples: parkinsonian syndrome (parkinsonism) versus Parkinson’s disease; depression as a symptom / syndrome / disorder.

CONSCIOUSNESS: REPRESENTS THE STATE OF BEING AWAKE AND IN CONTACT WITH THE ENVIRONMENT.

CONSCIENCE: represents one’s own moral compass, self-awareness regarding one’s own character, behavior, social status and insight (awareness of having an illness or disorder).

The UNCONSCIOUS PSYCHE is made up of two parts:

-Evocable: the information that is not conscious at present but can be evoked spontaneously or voluntarily in certain situations.

-Non-evocable: instincts.

WAKE STATE:

IS THE ORGANISM’S DEGREE OF RESPONSIVENESS TO STIMULI.

THE CURRENT STATE OF CONSCIOUSNESS has the following attributes:

1. INTENTIONALITY – attention focuses on a certain object / sector of reality in order to increase focus accuracy on this level.

2. STRUCTURED PERCEPTION of external and internal stimuli – the psyche organizes the perceived content according to its own existing models in order to give it meaning.

3. UNDERSTANDING THE SITUATION – the correct interpretation of the perceived objects leads in turn to an oriented and comprehensible behavior which is in accord to the stimuli.

4. ORIENTATION in time, space, situational, identifying self and others – correct placement of the perceived content in time and space and correctly identifying objects, people and situations.

**THE CURRENT STATE OF CONSCIOUSNESS** is characterized by:

THE AREA OF THE CURRENT STATE OF CONSCIOUSNESS – a certain perceived content which may be pathologically widened (ex.: intoxication with psychedelics) or narrowed (ex.: twilight state).

THE CLARITY with which the objective reality is perceived – clear vs altered.

THE HUMAN PSYCHE is subject to biologic rhythms and oscillates between two alternative states (sleep and being awake = circadian rhythm).

Regarding the circadian rhythms (with the duration of 24 hours), we will encounter:

ULTRADIANE RHYTHMS (with a duration under 24 hours):

Endocrine secretions, NREM or REM sleep rhythms

INFRADIANE RHYTHMS (with a duration over 24 hours): Menstrual cycle

SLEEP = a periodical and reversible physiological state characterized by a transient stopping of consciousness and decreased reactivity to stimuli (during REM sleep the CNS is reactive to internal stimuli).

SLEEP is very important for:

- Metabolic rejuvenation;
- Energy conservation;
- Improving memory functions.

SLEEP DEPRIVATION has the following consequences:

- Melatoninergetic dysfunction;



- Increased secretion of cortisol;
- Increased levels of pro-inflammatory cytokines TNF $\alpha$  and IL-6 (risk for cancer).

NON REM SLEEP: PREDOMINANCE OF THE PARASYMPATHETIC NERVOUS SYSTEM: decreased blood pressure, heart / respiratory rate and urinary excretion. It is a period in which vegetative functions are STABLE. Muscle tone does not diminish.

75 % of total sleep duration. Predominates in the first half of a night's sleep.

Serotonergic activity predominates on a CNS level. IMPORTANT ROLE IN METABOLIC REJUVENATION.

REM SLEEP: PREDOMINANCE OF THE SYMPATHETIC NERVOUS SYSTEM: increased blood pressure, heart / respiratory rate and urinary excretion. It is a period in which vegetative functions are UNSTABLE (risk for stroke, myocardial infarctions, sudden death, central sleep apnea. Muscle tone decreases (ex: hypnic paralysis).

25 % of total sleep duration. Predominates in the second half of a night's sleep.

Acetylcholinergic activity predominates on a CNS level. IMPORTANT ROLE IN IMPROVING MEMORY FUNCTIONS!

### **SLEEP DISORDERS:**

#### QUANTITATIVE:

Insomnias

Hypersomnias

#### QUALITATIVE (PARASOMNIAS):

Somnambulism;

Night terrors;

Nightmares;

INSOMNIAS (reduction of total sleep duration for 24 hours compared to the habitual sleep amount associated with the acknowledgement of sleep deficit and feeling tired in the morning).

Early Insomnia (latency before falling asleep > 30 minutes) in: anxiety, neurasthenia; non-pathological: after a difficult exam.

Late insomnia (waking up at 3-4 A.M. and not being able to get back to sleep) in: depression (specific).

Mixed insomnia in: mania associated with psychoactive substance use/abuse (coffee, amphetamines, cocaine), situations in which a reversal of the sleep-wake rhythm occurs (working in shifts, jet lag), comorbidity between anxiety and depression.

HIPERSOMNIAS: increased total sleep duration over 24 hours compared with the habitual sleep amount; sometimes it is compensatory after repeated insomnias.

Pickwick syndrome: hypersomnia (diurnal sleepiness), associated with obesity and right cardiac failure (chronic pulmonary heart disease).

Nocturnal sleep apnea syndrome: hypersomnia, nocturnal apnea (nocturnal crises with a duration of 10 seconds and snoring); the causes may be central or obstructive (narrowing of the retropalatine or retro-glossal space) associated with obesity.

NARCOLEPSY: unsurmountable sleeping crises with a duration of 20 minutes occurring in full wake state with or without cataplexy (loss of muscle tone).

Kleine-Levin syndrome: cycles of hypersomnia associated with bulimia, hyper-sexuality and irritability, which occur in some adolescents almost every other month.

PARASOMNIAS:

SOMNAMBULISM: "automated" nocturnal behavior (the person wakes up from the bed, moves through the house or the outside, moves objects) without being able to remember the episode (amnesia); the person is not conscious of what they do during the night; there is no specific treatment; risk factor reduction is targeted.

NIGHT TERRORS: an apparent wake-up from sleep of a child, accompanied by an intense anxiety and motor restlessness (cries, yells) coupled with amnesia and the inability to remember the dream.

NIGHTMARES: appear more frequently during REM sleep; they are more frequent in anxiety, depression and PTSD.

PTSD: simple-themed nightmares, with the same recurring theme (psycho-traumas) which predominate in the first part of sleep.

## **CONSCIOUSNESS DISORDERS**

QUANTITATIVE:

OBNUBILATION - (from Latin nubes = cloudiness, nebula = fogginess ) represents a decrease in the level of vigility. In normal individuals it can be seen in extreme tiredness situations and in hypnagogic

and hypnopompic states; in pathology: direct CNS involvement: CNS trauma, stroke, tumors, infections; indirect CNS involvement: respiratory / renal / hepatic failure or intoxications with CNS depressants (alcohol, psychotropic medication).

SOPOR STATE (first stage of come / vigil coma): a state of profound sleep from which the patient cannot be awakened without applying very strong stimuli. If waking the patient succeeds, it will only last for a short time, after which the patient will re-enter the profound sleep. It occurs in: direct and indirect CNS involvement (see above situations) or intoxications with CNS depressants.

COMA (from the Greek term “coma”, meaning profound sleep) – a state in which consciousness is abolished without the possibility of waking the patient by applying painful / luminous or auditory stimuli, with the loss of wake-sleep rhythmicity. The causes are the same as in obtundation and sopor state.

#### QUALITATIVE:

TWILIGHT STATE – is characterized by a punctiform decrease of the current state of consciousness with preserved motor automatism (the subject can walk, perform various tasks / activities), it has a paroxysmal and transient nature (abrupt onset and remission) with amnesia of the entire episode. The causes are organic (fronto-temporal epilepsy), induced by substances (pathological drunkenness) or psychiatric (dissociative states of the current state of consciousness from hysteria and acute reaction to stress).

#### CONFUSIONAL STATE:

Is characterized by the perturbation of the area and level of vigility of the current state of consciousness.

Abrupt onset, acute and transient evolution (if measures are taken), fluctuant intensity of symptoms (vesperal aggravation) It has the following clinical features:

Absence of intentionality, severe impairment of attention

Unstructured perception

Immediate understanding of the situation is impossible.

Disorientation in time, space, situational and regarding self and others.

Chaotic psychological processes, senseless and chaotic behavior.

Possible visual and tactile zoomorphic / micropsic / macropsic hallucinations (large animals / demons or panoramic hallucinations) or illusions associated with delusional behavior /// confuse-oniric state or delirium.

Hypomnesia, short term memory loss

Immediate (working memory) is severely affected: the patient does not understand the questions that are addressed to him; his language is incoherent

Psychomotor inhibition or agitation

Reversal of the sleep-wake rhythm

#### CONFUSIONAL STATE - CAUSES:

DIRECT lesions of the CNS: CNS trauma, tumors, strokes, infections, epilepsy.

INDIRECT lesions of the CNS: organ failure (hepatic, renal, respiratory), B1 deficiency, hypoglycemia, hydro-electrolytic disturbance, fever (febrile delirium that accompanies the fever), sepsis (infectious delirium).

Intoxication or withdrawals from: drugs and medication, toxic substances (intoxication or withdrawal delirium).

DELIRIUM ≠ DELUSION; in the elderly – differential diagnosis with dementia.

#### FUNCTIONAL LEVELS OF THE PSYCHE

- INSTINCTUAL LEVEL
- AFFECTIVE LEVEL (MOOD)
- COGNITIVE LEVEL
- VOLITIONAL LEVEL (WILL)
- SPIRITUAL LEVEL (specific to humans)

#### INSTINCTUAL LEVEL:

Common to both humans and animals

Instincts are born behavioral patterns/models which serve the adapting of a species, offering a finite number of solutions to the challenges raised by a relatively constant environment; to adapt, however, to an ever-changing environment, the intellect is needed in order to elaborate new solutions for new situations.

It is the headquarter of the instinctive impulses, which are urges (tendencies) that motivate the behavior of an individual; they have a high motivational power because they represent biological imperatives; instinctive impulses are a part of the unconsciousness psyche and are thus unconscious; they can become conscious only through the generation of affective needs that produce distress in the individual until they are completely satisfied.

Humans use the instinctual level to achieve the biological need to perpetuate their own species, but also their psychological need to obtain pleasure.

There are 5 instincts: sexual, social (to be part of a group), maternal/paternal, vital (self-preservation) and the instinct to feed.

### **SEXUAL instinct:**

A normal sexual act encompasses the following:

- Sexual desire (libido)
- Sexual excitement (manifested in men by the presence of erection and in women by vaginal lubrication)
- Orgasm
- "Resolution" phase
- Sexual instinct disorders are classified as follows:
  - Quantitative – sexual dysfunctions
  - Qualitative – paraphilias

### **SEXUAL DYSFUNCTIONS:**

- Disorders of the sexual desire: increased sexual desire (in men: satyriasis and in women nymphomania), decreased sexual desire.
- Disorders of the sexual excitement: erectile dysfunction or impotence / frigidity
- Orgasm disorders: premature ejaculation / delayed ejaculation / pain during ejaculation ; orgasmic dysfunction (in women)
- Other types of sexual dysfunctions: dyspareunia (pain during intercourse), vaginism (vaginal muscle contractions during intercourse).

## **PARAPHILIAS:**

Disorders linked to the preference of abnormal partner: the subject himself (masturbation – pathological when the subject avoids normal sexual partners and can only obtain gratification from masturbating); same sex partner (homosexuality / lesbianism); 1st degree relative (incest); unsuitably aged partner (children: pedophilia; elderly: gerontophilia); animal partner (zoophilia); an object as a sexual partner (statue / mannequin = pygmalionism); corpse (necrophilia);

Disorders in which sexual excitement occurs only in unusual conditions: exposing genitals in public (exhibitionism); in men- fondling / touching women's clothes (fetishism); in men: dressing up as women (transvestitism); contemplating / watching sexual scenes (voyeurism); producing / receiving pain for/from the sexual partner (sado-masochism); rubbing up against other people in public places (frotteurism).

## **MATERNAL INSTINCT:**

In women, the maternal instinct develops gradually even during pregnancy (if the child is wanted); in men, there is a paternal sentiment that develops gradually. Disorders of the maternal instinct occur most frequently when the child is unwanted: the child is considered a burden or has an unknown father or a father that doesn't want to recognize the child as his own (in young women); in these situations the mother rejects her child, going as far as abandonment (in the maternity ward, on the street or even in garbage bins) or neonaticide (killing of the newborn up to 24 hours after birth).

## **FEEDING INSTINCT:**

Has the biological purpose of keeping the individual alive.

Disorders of this instinct are as follows:

1. QUANTITATIVE:
  - Anorexia / inappetence
  - Bulimia
  - Hyperfagia
  - Potomania
2. QUALITATIVE: Pica

#### ANOREXIA:

- Refers to the absence of appetite; it is encountered in depression, anorexia nervosa (during the evolution of the disorder), anorexigenic drug abuse (amphetamines and cocaine)
- Anorexia nervosa is not an instinctual disorder per se, it appears during the evolution of the disorder, it is a body dysmorphic disorder like disorder (the inability of the individual to identify with his own body); the motivation to lose weight is stronger than the instinct to feed; the person shifts towards behavior which are meant to decrease body weight, even when their weight is normal or even way below normal (physical exercises, extreme calorie reduction, self-induced throw-ups; use of diuretics, laxatives and catabolic substances).

#### BULIMIA:

- Refers to an excessive and impulsive eating habit; it appears in bulimia nervosa, mania and Pick's dementia.
- Bulimia nervosa is characterized by recurrent episodes of impulsive eating of large quantities of food (especially sweets) in a short period of time (gorging), associated with the feeling of losing control; increased weight leads to adopting a corrective conduct (physical exercises, extreme calorie reduction, self-induced throw-ups; use of diuretics, laxatives and catabolic substances).

#### HYPERFAGIA:

- Refers to excessive, but not impulsive eating; appears in pregnancy, family or cultural habits in obese individual, anxiety; it may have organic causes (Kleine-Levin syndrome) or can be induced by iatrogenic substances (antipsychotics, antidepressants and mood stabilizers).

#### POTOMANIA:

- Refers to excessive consumption of liquids / a differential diagnosis with diabetes mellitus / insipid diabetes must be performed.

#### PICA:

- Is a qualitative disorder of the feeding instinct in which the subject ingests non-edible substances (mud, chalk, clothes, paper); can be seen in some women only during pregnancy (rarely), in advanced forms of dementia (the person cannot distinguish between edible and non-edible items) and in profound mental retardation.

## VITAL INSTINCT:

- Has the biological purpose of defending one's own life and body integrity. In this context, it can generate normal verbal or physical aggression (for defense).
- Aggression can be shifted towards other individuals (hetero-aggression) or towards the self (auto-aggression): self-harm, suicide.
- Aggression can have a verbal manifestation (irony, swearing, threatening, offending) or a behavioral one.

## SUICIDE VERSUS PARASUICIDE

### SUICIDE

More frequent in men and elderly people.

Preceded by a longer time-span during which suicidal risk increases progressively: ideation – plan – attempt

The firm desire to die exists, death is considered the only solution to resolve the problematic situation; subjects take extreme measures so that others may not save them!

Subjects usually leave written letters in which they assume responsibility for their actions, thus absolving others from blame/guilt.

More frequent in major depression with comorbidities

(depression + anxiety + addiction = major suicidal risk)

### PARASUICIDE

More frequent in women and in young people. Are carried out in an impulsive manner, usually triggered by interpersonal conflict; has a demonstrative character and is usually carried out with the family present.

There is no real desire to die, usually it's a type of "emotional blackmail" to resolve the conflict; subjects take measures to get saved and usually choose less dangerous methods.

If they leave a letter, they usually victimize themselves, blaming others for their actions.

More frequent in histrionic personality disorder or borderline personality disorder.



**SELF-HARM:**

Is a type of self-aggression that refers to the integrity of the body. Is seen in schizophrenic patients which have body dysmorphic disorders and in disharmonic personalities like histrionics (in order to impress) and emotionally unstable (impulsive and superficial cutting with blades, knives, which lead to multiple superficial scars, especially on the non-dominant limb).

**PATHOLOGICAL AGRESSION:**

Has the purpose of obtaining some benefits. Is seen in impulsive individuals with a low threshold for frustration, psychotic patients without insight: manic, schizophrenic patients, intoxications (for example: alcoholic intoxication), epileptics, sociopaths (they ridicule moral norms)

In educated persons, aggression manifests especially in the verbal manner (irony)

**SOCIAL INSTINCT:**

Refers to being part of a group, that constitutes a social support network for the individual; this network can be represented by the family micro-group or the neighbors/friends group; the social support network helps the individual and constitutes a filter / buffer for negative life events.

Socializing represents an imperative in the survival fight: humans are not strong enough to live alone and to oppose resistance to nature because when compared to animals, humans have a constitutional inferiority; thus, the child has an inborn feeling of social communication and at the same time the psychological development of the child is strongly influenced by his rapport with society (human stimuli).

Humans are aware of their constitutional inferiority by having a feeling of insecurity, which acts as a constant stimuli towards the adaption of life; in a group there exists a certain dynamic – the fight to occupy the position of the leader; physical defects or intellectual disabilities can generate feelings of inferiority, thus the person can adapt to this situation in two ways:

- Ostentative manifestations of individual weaknesses with the purpose to attract the other's solicitude.
- Compensating or overcompensating individual weaknesses.

## **AFFECTIVE LEVEL**

Present in both humans and animals.

Belonging to the conscious psyche.

Its energetic support is strong but weaker than that of instincts.

The affectivity is subjective in contrast to the reasoning which is objective.

Affective experiences:

Are generally polar (pleasure – unpleasant, love – hate, happiness – sadness)

Also, can be neutral experiences (affective indifference).

Also, at the affective level:

**EXOTHYMIA** represented by affective reactions to external stimuli but which are conditioned by endothymia. Affective reactions are:

Basal reactions: pleasure – unpleasant

Common reactions: sadness, happiness, fear, anger

Existential reactions: despair – ecstasy

Moral reactions: guilty, empathy

Transitive: love – hate, esteem – contempt

Non-transitive: excessive self-love – self-deprecating, proudness – shyness

## **HYPERTHYMIA**

EMOTION is an intense and of short duration affective experience, suddenly triggered and caused by external factors (oral exam, public speaking). It is accompanied by autonomous reactions (redness, tremors, urgently micturition, suddenly diarrhea)

AFFECT is an extremely intense affective reaction of ANGER which is triggered by a highly-significant person for the individual (e.g. a friend).

THE SENTIMENT is an affective experience, very intense and consumptive in the beginning (accompanied by insomnia, weight loss), but its intensity decreases gradually (e.g. the year of grieving). The sentiment

can be directed towards someone or it can have an abstract content (patriotism, science, different hobbies). It can be rationally controlled.

THE PASSION is a very intense affective experience, but in opposite with the sentiment it can't be rationally controlled.

HYPEREMOTIVITY represents a hypersensitivity which are accompanied by an affective hyperreactivity (the intensity of the affective reaction is excessive in regard to the intensity of the triggering stimulus). It can occur in manic state and histrionic personality.

PATHOLOGICAL AFFECT: is a very intense experience that especially occurs in a conflictual situation. The individual is not aware of what is he doing and does not estimate the consequences of his actions (e.g. criminal acts: destructions, homicide)

CYCLOTHYMIA refers to abnormally longer cycles of alternating hypomanic and sub-depressive periods of time.

DYSPHORIA is represented by a low mood accompanied by irritability.

IRRITABILITY represents the excessively susceptibility to explosive anger reaction that is disproportionate in relation with the intensity of the stimulus and suddenly occurs on an apparently calm mood.

DEPRESSION is a pathological sadness through its intensity, duration, way of occurrence and reactivity to positive stimulus.

- Depression is self-perceived as an intense unpleasant and "moral" pain, where everything loses its value: own life, the person (self-deprecating, feelings of incapacity, worthlessness, guilty)
- The individual has pessimistic feelings about future (no future plans) The present moment no longer offers any joy.
- The attractiveness for the painful past (failures, mistakes) which provokes feelings of guilt.

MANIC STATE – the pathological equivalent of joy but qualitatively different from it (the pathological character is determined by its intensity, duration, context of onset and reactivity to negative news

- The individual lives in a perpetual celebration (with the tendency to sing and dance)
- Overvalues himself and is excessively optimistic,
- Makes a lot of plans without any relation with the reality
- The exaggerated happiness may become disruptive for others

ANXIETY is an unjustified fear (fear without object). The person has the presentiment of danger that, however, cannot be named. This state of tensed expectance (apprehension) generates sleep onset insomnia, muscular aches and fatigability. It can occur in generalized anxiety, post traumatic stress disorder.

PANIC ATTACK is an intense and paroxysmic episode of fear with a certain theme: of dying, of losing control, of going crazy. It is accompanied by sympathetic and parasympathetic autonomous symptoms. It appears in Panic disorder, Phobic disorder or Acute stress reaction.

PHOBIA is a disproportionate irrational fear of certain situations; it is a pathological fear of an object or situation (phobogenic object or situation);

It is recognized as irrational in relation to the objects degree of dangerousness) but it cannot be controlled by the subject; it appears in Phobic disorders and Obsessive – compulsive disorder (obsessive phobias).

AFFECTIVE BLUNTING (ATHYMHORMIA) represents the incapacity to experience feelings accompanied by inertia, lack of will and inactivity. It appears in the simple form of schizophrenia (with negative symptoms)

AFFECTIVE ANESTHESIA (ANHEDONIA) represents the inability to experience pleasure from activities usually found enjoyable. It is seen in high-intensity depression. Affective anesthesia and self-deprecation deprecation may be a trigger for the decision commit suicide in some of depressive patients.

#### QUALITATIVE CHANGES OF AFFECTIVITY

LABILE AFFECT - the rapid passing from one emotional state to the opposite state (sadness – joy); it intensifies as the patient is getting older; it appears in histrionic personalities as a personality trait, neurotic pathology and manic state (should be differentiated from the depressive switch in bipolar disorder).

AFFECTIVE AMBIVALENCE – the existence at the same time, in the same person of two contrary sentiments/affective reactions; it is seen in schizophrenia

AFFECTIVE INVERSION – the inversion of the feeling of love into hate and contempt for the loved ones (parents, children, life partner) ; it is seen in schizophrenia

AFFECTIVE INCONGRUENCE (DISCORDANCE). An inadequate (paradoxical) affective reaction to a situation (the individual laughs when hearing bad news); it is seen in schizophrenia.

AFFECTIVE COLDNESS – the strict control of the manifestation of affective reactions; it is seen in anankastic and schizoid personalities.

AFFECTIVE INDIFFERENCE – the incapacity to show compassion for a person who is suffering; it is seen in antisocial/dissocial personalities

### **COGNITIVE LEVEL**

It is represented by the psyche's functions which help to get knowledge (attention, perception, memory, thought and intelligence)

It does not necessarily reflect the objective reality; it only STRUCTURES, ORGANIZES the human experience; it represents a useful INSTRUMENT in adaptation to the environment

Knowledge can be empirical based on senses involving perception

Knowledge can be rational based on intelligence.

### **ATTENTION (PROSEXIA)**

A function that orientates (directs) and focuses (concentrates) the conscious psyche towards a specific sector of reality (intentionality).

It is influenced by affectivity

Has 4 attributes (domains): concentration and persistence (directly proportional), dispersion and mobility (directly proportional). Concentration and persistence are reversely proportional with dispersion and mobility.

### **ATTRIBUTES OF ATTENTION**

**CONCENTRATION:** attention is focused on a certain stimulus (object) increasing the efficacy of perception.

It can be accomplished without effort (due to curiosity, interest). It may require an effort of will

**DISPERSION:** the area of superficial attention around the focus point, where objects are perceived less clearly

**PERSISTENCY:** the ability of maintaining attention at an optimum focus level

**MOBILITY:** the ability of commuting attention on a different object when necessity requires it

### **THE ATTRIBUTES OF NORMAL PERCEPTION**

- The existence of the object in reality
- Validation (the subjective awareness of the existence of the object, critique)

- Isomorphic mental image (identical) of the object (it is important for the significance attributed to perception)
- Esthesia (the intensity of perception): the mental image is less poignant
- Spatial projection (outside the body)

#### QUANTITATIVE DISORDERS OF PERCEPTION

HYPERESTHESIA (increased intensity of perception for a normal stimulus):

- Meningeal Syndrome
- Migraine
- Cephalgia after the intake of a quantity of alcohol that is not tolerated by the subject

HYPOESTHESIA (decreased intensity of perception for a normal stimulus): – Sensory organ deficits

(e.g. hypoacusis, presbyopia)

- Fatigue
- Obnubilation, confusional syndrome
- Normality: anger, overinvolvement in an activity

ILLUSION: a perception with object, but without isomorphism (a false significance is attributed to the perceived object)

HALLUCINATION: a clear, uncriticized perception without object, projected outside the individual

PSEUDOHALLUCINATION: a clear uncriticized perception without object, projected inside the individual

HALLUCINOSIS: a clear perception without object criticized by the individual (the individual does not lose contact with reality). In some definitions hallucinosis appears under the (incorrect) term of pseudohallucination.

#### HALLUCINATION

A clear perception without object, projected outside the individual and uncriticized (the individual is convinced that the perception is real)

Normal: only in the hypnagogic and hypnopompic states and lasting for a few seconds:

Hypnagogic hallucination: upon falling asleep

Hypnopompic hallucinations: upon waking up

## CLASSIFICATION OF HALLUCINATIONS

### VISUAL HALLUCINATIONS

### AUDITORY HALLUCINATIONS

- The most frequent in pathology
- Elementary: noises, cracks, bells, horns • Complex: voices
- Calling: the person is called by his/her name
- Commenting: the voices are ironically commenting on the patient's intended actions

### Schizophrenia

- Injurious: the voices are insulting the patient
- Imperative: the voices command the person to execute negative acts:  
to kill, to commit suicide (this type of hallucinations are the most dangerous)

### Paraphrenia

### OTHER EXTEROCEPTIVE HALLUCINATIONS

### PSEUDOHALLUCINATIONS

- Clear perception without object, projected inside the individual and uncriticized
- The object is not perceived by anybody else
- The subjective consciousness is very intense ☹️☹️There is no spatial projection
- The subject sees hallucinations in his/her head
- The subject hears voices in his/her head or various organs
- The subject feels animals inside the body
- Seen in Schizophrenia, and is associated with the transparency-influence syndrome

### HALLUCINOSIS

Clear and criticized perception without object, clear (the individual does not lose contact with reality)

The object is not perceived by anybody else

Ambivalence between what the patient perceives and criticizes

Esthesia can be weak

There is spatial projection

Appears in:

Elderly with cerebral atherosclerosis, chronic alcoholism

## **MEMORY**

Records the information in the current field of consciousness after the disappearance of the stimulus as long as is necessary for its processing (seconds, minutes) allowing simultaneous execution of multiple cognitive processes (reasoning, comprehending questions, etc.)

It depends on the functioning of the prefrontal cortex

MSD

stores information for a short period of time (MSD) or a long period of time (MLD)

Semiology

Short and long term memory

Information storage

May be done mechanically or logically and is scheduled.

programming is an unconscious process of storing short or long-term information

long term memory implies logical organization of information

storing new information is done by recirculating it through reverberating circuits like the circuit of Papez (hippocampus - fornix - mammillary bodies - thalamus cingulate gyrus - cingulum - hippocampal formation).

consolidating information is achieved by the phenomenon of long-term potentiation which implies stimulating the synthesis of new postsynaptic receptors.

MEMORY, cognitive function with multiple roles

Evoking information

Good evocation must be timely, accurate and complete, after mnestic content:

In MNESTIC STORAGE (MLD)

Acquired information is organized in cognitive schemes;



the latter generates rules which are underlying interpretations (meanings) or individual expectations about other people, situations or events; long-term memory involves the processing of information:

Comparison of the new information with the existing one in cognitive schemas. Only new information may be learned.

validation: Acceptance of new information as true and important to its subsequent assimilation in preexisting cognitive schemes, or rejection of new information as false or inconsequential with its removal. If the new information contradicts existing schemes, but is validated as true and important, then the process of adjustment to pre-existing cognitive schemas intervenes to harmonize them with the new information.

classification and encoding of new information by assimilation.

Memory impairment may be:

QUANTITATIVE:

AMNESIAS

HYPOMNESIAS /HYPERMNESIAS

QUALITATIVE

PARAMNESIAS

HYPOMNESIAS / amnesia:

Anterograde:

ONSET OF PATHOLOGICAL PROCESS

TIME

Normal: if the learning material does not make sense / LACKS LOGIC

OBNUBILLATION (concentration hypoprosexia)

Acute intoxications

Liminary intellect (by not understanding the information provided)

Depression (concentration hypoprosexia)

Anxiety (concentration hypoprosexia)

Retrograde:

ONSET OF PATHOLOGICAL PROCESS

Obnubilation (concentration hypoprosexia)

Depression (concentration hypoprosexia)

HYPOMNESIAS / amnesia:

Korsakov SYNDROME

Predominantly anterograde amnesia

retrograde amnesia

confabulation (Product of the imagination unconsciously used to fill mnestic gaps)

anosognosia (Lack of insight regarding the deficit) and euphoria.

use of the imaginary material is unconscious, unlike mythomania and lying.

Immediate memory (recording information) is not affected.

DEMENTIAL SYNDROME

short-term memory amnesia (anterograde) with good initial evocation of past events prior to deficit onset,

In the late stages amnesia is retrograde thus affecting long-term memory.

Lacunar amnesia

overlaps with the period of time the person has had abolished or uneven consciousness (ex. coma, grand mal seizures, obnubilation, twilight state)

Alcoholic "Blackout"

Time limited

Selective amnesia / ellective / dissociative

nability to remember a traumatic or a negatively charged event

Dissociative and conversion disorders (old term: hysterical neurosis): the unconscious repression of negative events: frustrations, disappointments

Acute stress reaction: inability to evoke psycho-traumatising events

Lapsus (lapse, slip)

an apparent evoking amnesia with an intrusive character, requiring an effort to find the right answer, appears in normal circumstances;

Should not be confused with the psychoanalytical meaning of the term (acts missed).

Temporary incapacity of evoking

HYPERMNESIAS:

FIXING HYPERMNESIA: is rare;

EIDETISM refers to the ability to lock in all details of obtained information and reproduce it perfectly correct. It is not considered pathological, it occurs especially in children;

EVOKING HYPERMNESIA appears in mania (mnestic avalanche), in substance abuse and near-death experiences. In the latter case, they have a panoramic character (a quick, rapid succession of important life events).

PARAMNESIAS:

ECMNESIA represents the placement of past events in the present. Can occur in dementia.

CRIPAMNESIA refers to the situation where the person unconsciously assumes a material made by someone else. Must be distinguished from plagiarism which is done knowingly.

DEJA / Jamais vu, connu, vecu (already seen or never known or lived) appears in normality and in the pathology of the temporal lobe (predictive of temporal lobe epileptic seizures).

The intellect: is that part of the knowledge required to adapt to a changing environment which offers various challenges (to which one needs to find new solutions), which overcome the adaptive ability of the primal instincts.

With the aid of the intellect one acquires rational knowledge which validates (or not) empirical knowledge and extends it beyond the limits of the senses.

Intellect involves several distinct faculties:

RATIONAL INTELLIGENCE (logical thinking):

- The ability to find the right solution in the shortest time to a given problem.
- intuition:
- ability to find solutions after the individual has stopped seeking them through the conscious psyche

THE IMAGINATION: the ability to form new images that are not perceived through the senses.

The intellect makes the following operations:

- Validation of information received from the exterior or interior

- learning new information
- Inner thoughts, inner language and expressed verbally, in writing and/or through gestures
- Rational knowledge of reality (understanding)
- motivation: Motivational instances of the cognitive level are curiosity and interest
- Creativity: the ability to create material and spiritual values manifested in science and culture
- Valuing: applying value (ethical, aesthetic) and the ability of selection

#### Intelligence quotient (IQ):

- It is an index by which to quantify the level of intelligence of an individual.
- Is calculated based on preset knowledge scales for each age-group.
- Depending on the average scores obtained in children of a certain age one determines the mental age which is then compared to the chronological age.
- The most used tests for measuring intelligence are Raven's progressive matrices and the Wechsler Adult Intelligence Scale.
- To avoid errors, calibration and validation is required for each population that the test is applied to.
- The average IQ score is 100. Normal variations of the IQ scores are between 70 and 130.

#### Mental retardation:

- It is an incomplete mental development or a stop in the development of the psyche as a whole.
- Impaired development of the psyche is congenital and unevolutive (unlike dementia which is a global, acquired and progressive deterioration of the psyche).
- Mental retardation can be mild (IQ: 50-69), moderate (IQ: 35-49), severe (IQ: 20-34) and profound (IQ <20).
- Factors affecting the development of the psyche can start from intrauterine life until the first three years of life. They are more likely: genetic and metabolic, endocrine, hypoxic, traumatic, infectious, toxic. The impact of the factors that interfere with the development of the psyche are of organic cause and are definitive.

## DEMENTIA:

- Is a global deterioration of the psyche, is acquired, progressive and spontaneously irreversible and mainly affects cognitive functions, emotional life and social conduct, leading ultimately to swallowing disorders, cachexia and loss of sphincter control.
- The causes of dementia may be unknown (degenerative dementias: Alzheimer's dementia, Pick's dementia and dementia with Lewy bodies) or known: genetic, metabolic, vascular, endocrine, toxic, infectious, traumatic, tumors.

## THE IMAGINATION:

- Operates with images, memories that through combination lead to a new content with an anticipatory function.
- It requires the acquisition and development symbolic thinking (End stage sensorimotor and then during subsequent stages: pre-operational stage, concrete operations and formal operations stage).
- Through mental representation of objects, people or situations (representative intelligence) a person can work with pictures and sentences, can solve problems or make provision for the consequences of decisions (operational intelligence).

## DISORDERS OF THE IMAGINATION:

### CONFABULATION

- It consists of story-telling strictly from imagination, without any connection with reality of life events related to past or present. Unlike the lie it is involuntary and unconscious. Can occur in Korsakov syndrome and participates in the genesis of delusions typical for paraphrenia.

MYTHOMANIA: Refers to the imaginative deformation of events with the aim of self-valorization.

The LIE, it consists of deforming the truth in order to mislead, confuse others or to obtain a benefit.

It's commonly used by antisocial psychopaths.

### MORBID IMAGINATION

Refers to imagining catastrophic outcomes regarding future events.

Appears in anxiety

## THINKING AND LANGUAGE:

Thinking is mental function supported by a logical and continuous ideational flow (flux).

This flow can have a verbal (as an inner speech) and / or imaginative character (mental images).

**RATIONALIZATION:**

It is a mental operation where two or more judgments (called premises) are summated to obtain a new judgment that follows logically from the first.

**JUDGMENT:**

The ability to think logically or a form of expressed thought through a sentence which affirms or denies something.

**DEDUCTION:**

It's a logical reasoning, independent of experience.

**SYLLOGISM** is deductive reasoning made up of three judgments, the third one representing the conclusion which is deduced from the first one with the help of the second: "All aquatic mammals are cetaceans; All dolphins are aquatic mammals; So all dolphins are cetaceans".

**INDUCTION:**

Is a type of reasoning which stipulates a general law from a large number of facts.

Is NOT a type of logical reasoning.

**INTUITION:**

Immediate form of knowledge based on experience and knowledge previously acquired, not by reasoning. The solution suddenly appears after the individual has ceased to seek it in the conscious psyche. Probably also relies on emotions connected with previous experiences.

Thinking can be described using its attributes, some quantitative, others qualitative:

Rich or poor in terms of content

Fast or slow in terms of the speed of ideational flow

Elaborate or simple, stereotypical

Abstract or concrete

logic or incoherent

synthetic or analytical

The content of thought is intimate, due to self-imposed censorship of written or verbal expression of thoughts.

The language is the basis of communication between individuals and represents selected expression of thought.

Words are abstract symbols of phenomena, objects or the conclusions drawn up through abstract thinking.

Language can be verbal or nonverbal.

Nonverbal communication is achieved by: facial expressions, gestures, posture, rhythm and intonation of speech.

### **THOUGHT DISORDERS:**

QUANTITATIVE (in terms of quantity and rhythm of the thoughts)

- Flight of ideas
- Slowing of the ideation flow

QUALITATIVE (abnormal content)

- obsessive idea
- prevailing idea
- delusional idea

FORMAL

- digressive thinking,
- circumstantial thinking
- ideo-verbal dissociation

QUANTITATIVE DISORDERS OF THINKING

Tachypsychia – in normality: when one is in a good mood (humorous mood); pathological - intoxication with stimulant drugs or alcohol in small quantities;

Flight of ideas = quick thinking + increased content of ideas (volume ideation) - in mania; ≠ ideo-verbal dissociation in schizophrenia; in mania one can also encounter:

SPEAKING telegraphically: a situation where the individual can not speak in the rhythm in which he thinks and thus eliminates superfluous words

TACHYLALIA (accelerated rhythm of speech)

Logorrhea (rich content of speech)

GRAPHORRHEEA: the need to write more (sometimes long lists of meaningless words).

Depending on the wealth or poverty of thought and speech:

Is associated with slowing of speech = BRADYLALIA

In depression, slow thinking is associated with poverty of thought content.

Depressed patient speaks slowly (bradylalia), with a higher latency between question and answer. Usually does not initiate dialogue and responses are short, monosyllabic (laconic speech).

Epileptoid personalities are characterized by slow, non-selective thinking.

Depending on the wealth or poverty of thought and speech:

- Speaking with a rich content: logorrhea in mania
- Speaking with poor content: Laconic SPEAKING: concise, with short answers, sometimes monosyllabic (yes / no): in depression
- Speaking null (void) content: MENTAL BLOCK. This refers to the sudden and unjustified interruption of the flow of thought and speech, the patient feels like a "void" (head feeling empty). Thinking and speaking can be resumed after a pause. Can occur in schizophrenia or individuals who do lots of digressions.

MENTAL fading is characterized by progressive slowing of the ideational flow leading up to mental block.

MENTISM is the sudden appearance of a large number of thoughts which unfold quickly and uncontrollably like an avalanche of disturbing thoughts unstoppable by the individual.

#### DISORDERS OF FORMAL THINKING

Digressive THINKING is a deviation from the theme of the speech by digressions ("brackets"), but with the final return on the topic. Sometimes correlates with tachypsychia.

Circumstantial thinking consists of a rich discourse that abounds in unimportant details. Is due to an inability of synthesis and selection (unimportant details are raised to an essential status) associated with a strong adhesion to the theme (once the topic has been changed, the person answering the question then pops back to the old theme from where it was interrupted). Correlates with bradypsychia.

Ideo-verbal dissociation consists of a "cleave" in both the thinking and speech so that patients lose their coherence. In less severe forms persons jumps from one idea to another without logical explanation. In



severe forms ideas associate randomly and words associate with any rules. There is a loss grammatical structure of sentences and discourse meaning. In the speech, the so called "word salad" can appear.

Sometimes words are associated with rhyme. Sometimes words are broken into syllables. The subject may invent new words called "neologisms" (which have no real connection with real neologisms) or assign other meanings to words which normally have another meaning known by others.

Ideo-verbal dissociation occurs mainly in schizophrenia. Loss of coherence can be also found in mental confusion (delirium).

Obsessions are thoughts, ruminations, images, impulses or intrusive character doubts persistent, recurrent and egodystonic, parasitizing conscience of the individual. Unlike delirium, obsession is recognized by the subject as irrational. Also, unlike syndrome transparency-influence, the subject recognizes obsessions as being his own thoughts.

Obsessive ruminations are long and sterile thoughts (without purpose) on abstract or trivial themes.

Obsessive impulses are tendencies to self or hetero-aggressive acts, embarrassing, shameful (swearing, profanity) or sexual.

Obsession's content can be:

- Abstract in the case of obsessive ruminations (metaphysical themes: where is
- God ?, Where is the end of the universe?)
- Trivial: obsessive ruminations regarding order and symmetry.
- shameful, aggressive impulses.

In normality: obsessions can be generated by moral conscience or a song which one cannot forget. If there's a lapse (lapsus) an obsession regarding the lost term might appear.

In pathology: in obsessive-compulsive (obsessions with or without compulsions), depression (depressive rumination); in posttraumatic stress disorder (flashbacks) and schizophrenia (with a bizarre character)

THE DELUSION: It is a pathological belief (absolute) without real substrate (a false idea) that cannot be countered by logical argument.

- Delusions occur when the individual has a clear wake state (unlike delirium / confusional state). It should also be differentiated in regards to socio-cultural beliefs that a person adheres to.
- Subject's behavior corresponds to the delusion (delusion induced behavior).

- Delusions take over the mind of the subject, the patient lives through and for his delusion. occur in psychoses (schizophrenia, paraphrenia, paranoia, affective depressive or manic episodes of psychotic intensity)
- Prevalent idea: starts from the idea that a true fact of life of the patient, which the patient solely focuses on (the subject cannot focus on other aspects of life, the prevalent idea dominates the patient's life). The subject does not consider the idea as pathological, but can accept counter-arguments.

Mimicry refers to the subject's facial expression, movements and gestures ☞ Quantitative disorders of expressiveness and mimicry:

HYPEREXPRESSIVITY: seen in histrionic personalities and manic episodes

HYPOEXPRESSIVITY: depression / simple schizophrenia.

QUALITATIVE DISORDERS OF EXPRESSIVITY AND GESTURING:

ECHOPRAXIA and ECHOMIMIA: imitating gestures and mimic other people. occurs in: Catatonic schizophrenia

Grimaces is a voluntary or involuntary contraction of facial muscles. Seen in: pain, as a side effect of medication or incisive neuroleptics in HEBEPHRENIC schizophrenia (as "schizophrenic snout")

Mannerisms are exaggerated gestural signs that have lost functional significance. Seen in hebephrenic schizophrenia

MIMICRY DISORDERS

Depressive facies: with lowered corners of the mouth; and on the forehead, between the eyebrows appears the so-called "omega melancholy".

Anxious facies: frowning, tense, that expresses fear.

Semiology

POSTURE - refers to the positions taken by the patient.

Among posture disorders we can encounter:

- Secondary dystonia incisive neuroleptic medication are:
- Oculogyric crises: eyeballs blocking or capping sideways gaze, stiff neck, opisthotonus
- Parkinsonism (shape of question mark) is characterized by flexing head, elbows and knees. It is a side effect of antipsychotic medication.

- depressive: is characterized flexing the head downwards, gazing downwards, hands located on the lap.
- waxy flexibility: manifested by maintaining uncomfortable postures induced by the examiner for a long period of time (raised upper limb, “psychogenic pillow”).

## **THE SPIRITUAL LEVEL**

is characteristic for humans;

Each individual has a hierarchical system of values which may or may not coincide with the values of the family of origin, the group that he adheres to, culture to which he adheres, or with universal values. The latter can be reduced to three fundamental values:

- good (Ethics, morality)
- truth (Logic) and
- beautiful (Aesthetics)

In the ethical level we have moral conscience:

This represents all the values and moral norms that underlie the functioning of society. It develops gradually.

3 year old child is egocentric and has no concept of right and wrong.

At 7 he learns to obey rules, to distinguish between right and wrong and to control.

In adolescence a reorganization of values occurs (by challenging rules imposed by the parents, school, society) and by building his own system of values.

As an adult, the subject assumes a certain value system that may or may not coincide with society's values.

Thoughts, words and acts of a person are subject to moral judgment. When they are in accordance with moral norms there arises a pleasant feeling of gratification, accompanied by increased self-esteem and a desire to repeat good deeds. Otherwise, there is an unpleasant feeling of shame, remorse, guilt, accompanied by lower self-esteem and a desire to refrain from bad deeds in the future or to redeem themselves.

motivational instance: generated by the moral conscience; is the aspiration towards fundamental values. It motivates the individual to behave within the rules of moral conduct and sometimes self-improvement.

Individuals with mental retardation have an IQ that does not allow them to distinguish between right and wrong and are not responsible for their acts (disharmonious people with mental retardation).

Individuals with dissocial personality disorder (or antisocial behavior) have an IQ that allows them to distinguish between right and wrong but choose evil and ARE responsible for their acts.

In depression, the individual's value system is disrupted. The loss of ability to enjoy life and with the loss of meaning to that life worth living can lead to suicide attempts.

## **THE VOLITION, MOTIVATIONAL SYSTEM AND BEHAVIOUR**

The instinctual and affective levels have enough energy to trigger a behavior

Unlike the first, the cognitive and spiritual levels do NOT and require WILL to trigger behavior.

Motivational instances are those forces that are capable of generating behaviors. They are:

- instinctual drives or needs at an instinctual level,
- desires at the emotional level,
- interest and curiosity at a cognitive level
- Volition (will) at a volitional level
- Aspirations at spiritual level

motivational process = Sequence of steps:

1. Enabling motivational instances – weak in depression and simple schizophrenia; mild in mania
2. Deliberations: Cognitive level (strategies, value judgments, calculating the consequences) - prolonged in schizophrenia and depression, hasty in mania and nonexistent in the impulsive personalities
3. the decision phase - Difficult for dependent personalities
4. Switching to the act
5. Persistence to the act: needed to attain the goal

## **QUANTITATIVE DISORDERS OF VOLITION**

HYPERBULIA is represented by a strong will, not considered pathological. Hiperbulia pathology may occur in some patients with paranoia characterized by a high tenacity in claiming their rights.

HYPOBULIA and ABULIA represents weak or absent will. It could be a personality trait or may occur in depression, simple schizophrenia, Pick's dementia.

#### QUANTITATIVE BEHAVIOR DISORDERS:

Psychomotor restlessness that occurs in generalized anxiety disorder (person cannot sit still, move more, rubs his hands); in hypomania; AKATISIA: restlessness induced by incisive neuroleptic medication.

Psychomotor agitation is the maximum degree of psychomotor restlessness, meaningless and accompanied by aggression. Appears in intense anger, very intense panic attacks, mania: where they occupy the entire space available to and influenced by events ( "furor maniacalis"), secondary to hallucinations and delusions in schizophrenia catatonia (agitation confined to a small space, stereotypical, uninfluenced events and short - raptus), confusional state (agitation is chaotic; non-stimulant drug intoxication or withdrawal from sedative drugs).

PSYCHOMOTOR INHIBITION occurs in depression (slow movements, slow responses with greater latency period), epileptoid personality (great slowness in everything he does), in fatigue and the confusional state (sedative drug poisoning).

STUPOR is the maximum degree of inhibition with no spontaneous movements. It may be a:

- Depressive hypotonia in severe depression
- Catatonic with hypertonic and waxy flexibility in catatonic schizophrenia
- Reactive in panic attack
- Organic CNS lesions

Negativity is resistance to external or internal stimuli. Occurs mostly in catatonic schizophrenia.

Negativity can be:

- Passive: subject ignores commands from the examiner
- Active: the subject does the opposite of what is asked.

Tremors: characterized by rhythmical involuntary movements of the extremities, or limbs and head (generalized tremor). It may be a:

- Parkinsonian type caused by incisive neuroleptics administration
- Anxious (the panic attacks)
- Conversion

Tics are sudden, repetitive and involuntary. Appear in:

- Tic disorders (Tourette): motor and verbal tics.

- Tics caused by anxiety (in children).

Dyskinesia: characterized by involuntary buco-lingual movements (gum, splash, tongue darting) or choreo-athetotic movements induced by neuroleptics.

Choreic Movements: large and sudden movements at the root of the limbs (St. Vitus dance)

Athetotic movements: movements of small amplitude, slow, occur in the lower limbs.

Stereotypes characterized by repeating senseless movements or words that have never sense. appear in catatonic / hebephrenic schizophrenia, or mental retardation

Persevering: characterized by repeating senseless movements or words that were appropriate initially. occur in HEBEPHRENIC schizophrenia

Bizarre behavior:

- Secondary to ideo-verbal disruption in HEBEPHRENIC schizophrenia
- Secondary to hallucinations (the patient executes orders given by the imperative hallucinations)
- Secondary to dellusions (paranoia)
- Behavior that is remotely induced (in mental automatism).

DRAMATIC BEHAVIOUR: theatrical gestures and exaggerated movements; occurs in histrionic personalities

UNCENSORED BEHAVIOR: characterized by disinhibition in social behavior (the subject addresses strangers overly familiar, sings, dances, tells jokes or inappropriate situations; "truths" that bother). It occurs in mania and Pick's dementia.

Compulsive behavior is represented by compulsions. These are acts of physical or mental topic used to reduce the inner tension generated by obsessions or unrelated obsessions (obsessive compulsive disorder)

Impulsive behavior is characterized by short-circuiting deliberation with immediate relief by switching to the act.

Appears in

- Impulse control disorders: arsonist, trichotilomania, kleptomania
- bulimia nervosa
- Emotionally unstable-type personalities, histrionic or antisocial

The avoidance behavior is to avoid situations which produce phobia (phobic disorders) or relations with strangers (anxious-avoidant personalities)

“Securing” behavior: consists of having “guardians”, wearing token / amulets to deal with the exposure to stressors which cannot be avoided.

## Chapter III – PERSONALITY AND PERSONALITY DISORDERS

### HISTORY

Individuals with various types of temperament or personality were classified starting from antiquity (ex. The zodiac, the humoral theory of temperament - Empedocle and Hippocrates);

Personality = the habitual way the individual thinks, feels, acts and reacts. It has 3 components:

- body
- psychological (cognitive, affective <mood> and behavioral)
- spiritual

Bodily (body) perspective (Ernst Kretschmer)

- "Picnic" - Cyclothym - Prone to cyclothymia
- Leptosom / Asthenic - Schizothym - prone to schizophrenia
- Athletic - epileptoid - Prone to epilepsy

Psychological component

- The cognitive aspect - how the person perceives themselves and others
- Affective (mood) aspect - the ability to resonate emotionally, to control their emotions (or not), to orient affection towards himself or others.
- The behavioral aspect - refers to relations with others and the ability to control impulsivity)

The term personality comes from the mask used in antiquity by actors to amplify sounds ( "per sonare") and to change multiple characters (initially referring to the visible behavior).

Today the term refers to the real and hidden appearance (aspect) of an individual.

### DEFINITION

CHARACTER is the visible aspect of personality (behavior). The term was used in psychoanalysis under the term "character structure" reuniting motivational traits, which are in close correlation between them and form a structure resistant to change. Other meanings for the term "character" are: the moral aspect of personality (pleasant or unpleasant character), or the tenacity of an individual: "strength of character".

The temperament refers to simple features, of biological origin, observable in infants in opposition with the more complex notion of adult personality: regularity of biological functions, activity level, quality of



affective mood, response to sensory stimuli, closeness or distancing towards new situations; adaptability in new situations.

PERSONALITY GENESIS: Personality is formed in childhood and ends after adolescence. After 18-25 years of age personality genesis is considered to be over. A diagnosis of personality disorder may be made only after the age of 18!

PERSONALITY - psychoanalytic perspective

Sigmund Freud considered psyche as having three components:

- I. The Self (or id) - Entirely unconscious - the headquarter of repressed impulses
- II. The EGO - Both conscious and unconscious – differentiates itself from the self through contact with the surrounding reality.
- III. The Superego – both conscious and unconscious – differentiates itself from the ego by interiorizing of interdictions (moral conscience) and expectations from the parents (ideal ego).

During psycho-sexual development a child's needs can be adequately met by the parents to help the transition to the next stage of development.

In the case in which the child's needs are not met (the child is frustrated) or excessively fulfilled by the parents, development stops. Stopping the evolution in one of the normal stages of development leads to the appearance of the following traits/characters: oral (dependent), anal (anankastic) or phallic.

PERSONALITY - Jung

Carl Gustav Jung introduces the concept of collective unconscious of which the individual unconscious is part of.

HE also describes eight types the personality in connection with 2 attitudes (extraversion - importance given the external world and introversion importance given to inner perception) and 4 functions: taking decisions (based on thinking or feelings), and the perception of information (based on feeling or intuition).

Behaviourism

Behaviourism downplayed the importance of the psyche (which could not be known) and focused on behavior (which can be measured). From the view-point of radical behaviourism - human behavior is not the result of unconscious processing (Psychoanalytic theory) nor a result of conscious processing (Cognitive theory), but is the result of learning whilst being in contact with the environment.

Cognitivism

The cognitive theory pleads the existence of an unconscious storage of cognitive schemas, which are rules after which information is organized and processed so that they acquire meaning and can be stored in mnemonic storage.

Based on individual schemas the individual makes assumptions (has expectations) about themselves (their own abilities), towards others, or the future. These assumptions are the basis of automatic thoughts (in the preconscious or the evocable unconscious) which is reflected in conscious thinking. Cognitive processing generates emotions, vegetative reactions and behavior in an individual. In cognitivist terms, personality disorders are based on distortions of thinking caused by maladaptive cognitive schemas formed during the development of the psyche.

#### GENETIC AND BIOCHEMICAL THEORIES

Genetic studies have highlighted a genetic component for antisocial personality disorder.

Biochemical theories stipulate that the dysfunction of some neurotransmitters can be correlated certain temperamental traits, for example exploring the new and impulsivity have been correlated with a dopaminergic hyperfunction and a serotonergic hypofunction.

#### ADLER AND FRANKL

Alfred Adler brought forth social factors, which influence behavior dominated by the need for power that is generated by feelings of inferiority;

Viktor Frankl considered the predominance of the spiritual-value factor and in his views human behavior is dominated by the need to give meaning to its existence.

CHARACTER = is based on temperament, on which learned aspects (through contact with the environment) occurring during development overlap.

Temperament = innate (inborn), biologically conditioned

The current description of personality disorders is based on the descriptions of Kurt Schneider.

The borderline type of personality has been described by Otto Kernberg.

According to DSM-IV criteria, personality disorders (PD) have been classified in three distinct groups (clusters):

- I. cluster A (the bizarre): paranoid PD, schizoid PD
- II. cluster B (the extravagant): Histrionic PD, emotionally-unstable PD and antisocial PD
- III. cluster C (the uncertain): anankastic PD, anxious-avoidant PD and dependent PD.

Personality disorders are unevolutive but predispose (increase the vulnerability of the individual) towards neurotic, psychotic or addictive psychopathology.

Personality disorders from the cluster C predispose the individual to anxiety disorders and depression.

Personality disorders from the A cluster predispose the individual to psychotic disorders

Personality disorders from the B cluster predispose the individual to affective (mood) disorders, addiction and suicidal behavior (emotionally unstable personality disorder, borderline type).

#### GENERAL CHARACTERISTICS OF PERSONALITY DISORDERS

Features personality are globally and excessively accentuated

Egosyntonic: Subject is content (happy) with himself (lack of insight)

Behavior is rigid (inflexible a large variety of situations), so it has the characteristic of being predictable.

Alloplasticity: Subject does not feel the need to change, but tries to make others adapt to their own personality.

Maladaptive behavior: affects the functioning of the individual in society, family and the workplace .

Pathoplasticity: clinical features of comorbid disorders are influenced by the personality disorders (by either masking <dissimulating> symptoms or exaggerating them.

#### **PARANOID PERSONALITY DISORDER**

Is characterized by a “hypertrophy” of the ego (megalomania).

Personal failures are blamed on bad intentions or plots of others (extrapunitivity). Therefore, individuals with this disorder are hypervigilant , constantly on alert to detect and thwart possible malicious acts.

Are suspicious about other’s intentions (anyone can be a potential enemy).

DO NOT CONFIDE even to friends, because they are afraid that what they say might be used against them.

They tend to interpret everything against them, even neutral or benevolent words or gestures, are very sensitive to criticism (sensitivity) with a tendency to bear a grudge and taking revenge (they do not forgive or forget real or imaginary offenses), tend to have a revendicative behavior (they fight for their rights) are cverullent (prone to quarrel) or extremely tenacious in suing others.

Paranoid personality disorder predisposes the individual to persistent delusional disorders (paranoia)

Individuals show lack of interest towards tight, intimate relationships, which are interpreted as intrusive, preferring a solitary life-style.

They display an emotional coldness that discourages social relations. Most times their social network comprises of just their own family. The gap or lack of interhuman relationships is compensated by their preoccupation for phantasies and introspection.

### **SCHIZOID PERSONALITY DISORDER**

Lack of affection is compensated by the preference for abstract activities (related to domains such as philosophy, psychology, mathematics).

Schizoid individuals are eccentric, nonconformist and indifferent to any criticism or praise.

Schizoid personality disorder does not predispose these individuals for developing schizophrenia per se, but studies have shown that in the families of schizophrenic patients there are a lot of members with schizoid personality disorder.

### **EMOTIONALLY UNSTABLE PERSONALITY DISORDER**

Comprises of two types:

- Impulsive type characterized by emotional instability and lack of impulse control
- Borderline type characterized by instability of interpersonal relationships (Intense interpersonal relationships and unstable with the subject's desperate efforts to avoid real or imagined abandonment) through an unstable self-image or regarding other persons (hyper-idealization or hyperdevaluing) and by emotional instability with intense emotional reactions (euphoria, anxiety, irritability, anger).

Another feature of this type is the impulsivity with potential self-destructive behavior (excessive spending, inappropriate sexual life, drug abuse, bulimia, careless driving).

Often the subject has a self-harming behavior (Notches, prickling in the limbs), suicidal threats and suicide attempts.

Is associated with feeling empty inside and sometimes transient paranoid ideation.

Predisposes the individual to depression, suicide and abuse.

### **HISTRIONIC PERSONALITY DISORDER**

Is characterized by selfishness (with the need to be in the center of attention, to be admired, loved, courted) with poor affective transfer ability.

They are very sociable and charismatic making friends easily, but their shallow transitive affectivity makes keeping friendships difficult.

In order to get the attention they require, they adopt a dramatic behavior or a manipulative behavior (through seduction or emotional blackmail

<parasuicide or suicidal threats>)

Is characterized by immaturity coupled with superficiality, emotional lability, reduced tolerance for frustration with hyper-emotivity (Exaggeration in expressing emotions), easily crying. Are very suggestible.

Histrionic personality disorder predisposes an individual to conversion and dissociative disorders and somatization disorder.

### **ANTISOCIAL PERSONALITY DISORDER**

The antisocial personality type is characterized by contempt towards the rights and feeling of others, and by contempt towards laws and social norms (and without hindrance in breaking them)

These individuals are unable to empathize (to feel compassion) for other individuals, sometimes causing harm to others produces pleasure for them (malignancy).

For personal benefit, they might resort to lies, intrigue, extortion, complicity.

Antisocials are both irresponsible at work which they lose easily (they can not adapt, and change many jobs) and in the family (they leave their partners and children and aren't interested in neither).

Tolerance for frustration is reduced, with increased impulsivity and aggressivity.

Their IQ score is high enough for them to make the difference between good and bad, but through their lack of moral dimension they choose to do evil. Are incapable of feeling remorse and to learn through punishment (they cannot be reeducated).

Antisocial personality disorder is preceded in childhood by conduct disorders and may be complicated by substance abuse.

### **ANANKASTIC (OBSESSIVE-COMPULSIVE) PERSONALITY DISORDER**

Is characterized by high self-imposed standards and imposed onto others aswell (increased requirements). They have an unjustified devotion to work in terms of volume and time at the expense of leisure (their sacrifice moments of relaxation).

Their inner uncertainty is compensated through order in time (plans, agendas) and space (arranging / order regarding objects) and pedantry. Are very attached to material objects and are incapable of throwing away useless objects or objects that have sentimental value.

They adhere the rules, regulations, conventions and moral norms (punctuality, honesty, sacrifice) and are characterized by a marked psychorrigidity (stubbornness, intransigence) with the risk of sacrificing

relationships. Regarding affectivity they appear to be emotionally cold or they adopt a very serious mimicry / gesturing.

In relations with colleagues they are authoritarian and are reticent in passing on responsibilities to others.

In their desire to achieve perfection they pay great importance to details and verifying (self-checks but also checking others).

These individuals are more vulnerable to anxiety or depressive disorders (and secondary to these towards alcoholism).

### **ANXIOUS-AVOIDANT PERSONALITY DISORDER**

Present an excessive fear and concern of being criticized or rejected. They live with a feeling of inferiority and consider themselves socially inadequate.

From here comes reluctance in trying new interpersonal relations if the person is not sure whether she/he is accepted or liked hence the aversion towards intimate relations.

These people do not reject relationships similar to schizoid personalities, they just want to make sure that they are accepted as they are.

In regards to a new relationship, these individuals are inhibited, preferring to avoid activities which involve interpersonal relationships.

Uncertainty makes them reluctant in taking risks or responsibilities.

These individuals are predisposed to anxious and phobic disorders (especially social phobia).

### **DEPENDENT PERSONALITY DISORDER**

These individuals live with distrust in their capability to make their own decisions, requiring that others make decisions for them.

As a result dependent personalities encounter difficulties in decision making without supervision or to initiate their own projects.

When they need to make a decision for themselves, they feel helpless.

In order to avoid losing support from the person who takes or supervises their decisions, these individuals are incapable of expressing disapproval towards these persons, forego their principles or accept menial tasks which humiliate them.

These individuals live in fear of being abandoned or being left to fend on their own.

They immediately search for a new supervisor (or life partner with those traits), as soon as the current relationship ends.

Are more predisposed to anxiety disorders, depression and addictive behavior (secondary to anxiety / depression).

### **DIFFERENTIAL DIAGNOSIS**

- Personality disorders must be differentiated from the accentuation of personality traits and personality changes from an organic cause like the fronto-temporal syndrome (caused by tumors in the frontal lobe) or Pick's dementia (prefrontal degeneration of neurons in the frontal lobes with the atrophy of the frontal lobes).
- Psycho-active substance abuse may be complicated with antisocial behavior (offering drugs to friends to raise money, theft and sale of goods obtained illegally, robbery, verbal aggression and even murder).
- Other causes of changes in personality are the durable changes of personality caused by a psychotrauma: the whole life philosophy of an individual changes in the sense that he might become hypervigilant, sensitive, isolated or dependent on others, to reconsider or reconsider moral values.
- Personality disorders are unevolvable. Anankastic personality disorders might worsen with age.

### **COMPLICATIONS**

- Personality disorders can be complicated with anxiety disorders, depression, conversive-dissociative disorders, food disorders, psychotic disorders and addictions.
- The presence of a personality disorder worsens the prognosis of associated disorders and it complicates the treatment.

### **TREATMENT**

Individuals with personality disorders do NOT have insight of their disorder, thus they do not seek medical help.

Results regarding improvement of personality disorders through psychotherapy (psychoanalysis, cognitive-behavioral or familial psychotherapy) is controversial.

When a personality disorder leads to the onset of other disorders (anxiety, depression, psychosis or drug abuse), pharmacological treatment might need to be administered (anxiolytics, antidepressants, mood stabilizers)

## Chapter IV - ACUTE STRESS REACTION AND ADJUSTMENT DISORDERS

All disorders in this nosological category are considered to appear as a direct consequence of an acute stress or a persistent trauma. Stressful events are causal factors and the disorders would have never appeared if it weren't for them. The link between the type of event, its significance to the subject and the clinical aspect of the reaction are to be understood in the sense that any subject could have reacted similarly to this type of event. The difference between a normal and a pathological reaction lies in the intensity, the way symptoms present themselves, and time span.

Psychopathological are maladaptive responses to severe or continuous stress because they interfere with coping mechanisms and lead to social functioning impairment. They are more frequently seen in more vulnerable subjects (people who've accumulated vulnerable psychosocial and biological influences), fact driven by the observation that not all subjects exposed to severe stress or persistent trauma develop psychopathological reactions. Also, other predisposing factors might be other repetitive traumatising events that occurred prior to the indexed stressful event, prior psychiatric disorders (relapses of pre-existing psychopathological disorders are excluded except personality disorders). Depending on the stressful event and the duration of the psychopathological changes, they can be classified as follows: acute reaction to stress, post-traumatic stress disorder and adjustment disorder.

### **Acute stress reaction**

Acute stress reaction is a transient disorder but with a significant severity which develops in subjects without a prior apparent mental disorder on impact with physical or mental stress, which enters remission hours or days after the initial event. There has to be an immediate and clear temporal link between the causal event and the development of symptoms. The stressor might be a traumatic experience that involves a serious threat to the physical integrity or security of the subject or loved ones or unusually abrupt or threatening change in the social position of the subject (ex. Natural catastrophes, accidents, criminal attacks, fights, rape).

Symptoms are varied but typically include a state of perplexity with some narrowing of consciousness, an inability to understand external stimuli and lack of orientation. This state can be followed by dissociative stupor or by agitation and hyperactivity (isolation or flight/fugue).

The following vegetative anxiety symptoms might be present: tachycardia, profuse sweats, facial erythema. Also, derealisation, depersonalisation, partial selective or complete amnesia of the episode (dissociative amnesia), depression, anger and despair, may be observed. Generally the clinical picture is



volatile and neither type of symptoms is predominant for a long period of time. Symptom remission occurs usually within a few hours if the stressor is removed or they can last for a few days/weeks if the stressor persists. If symptoms last for over a month, the diagnosis changes to post-traumatic stress disorder.

**Psychological treatment:** Supportive psychotherapy is usually sufficient. It comprises of detailed discussions about the stressful event in a secure emotional context by reassuring the patient and by learning methods of problem solving.

**Pharmacological treatment:** Anxiolytics are useful especially in cases in which the stressor persists and the patient is severely affected. In patients where benzodiazepines are contraindicated, small doses of sedative antipsychotics may be used.

### **Post-traumatic stress disorder**

Post-traumatic stress disorder (PTSD) appears as a late (weeks/months, rarely over six months) and prolonged response to a stressing situation or an event of menacing or catastrophic nature which can cause profound suffering for almost anyone (violent attack, including rape, capturing, kidnapping and torture, survival of a criminal attack, unexpected death of a loved one and, rarely, man-made or natural disaster).

The clinical picture consists of: flashbacks (repeated memories of trauma), insomnia, fragmented sleep (interrupted by repeated dreams and nightmares which are replicas of the traumatic event), heightened motor activity during sleep. Other symptoms include emotional numbness or blunted affect, detachment from other people, decreased interest towards pleasant activities, lack of reactivity towards the ambiance, avoidance of everything that reminds the subject about the trauma (thoughts, feelings, conversations, activities, individuals or places), irritability, aggressive outbursts, hyperactivity, difficulties in concentration, hyper-vigilance.

Anxiety and depression are usually present, as are suicidal thoughts and suicide attempts. Excessive alcohol and drug use is common and worsens the outcome. The outcome is volatile but complete remission is possible in most cases.

A small number of patients can have a chronic evolution across several years even after decades from the traumatic experience which represents a transition towards a durable personality change.

**Psychological treatment:** Behavioural psychotherapy combines imaginative exposure to memories about a trauma and in vivo exposure to what the subject avoids. Cognitive techniques are less efficient as are relaxing techniques.

Pharmacological treatment: Antidepressants (especially SSRI's – Escitalopram, Sertraline, Paroxetine, Fluvoxamine), but also dual antidepressants (Venlafaxine, Duloxetine) have proven to be effective. Benzodiazepines are apparently not efficient in the treatment of PTSD, bringing just a partial remission of the anxiety symptoms. Administering these drugs in the long term increases the risk of abuse and addiction to benzodiazepines and thus non-benzodiazepine drugs (Buspirone) are needed. Other classes of drugs that may be used are mood stabilisers and beta-blockers.

As an alternative to a pharmacological treatment repetitive transcutaneous magnetic stimulation of the right frontal cortex was proposed and it is efficient in decreasing anxiety symptoms.

## **Adjustment disorders**

Adjustment disorders are subjective suffering and emotional distress which interfere with social performance and functioning that are triggered by identifiable stressors. The types of stressful events that can trigger adjustment disorder are the loss of a loved one (mourning reaction), separation, significant life changes (emigration, refugee), the presence or possibility of serious somatic disorder. Individual predisposition or vulnerability plays a higher role in the risk of a clinical manifestation than in the other types of psychopathological reactions.

Clinical symptoms are varied and include: depressive disposition, anxiety, feeling of incapacity to handle the situation or to plan the future. Also, in some cases (rarely), dramatic behaviour or outburst of violence are also possible. Symptoms appear less than a month after the traumatic event or the life change and duration of symptoms isn't longer than six months except the prolonged depressive reaction.

### Clinical types

- Short depressive reaction – transient mild depressive state with a duration under a month
- Prolonged depressive reaction – mild depressive state which appears as a response to a prolonged exposure to stressful situation that lasts under two years
- Mixt depressive and anxiety reaction – both syndromes are present, mild intensity

### Differential diagnosis

- Normal reaction to stress – not every stress induced type behavioral or emotional reaction represents a psychopathological disorder. Differentiating a normal reaction from a psychopathological one is made by assessing symptom intensity, forms of manifestation of symptoms and duration

- PTSD – is characterized by the presence of a severe stress and by the specific association of symptoms

Psychological treatment: Psychotherapeutic approach centered on its specificity and the way the subject perceives and controls this stress is paramount. Cognitive orientation techniques are especially efficient because they aim to correct dysfunctional strategies in regards to overestimating danger.

Pharmacological treatment: Symptomatic medication has an auxiliary role by reducing symptom severity and facilitating the psychotherapeutic approach.

## Chapter V – ANXIETY DISORDERS AND PHOBIAS

Anxiety is an emotional state, that up to a point is considered normal, and is correlated with a state of alert, which any individual might encounter in situations which might pose real physical danger or evaluative social situations. Anxiety which appears in the absence of such objective situations or when the emotional response is disproportionate (high intensity / duration) is considered pathological.

In this chapter, generalized anxiety disorder (GAD), panic disorder (P) and phobic disorders (PD) will be defined and discussed.

### **Epidemiology**

Anxiety disorders are one of the most frequent psychopathological disorders in general practice. Life-time prevalence of GAD is 2.5-6.4 % in the general population, PD 1.4-7.0 % and P 0.6-1.2 %. Mean age at onset is usually 25 ( $\pm$  10 years) and females are more at risk to develop the aforementioned disorders than men.

### **Etiology**

Numerous psychosocial factors can cumulate in a vulnerable subject and contribute the onset and clinical manifestation of anxiety disorders. The vulnerability for a subject to develop a psychopathological disorder has a biological and psychosocial conditioning.

### **Psychosocial theories**

Psychosocial influences play an important role in generating vulnerability for psychopathological disorders if they act early on in life and are persistent / prolonged. During the first years of childhood, an important role may be played (in regards to becoming a vulnerable person) by: insufficient or deformed identifications with the parents or later on, teachers, close friends, and the types of “heroes” brought forward by socio-cultural movements. Also, repeated psycho-traumas, stressful long-lasting familial atmosphere and multiple frustrations may contribute in the vulnerabilization of a person. In this context, pathological teachings may be vulnerabilizing, because of identifications with adults with an absurd

behavior, dysfunctional attitudes of parents and/or teachers (ex: parental rejection, punishment, hypercriticism, hyperprotection), which can lead to dysfunctional beliefs about the world in general and about the subject's self. Dysfunctional parental attitudes may lead in delayed psychological development of the subjects, the young adult being highly dependent on his parents, familiar protective places and close friends. Such deficits can be seen frequently in subjects who have anxiety disorders.

**Psychoanalytic theory:** Freud, the founder of the psychoanalytic theory, mentioned the role of psychosocial influences from a developmental perspective. He underlined the role of deformed identifications with parents and/or teachers in early childhood and the intra-psychic conflict (Oedip and Electra complexes), both for the harmonic and inharmonic types. He considered that if intra-psychic conflicts are less integrated or repressed during the formative period (childhood – adolescence), then during adulthood the significance of events may trigger anxious responses which will in turn activate psychological defense mechanisms. The first mechanism that gets activated is repression, which could have partial efficiency, situation in which auxiliary mechanisms come into play, such as: displacement, projecting, isolation, etc. Through displacement, anxiety is attached to a situation or object which symbolically represents the intra-psychic conflict (ex: phobias). Psychological defense mechanisms prevent the “update” of the dangerous situation. For example, in panic attacks, anxiety isn't triggered by the repressed affect, but by the fear of affect, the fear of repetition of a dangerous situation to which the affect is associated and the anticipation of a dangerous situation. In GAD the cognitive content of a situation similar to a previous experience is fragmented and repressed, and the content of affect has access to the conscience.

Learning theory (conditioning theory): Has a particular relevance for phobias. According to the conditioning theory, a neutral stimuli triggers anxiety as a result of classic conditioning. The conditioned response will be protected of extinction through the intervention of the avoidance behavior, which reduces the anxiety and thus gains a status of reinforcement. Avoidance becomes a stable and persistent symptom, because it is efficient and protects the subject from anxiety. The maladaptive anxiety response may be acquired indirectly through imitation as well. The information which induces fear, may be transmitted even through language. In this situation, the type of conditioning is semantic.

For GAD it seems there might exist a certain style of reactivity (characterized by hypervigilance and anxious anticipation), that has been learned from previous experiences, when the subject went through a stress which he interpreted as uncontrollable and unpredictable. The response is triggered unspecifically by a large diversity of stimuli, according to the principle of generalization.

**Cognitive theory:** the first pathological link that appears is represented by dysfunctional cognitive structuring. Cognitive schemes are the result of learning from one's own experiences, direct observation, identifying and implicit and explicit messages received from other subjects. On top of these, nuclear beliefs about the self and the surrounding world can be formed, some stable, some less stable and who vary in exactness and functionality from one individual to another. Correlated with these nuclear beliefs are: presumptions, attributions and attitudes, which operate as rules and, automated thoughts (quick, evaluative, partially conscious thoughts) which are triggered by specific stimuli and which can influence emotions and behavior. According to the model proposed by Beck and Clark, in anxiety disorders, cognitive schemes that have become dysfunctional are mildly activated by stimuli, and distortions in selecting and processing information may appear.

Thus, more attentional resources are needed to process the negative stimuli. In the next phase the processing of information continues, both automatically and through controlled processes. The results of this phase are the automated thoughts, with themes of threat and danger, and errors of thought specific for anxious subjects. The most frequent logic error is selective information extraction which validates danger schemes in a repetitive fashion, followed by a catastrophic interpretation of benign situations and an erroneous assessment of their ability to handle the situation.

Dysfunctional beliefs more specific to patients with GAD refer to: social acceptance, competency, responsibility and control of their own anxiety. For subjects with panic disorder, catastrophically interpretations of normal body sensations / functions (as a sign of a imminent catastrophe) are characteristic. In this way, varied stimuli are interpreted in a distorted manner and the result is a rise in apprehension and bodily sensations, thus creating a vicious circle which amplifies anxiety, leading to a panic attack. In regards to what maintains the symptomatology and the negative interpretation, two processes have been found: focusing the attention on the body and some forms of cognitive avoidance.

### **Biological theories**

Genetic data: given the high comorbidity rate between anxiety disorders amongst themselves and with depression, quantifying just how much genetics play a role in the etiology of anxiety may prove rather difficult.

-familial studies: life-time prevalence of panic disorder in 1st degree relatives is 7.9-14 %, whilst in GAD it's 3.5-4.8 %. Aggregation of anxiety symptoms within the family is suggestive, but not conclusive,

because familial studies show intergenerational transmission and contribute to inherited phenotypes, but cannot make the distinction between genetic and environmental influences.

-twin studies: for panic disorder, concordance rates in monozygotic twins (MZ) are 25 % and for dizygotic twins (DZ) 11 %. For GAD, MZ rates are 21 % and 10 % for DZ. Segregation and genome scanning studies suggest the idea of genetic transmission, with the involvement of several chromosomes. These studies show the involvement of a genetic component in anxiety disorders, more for panic disorder and agoraphobia than GAD and phobic disorders.

### **Aspects regarding neurotransmission**

Data regarding the implication of neurotransmitter dysfunction in the etiology of anxiety disorders is at best described as circumstantial and based upon speculation regarding the efficacy of some pharmacological compounds.

- Noradrenergic transmission: the somatic nature of some symptoms such as: increased respiratory and heart rate, sweats, dizziness, paresthesia suggest a hyperfunction of the autonomous nervous system. It's considered that these peripheral phenomena appear as a result of a neuronal discharge from the brainstem (more specifically, the locus coeruleus, which contains 50 % of noradrenergic neurons). From there, numerous efferences to towards different areas of the CNS, including the prefrontal cortex, limbic system and the thalamus (areas involved with emotion control and disposition). The role of the noradrenergic system in the etiology of anxiety disorders is backed up by several studies (both pharmacological and experimental). Because of these studies, several hypotheses have been proposed, such as the noradrenergic system hyperactivity and dysfunction of alpha-2 and beta receptors, especially in the etiology of GAD.

- GABA-ergic (gamma-amino-butyric acid) neurotransmission: the idea of the gaba-ergic involvement in the etiology of anxiety disorders came from the observation that benzodiazepines (BZ) are effective in the treatment of these disorders. BZ facilitate gaba-ergic neurotransmission by interacting with GABA-A receptors. GABA is the most important inhibitory neurotransmitter on the CNS. There are several hypotheses regarding GABA-ergic dysfunction in anxiety disorders, one being the existence of a basal abnormality and the other an adaptive one, with a pathological significance in both panic disorder and generalized anxiety disorder.

- Serotonergic transmission (5-HT): serotonergic dysfunction in anxiety disorders was postulated more than 4 decades ago. Two competing theories have emerged, one supporting excess 5-HT and the other 5-HT deficit. Serotonin has an excitatory role upon the CNS. 5-HT receptors have a very wide distribution, in practically all regions of the CNS.

The high effectiveness of pharmacological substances which interfere serotonergic neurotransmission (ex: SSRI's) constitutes an important argument in the implication of this neurotransmission system in the etiology of anxiety disorders.

- Neuro-endocrin aspects: some patients with anxiety disorders have been found to suffer from nocturnal hypercortisolism, non-suppression to dexamethasone and a certain degree of sensitivity reflected by the ACTH-cortisol level (which was found to be lower in patients with severe forms).

- Neuroanatomy aspects: the results of recent neuro-imagery studies have shown that there are some abnormalities in the functioning of several areas of the CNS in patients with panic disorder (more specific: amygdala, hippocampus, thalamus, hypothalamus, locus coeruleus and other structures of the brainstem) and generalized anxiety disorder (frontal and temporal lobe, basal ganglia)

### **Vulnerability-stress theory**

The aforementioned etiological models (presented from a psychosocial and biological point of view) each offer partial explanations. Vulnerability-stress theory creates connections between the two competing models.

According to Zubin, the vulnerability of a person for psychopathological disorders in general or for a certain type of disorder is constituted by a sum of biological and psychosocial experiences which occur during ontogenesis. Through genetic determinism, certain genetic or biological predispositions can occur, which will leave an imprint on the later bio-psychological development of the individual. Thus, certain temperamental traits may influence the manner in which the individual selects information and the way the interpersonal relationships develop. Functions like: attention, memory, reasoning and imagination may be genetically influenced. Dysfunctions or fragility of some neuroendocrine or neurotransmission systems may also be genetically transmitted.

Psychosocial influences play a major role in the development of vulnerability for psychopathological disorders if they appear early and are persistent, leading to a fragile personality.

Regarding anxiety disorders, the scenario of the aforementioned factors might play out as follows: if a subject that is genetically predisposed for anxiety disorders goes through one or several psychotraumas



in early childhood or adolescence he may become sensitive towards these types of events and there may also be alterations regarding the functioning of different neuronal and neuro-endocrine circuits. In other words, a individual with genetic or acquired vulnerability will be more susceptible than the general population to develop an anxiety disorder in adulthood.

Psychosocial influences also have a role as triggers. Such situations might be: many negative life events developed in a short period of time (linked to family, the work place, study, social life), life changes, failure.

## **ANXIETY DISORDERS: DIAGNOSIS, OUTCOME AND TREATMENT**

### **1. PANIC DISORDER**

The essential traits of this disorder are recurrent severe anxiety attacks (panic attacks), which are unpredictable, apparently triggered spontaneously. This disorder is more common in insecure, hyperemotional subjects, who tend to excessively control the functionality of their own body and who strive to avoid new and stressful events.

Characteristic for the panic attack (PA) is the sudden onset of a feeling of imminent death or catastrophe, preceded and accompanied by severe neurovegetative and somatic symptoms. During the attack, the patient may lie still and terrified or may enter a state of psychomotor agitation, with a hyper-expressive cry for help to those who surround him or to emergency services.

Somatic and neurovegetative symptoms: palpitations, tachycardia, chest pain, breathing discomfort (described as: feelings of suffocation, tachypnea), generalized tremor, erythema, dry mouth, tinnitus, abdominal pain, nausea, blurred vision, vertigo, accelerated bowel movements, muscular hypotonia, derealisation, depersonalization. The duration and intensity of panic attacks vary from one individual to another, the onset and remission are abrupt, and the duration is seconds or minutes, rarely hours.

For the positive diagnosis of panic disorder, the following criteria must be fulfilled:

- 4 or more panic attacks / month.
- The panic attacks do not appear in circumstances where there is real danger present; the panic attacks must not be triggered by specific or predictable situations.

- Between two panic attacks there must be anxiety-free periods of time.

Differential diagnosis: an organic cause must first be excluded, as anxiety may be a part of many somatic disorders, like:

- Asthma, chronic obstructive pulmonary disease, pulmonary embolism, pulmonary oedema.
- Coronary disease, cardiac arrhythmias, high or low blood pressure.
- Hyperthyroidism, hyperglycemia, hypercortisolism, hypercalcemia, hypocalcemia, paraneoplastic syndrome, porphyria.
- Temporal lobe epilepsy, cerebral tumors, Parkinson disease.

Anxiety syndrome may also be triggered by psychoactive substance use / abuse and may a consequence of either intoxication or withdrawal to these substances, such as:

- CNS stimulants: amphetamines, aminophyllin, methylfenidate, caffeine, tricyclic antidepressants.
- Sympathomimetics: ephedrine, epinephrine, phenilpropanolamine.
- Dopaminergics: L-dopa, neuroleptics, metoclopramide, bromocriptine, amantadine.
- Withdrawal: benzodiazepines, barbiturics, sedatives, alcohol.

After excluding all possible organic causes and/or psychoactive substance use / abuse / withdrawal, we must differentiate panic disorder from the following afflictions:

- phobic disorders – the panic attack is triggered by phobogenic objects or situations.
- Obsessive-compulsive disorder – mental and behavioral phenomena are specific.
- Primary depression – differentiating might prove difficult. A longitudinal approach regarding symptoms (temporal link) might prove useful.
- Schizophrenia – may debut with anxiety symptoms, who are usually associated with the feeling of “losing one’s self”, followed by a period of various thought and perception disorders (delusions, hallucinations).

## **Outcome**

Panic disorder has an episodic character, with remissions which can last long periods (years) and relapses, but it can also be healed. Prognosis is usually favorable. Clinical observation reveals a high comorbidity rate with depression, GAD, hypochondria, psychoactive substance abuse (with or without addiction), comorbid disorders / behavior with a variable onset after the debut of panic disorder.

## **Treatment**

In panic disorder, both psychotherapeutic and pharmacological approaches might be useful, depending on the particularities of the case.

### **Pharmacological treatment:**

- benzodiazepines: very efficient (alprazolam) – they reduce the frequency of panic attacks, anticipatory anxiety and the potential associated agoraphobia. The anxiolytic effect is quick, which explains the good adherence of the patients. Other benzodiazepines (diazepam, lorazepam, clonazepam) are also effective. There are few side effects and if they occur, they are not of a serious nature, but extreme attention has to be given to cases who have been on benzodiazepines for a long period of time, because there is the risk of biological addiction (and thus, risk of withdrawal if the medication is stopped abruptly). Therefore, benzodiazepine administration should not exceed 1-3 months and antidepressants should be used if further treatment is necessary. Stopping the administration of benzodiazepine should be done gradually, to avoid rebound / withdrawal. Recommended therapeutic doses are: alprazolam 3-10 mg/day, clonazepam 1-2 mg/day, lorazepam 2-7 mg/day and diazepam 10-40 mg/day.

- Antidepressants: tricyclic antidepressants which are effective in panic disorder are clomipramine and imipramine. Tricyclics have numerous side effects and thus other classes of antidepressants (such as SSRI's) should be preferred as a first line of treatment, because they have fewer side effects and are well-tolerated by patients. Initial doses for SSRI's are: fluoxetine 10 mg/day, sertraline 25 mg/day, paroxetine 10 mg/day, fluvoxamine 20 mg/day and escitalopram 10 mg/day. Another class of antidepressants used are SNRI's (dual antidepressants). Venlafaxine is a frequently used SNRI, dose range 50-150 mg/day. The aforementioned doses must be progressively increased until the therapeutic effect is obtained.

Treatment duration in the acute phase is 6 to 12 weeks. Maintenance treatment should be 6-12 months. Antidepressants in general are indicated even when depression is not present because they help prevent the frequency of panic attacks.

- Anticonvulsants: their efficiency is still unclear, some authors consider that in some cases sodium valproate and carbamazepine reduce the frequency of panic attacks.
- Adrenergic beta-blockers: are useful as a secondary short-term treatment (in coupled with benzodiazepines) in cases where cardiovascular symptoms are predominant. Recommended doses are according to the therapeutic effect and monitoring of heart rate and blood pressure are paramount.

### **Psychotherapeutic treatment**

In the treatment of panic disorder the most effective psychotherapeutic interventions are cognitive-behavioral therapy, individual and/or group therapy. The main components of these interventions are: psycho-education, continuous monitoring of anxiety symptoms, respiratory control, distraction of attention, cognitive restructuring based on correcting catastrophic interpretation / thoughts and exposure to anxiogenic stimuli. Treatment duration is 4-16 weeks. In some cases, where there are familial problems, familial psychotherapy or couples therapy might be needed as well.

## **2. GENERALIZED ANXIETY DISORDER**

GAD has an insidious onset, most patients have difficulty of saying when exactly the symptoms started and in what circumstances. Subjects who are predisposed to GAD have the same traits as those described earlier in the panic disorder section.

The symptoms of GAD are numerous and varied and can be grouped as follows:

-subjective: the feeling of a diffuse, unspecifiable danger, unjustified worries about hypothetical circumstances, irritability, insomnia (trouble falling asleep), interrupted sleep, attention difficulties (concentration and persistence), which determine hypomnesia.

-somatic and vegetative symptoms: are moderate in intensity when compared to those encountered in panic disorder. They can be: increased heart rate, palpitations, breathing discomfort, tachypnea, tremor (usually not noticeable by others), sweating (hands, feet), inability to relax, abdominal discomfort, dry mouth, head ache, dizziness, articular pain.

-behavior (noticed by others): psychomotor restlessness, hyperinvestigative eye movements, mimic that expresses worry.

Generally, anxiety levels rise during the evening/night and when the subject visits unknown places.

Positive diagnosis: most symptoms previously described need to be present on most days for at least a few weeks for a positive diagnosis.

Comorbidity: the most frequent comorbid afflictions are: depression and psychoactive substance use / abuse (drugs, alcohol).

The incidence of depression in subjects with GAD is estimated at 31-71 % of cases. Depressive states are episodic, of variable intensity and in most cases are secondary to GAD. They're considered to be reactions to the anxiety disorder. In other cases though, the two independent nosological entities are co-existent. Alcohol use / abuse and self-medication (usually sedatives) is reported to have a prevalence of 27-35 % of cases. If during the initial phase alcohol consumption has an anxiolytic effect, maintaining chronic use (or abuse) actually increases symptom severity and maintains symptoms in time. Thus, a vicious circle of reciprocal potentiation is created, which has serious therapeutic implications and worsens the outcome.

Differential diagnosis: has to be made with somatic disorders, substance use / abuse (including addiction and withdrawal, which are described in the panic disorder section of this chapter).

-differentiating GAD from panic disorder may be difficult in cases with GAD who have spontaneous panic attacks. The difference can be made by determining focus expectancy and worry.

-depression: patients with GAD may have secondary depression, but, on the other hand, the anxiety symptoms may be a manifestation of a depressive disorder. In differentiating the two nosological entities we must determine which specific symptom groups appeared first.

-patients with GAD may have increased focusing on somatic symptoms and therefore will solicit (emergency) medical services repeatedly. In such cases, differential diagnosis with somatisation disorders and hypochondria has to be made.

Evolution / outcome: is chronic, fluctuating, but with a favorable outcome. The fluctuant aspect is explained by the interference with stressful events / time periods and/or the appearance of complications and/or comorbid states.

## **TREATMENT:**

### Pharmacological treatment:

-benzodiazepines: mild/moderate doses of benzodiazepines are indicated (ex: 20-30 mg diazepam / day)

-azapirone / buspirone: are non-benzodiazepinic anxiolytics, well tolerated by patients, who present no risk of biological addiction, usual doses 15-40 mg/day. In doses over 40 mg/day they have antidepressant effects and can thus be used to treat mixed (anxious-depressive) symptomatology.

-antidepressants: may be useful in reducing anxiety symptoms and/or depressive ones. The most used classes are: SSRI, SNRI, tricyclics.

The duration of treatment is usually 6-12 months. Because most cases have a chronic evolution of the disorder, dosage reduction or stopping administration altogether might prove useful, with re-initiation if needed.

### Psychotherapeutic treatment:

-supportive psychotherapy: can be efficient in some cases. The fact that the patient can discuss about his/her problems and difficulties in a secure environment can help reduce symptoms, as does the fact that the therapist will explain and teach him/her some physiological aspects of anxiety.

-cognitive-behavioral therapy: behavioral techniques like relaxation (self-control techniques) may reduce anxiety symptoms. Cognitive techniques – aim to reduce the frequency of negative thoughts by altering

dysfunctional beliefs from which they derive. Dysfunctional beliefs and attitudes can be altered through arguments and learning.

In some cases, both pharmacological and psychotherapeutic treatment is necessary.

### 3. PHOBIC DISORDERS

Phobia is defined as persistent and irrational fear of specific stimuli. Exposure to these stimuli triggers an anxious response, which can vary in intensity, from a discomfort to a panic attack, which create behavior of avoidance and assurance. These behaviors interfere with normal day-to-day functioning (social, relational and professional activities).

Subjects predisposed to phobic disorders are unsure of themselves, especially regarding new and uncharted events / places, which they tend to avoid. They can have an excessive preoccupation for order, cleanliness. Besides the different events, an important role in triggering phobic disorder may be played by factors who modify or interfere with the social support network.

Phobic disorders are classified as follows: agoraphobia, social phobias and specific phobias.

#### AGORAPHOBIA

In a broad sense, is defined as: an irrational fear of any space or situation in which the possibility of escape or to get help is not immediately accessible in case of the sudden onset of anxiety symptoms. The most frequent stimuli that trigger an anxious response are: streets, squares (empty or full of people), other public spaces, transport vehicles (buses, trams), being far away from home. Patients with agoraphobia have assurance (they ask for company when they need to visit such places) and avoidance behaviors. They tend to diminish the area in which they are active throughout the day (or night), preferring to stay home most of the time. In some cases, they isolate themselves completely. Mean age at onset is 20 to 30 years of age and the disorder is more common in females.

Differential diagnosis - must be made with:

- GAD – in phobias, the symptoms are triggered by specific situations and symptoms disappear in the absence of these specific situations.
- Depressive disorder: differentiating them might prove difficult, but disorder history usually clears things up (if phobias appeared after the onset of depressive symptoms, depression will be the primary diagnosis).
- Schizophrenia and other paranoid psychoses: subjects may present some behavior similar to agoraphobia (like refusing to leave the house), but their arguments are of a delusional nature.

## **SOCIAL PHOBIAS**

Are correlated to situations in which the subject might be exposed to a (public) scrutiny. Exposure to these stimuli triggers an intense anxious response, which is accompanied by neuro-vegetative symptoms and behavioral inhibitions.

The onset of the disorder is usually in adolescence, and, in contrast to other phobias, gender prevalence rates are similar. Social phobias may be distinct, isolated, for example limited to talking, writing, eating in public or diffuse, implicating all social situations outside the family circle. Avoidant behavior is sometimes extremely severe and may sometimes lead to total social isolation.

Differential diagnosis:

- Normal anxiety that occurs during public speaking (stage fright, timidity).
- Generalized anxiety disorder – in social phobia symptoms occur only during the specific situation.
- Avoidant personality disorder – characteristic for this disorder is the general avoidance of social situations, behavior which is not limited to specific circumstances.
- Delusional / hallucinatory psychoses (schizophrenia, persistent delusional disorders) – subjects may manifest a phobia-like behavior, but this behavior is motivated by delusions and/or hallucinations.



## SPECIFIC PHOBIAS

Represent a heterogenous group which includes many phobias. Specific phobias frequently reflect universal reaction to stimuli, which many people find uncomfortable, but which generate extreme anxiety in subjects with specific phobias.

Onset is usually in childhood or adolescence, and if untreated, can last for decades. Global functioning impairment depends on how easy the individual can avoid the phobogenic object / situation.

Subtypes:

- Phobias of small / large mammals, reptiles, insects.
- Phobias of natural elements: thunder, lightning, height, water, fire.
- Situational phobias: airplanes, elevators.
- Phobia of seeing blood or wounds, phobia of infections, dental procedures. These may be couple with vaso-vagal syncope. There is also a phobia of getting diverse diseases. It'll be considered a phobia if there are correlations with specific situations where one might get that disease.

Differential diagnosis:

- Hypochondria & persistent delusional disorder with hypochondriac delusion – there is a fear of specific diseases, but it's not linked with a specific situation where one might get that disease.
- Obsessive-compulsive disorder – some types of phobia, like the phobia of sharp objects and being contaminated are determined by obsessive phenomena belong to the nosological group of obsessive-compulsive disorder.

## Treatment

Psychotherapeutic treatment: cognitive-behavioral psychotherapy: the most efficient behavioral techniques are of the desensitizing type (through progressive exposure to the anxiogenic object / situation), through “invasion” or “flooding” (“brutal”, non-progressive exposure), positive and negative reinforcement. The cognitive technique is used to stop negative/intrusive thoughts and to neutralize their effect. Thoughts regarding being afraid (“afraid of being afraid” – ex: fear that he/she will faint or lose control) and thoughts that other people will assess him/her in a negative way (social phobia) can be modified / neutralized using these techniques.

Pharmacological treatment:

- Antidepressants may be used in cases with secondary depression and even if depression is not present, because this medication class helps in reducing the frequency of the panic attacks (especially in agoraphobia). SSRI's are the most helpful in social phobia, as are beta-blockers (taken 30 minutes before the performance), because they help reduce the vegetative symptoms of anxiety.
- Benzodiazepines are only used for a short period of time – to reduce anxiety whilst the patient is undergoing behavioral desensitizing.

## Chapter VI - OBSESSIVE COMPULSIVE DISORDER (OCD)

### Epidemiology

Prevalence in the general population is 1-2 %, with equal distribution among both sexes. Mean age at onset is most frequently between 20 and 35 years, with a slightly earlier onset in males. OCD is not considered to have a link with the intelligence level.

### Etiopathogeny

#### Biological aspects

##### a) Genetic factors:

-Greater concordance in monozygotic when compared to dizygotic twins. – Rank I relatives prevalence is estimated in some studies up to 35%.

-The obsessive-compulsive spectrum comprises of other disorders similar to OCD (Gilles de la Tourette disease, Huntington's chorea).

##### b) Pathologic studies:

-Revealed changes in the frontal lobe, cingulum or caudate nucleus.

-The level of such formations, PET (positron emission tomography) revealed an increase in their activity by increasing blood flow and glucose consumption.

-Brain imaging studies also revealed the involvement of prefrontal cortexbasal ganglia-thalamus circuit.

##### c) Pathophysiology:

-in OCD we encounter a reduction of serotonergic activity coupled with an increase of dopaminergic activity.

##### d) Autoimmune factors:

-The hypothesis is supported by the association of obsessive-compulsive disorder with symptoms of autoimmune diseases of the basal ganglia, as well as Sydenham's Chorea; as are associations of G. de la Tourette disease with OCD symptoms and anticerebral antibodies.

### Psychological aspects:

Psychodynamic theory (Described by Freud)

The disorder is seen as a regression to early developmental stages from the oedipal phase to the anal phase, for which ambivalence is characteristic.

Originally Freud suggested that the symptoms of obsession result from unconscious impulses of an aggressive and sexual nature. These impulses create an extreme anxiety that activate defensive mechanisms.

In OCD the main mechanisms of defense are considered to be: isolation, reactive formation and cancellation. When these mechanisms fail in the face of anxiety, neurotic symptoms of the anxious type appear.

## Vulnerability-stress theory

Implies a predisposing terrain, which under the action of stressful stimuli determines the onset of this disorder.

In this case it is the anankastic or psychastenic type of personality that acts as the predisposing terrain.

## Learning theory

Presumes the existence of the obsession as the conditioned stimulus.

In the first stage, neutral stimuli (words, images) are associated with anxiety becoming conditioned stimuli

(classical conditioning).

In the second stage, the person discovers that a certain action reduces anxiety accompanying the obsessive thoughts, and thus compulsions and rituals are learned as a way to reduce anxiety (operant conditioning).

## **CLINICAL PICTURE**

-It is marked by the presence of obsessions and compulsions that cause anxiety or considerable distress (Obsessions)

-are time-consuming (more than one hour per day) and interfere significantly with normal routine and normal social activities, work or school.

-Obsessions are thoughts, impulses, ruminations, doubts, phobias or images that are recurrent and persistent and that are experienced as being intrusive and inappropriate, parasitizing thinking and causing distress.

-Ruminations are sterile thoughts without finality (end) on trivial or sophisticated themes.

-Obsessive phobias are precise fears (the individual can name the object that induces fear), but which may also appear outside of phobogenic situations.

-Obsessive impulses are tendencies towards acts, of a dangerous or embarrassing nature, that the patient never puts into practice.

-Compulsions: are mental acts (counting, prayers, etc.) or behavioral (hand washing, collecting, checking, correcting, avoidance, etc.) used to reduce patient anxiety, pain or prevent a dreaded event or situation.

-They can be correlated with obsessions (or not).

Compulsions have a repetitive, stereotypical, excessive and parasitizing character and are very time-consuming.

## Differential diagnosis

-With organic pathology: temporal lobe epilepsy, posttraumatic or post-encephalitic complications.

-Psychiatric diagnoses: addictions, anxiety disorders, delusional disorders, schizophrenia, depressive disorders, impulse control disorders (trichotillomania, kleptomania, pyromania), paraphilias, eating disorders, body dysmorphic disorder, hypochondriasis.

## Evolution and prognosis

The evolution of the disorder is variable, most commonly chronic.

Evolution might be phasic (episodes separated by periods of remission), fluctuating (incomplete remissions and exacerbations), constant or progressive .

Patients with OCD are prone to depression and sometimes suicide, isolation with celibacy or anxiety.

## Treatment

Pharmacological treatment:

The first treatment with positive results was the tricyclic antidepressant clomipramine (Anafranil) in recommended doses of 75-250 mg / day. It should be noted, however, that there may be significant side effects.

The most widespread current SSRI antidepressant treatment options are:

- Fluvoxamine: 100-300 mg / day
- Fluoxetine 30-60 mg / day
- Paroxetine 40 mg / day
- Sertraline 50-200 mg / day
- Escitalopram 20 mg / day
- Citalopram 20-40 mg / day

Effectiveness of SSRIs is independent of depressive symptoms.

In OCD therapeutic doses are double to those needed to treat depression.

Treatment efficacy should be assessed after 4-12 weeks.

Several months of treatment are needed to notice the maximum therapeutic response.

SSRI's are considered to be of similar efficacy to tricyclics, and have the advantage of being better tolerated than the latter.

In case of therapeutic failure, severe avoidance behavior or atypical depression the use of MAOIs (monoamine oxidase inhibitors) antidepressants might be recommended.

Anxiolytics (like clonazepam) might also be recommended, but although they are efficient, the problem of dependence arises, as the treatment needs to be long-term.

Beneficial effects have been noticed by the combination of antipsychotic medication with a serotonergic antidepressant.

These intervene in dopaminergic neurotransmission.

Patients with OCD should be maintained on medication for a long period of time, at least one year before attempting a gradual reduction or its discontinuation.

Biological, but non-pharmacological treatment:

-Psychosurgery procedure which interrupts the connection between the prefrontal cortex and the basal ganglia.

-Cingulotomy may help some patients in the short-term, but long-term prognosis is uncertain.

Psychotherapeutic :

- Supportive psychotherapy (focused towards trust)
- Psychodynamic and familial psychotherapy
- (with inconclusive results).
- Cognitive and behavioral psychotherapy

## Chapter VII - DISSOCIATIVE AND CONVERSION DISORDERS

### General considerations

Dissociative [conversion] disorders (previously known as “hysterical neuroses”) have been described since antiquity. The terminology has changed recently due to the multiple negative connotations associated with the term of “hysteria”.

The prevalence of dissociative [conversion] disorders is situated between 0.1 and 3% of the general population and is higher in women.

Dissociative [conversion] disorders appear more frequently in subjects that have a personality disorder or histrionic personality traits (hyper-expressive individuals, that always want to be in the center of attention, to be admired or pitied, that have a florid imagination, suggestible subjects, emotionally immature, with an excessive preoccupation for their personal prestige – “egocentrism”).

In the development of the dissociative [conversion] disorders, psychosocial factors such as failures, frustrations, intra-psychic conflicts, that lead to low self-esteem intervene. Characteristic to these disorders is the repression of tendencies, of the unpleasant and tense feelings unacceptable for the conscious self from where they manifest indirectly, sometimes symbolic, through “impressive symptoms”. Neither conversion nor dissociative symptoms are produced deliberately by the patients, they often represent the patient’s ideas and knowledge of different somatic or psychiatric illnesses. There is always an obvious discrepancy between the patient’s display of symptoms and the ones present in a somatic/psychiatric illness.

Although there is an impressive show of reactions, anxiety is rarely present, the patient expressing an apparent indifference for his/her symptoms (“la belle indifference”) and leaving them to the care of others. This release from duties, from the responsibility of healing is done in the context of a regression to the state of infantile dependence which expresses itself by self-pity tendency, by inclusion in the “sick statute” (this statute offers some advantages, like sympathy and attention from others).

The main groups of symptoms are: conversion symptoms and dissociative symptoms.

#### 1. Conversion symptoms

Conversion symptoms refer to the transformation (“conversion”) of the unpleasant and unacceptable feelings into physical symptoms that mimic certain somatic diseases. They are functional symptoms, without an organic substrate. They can be grouped into motor and sensory symptoms.

a. Motor conversion symptoms: The most frequent versions are: psychogenic paralysis (monoplegia, paraplegia, quadriplegia), psychogenic paresis, movements that mimic certain neurological disorders (abasia, tremor, chorea-like movements, apraxia, dysarthria, aphonia, dysphonia, mutism, convulsions). The onset usually is a conflictual (reactive) context. These are functional symptoms (psychogenic determinism) and thus no alterations of reflexes can be observed. The manifestation forms unravel in conformity with ideas and false knowledge about somatic disorders that they mimic and according to the patient's imagination.

b. Sensory conversion symptoms: anaesthesia, paraesthesia, hyperesthesia, cutaneous hypoesthesia, blindness, deafness, anosmia. Conversion symptoms are different to those of somatic disorders by the fact that distribution does not respect the metamers through variations of intensity and through their response to suggestion. Hyperesthesias are more frequently in the cephalic or abdominal regions and are described by patients as pain or burns. Psychogenic blindness can take the form of a concentric diminishing of the visual field (tunnel vision), loss of visual acuity, general visual loss, without any changes to the pupillary reflex. There are indirect signs that show that the patient is still able to see (ex: avoiding a chair that is in front of him/her). The same consideration can be applied to psychogenic deafness. Also described are gastrointestinal conversion symptoms (abdominal discomfort, vomit) or respiratory conversion symptoms (pseudo-asthmatic crisis).

## **2. Dissociative symptoms**

Are centered by the dissociation of the actual consciousness field and are of psychogenic nature. They usually debut in stressful situation that are long-lasting and insoluble. They're characterised by a sudden onset and remission, a fluctuating diurnal evolution, a variable duration (hours – years) and have the following clinical forms:

### ***Dissociative amnesia***

The main symptom is memory loss tied to recent important/stressful events. The amnesia that's presented is too intense to be explained by normal forgetfulness or fatigue and is not caused by an organic mental disorder.

The amnesia is centered on traumatic events like accidents or sudden loss of loved ones and is, usually, partial and selective. In contrast to a normal state, where an event with an emotional surcharge is better remembered, in dissociative amnesia just this kind of event is forgotten. Affective symptoms which surround the amnesia are varied: anxiety, mild or moderate depression, varied types of behaviour that is meant to attract other people's attention.



**The differential diagnosis** is made with: organic mental disorders (which present other signs of CNS impairment), acute intoxications with psychoactive substances (symptoms are closely associated with the time span of the substance abuse and the lost information can never be recovered), Korsakov syndrome (immediate memory is normal but short-term memory is lost) and conscious amnesia simulation (associated with obvious financial problems, possible jail sentences, vital risk during war time).

### ***Dissociative fugue***

Includes all the traits of dissociative amnesia and an abrupt “escape” from home or work outside of the usual places the individual frequents, with maintaining of the basic self-sustenance and simple social interactions. In some cases, the individual might assume a different identity, usually for a few days. Total amnesia of the episode will occur. The subject’s behaviour during the dissociative fugue may appear normal to independent observers.

**Differential diagnosis** is made with: temporal lobe epilepsy (post-ictal fugue) in which there is a known history of epilepsy and a lack of stressful / traumatic events, with reactive fugue and pathological alcohol intoxication. As well as for dissociative amnesia, differentiating dissociative fugue from conscious simulation may prove difficult (in the absence of the aforementioned associated problems).

### **Differential diagnosis of the dissociative and conversion disorders**

Dissociative and conversion disorders must be differentiated by many somatic diseases that present similar symptoms. The most difficult to differentiate are organic disorders of the CNS (like: diffuse cerebral pathology and temporal lobe epilepsy). Dissociative and conversion disorders may be comorbid or can mimic depression or anxiety (paroxysmic anxiety – “panic attack”), situation in which differentiating these disorders is necessary. Also, differentiating these disorders from conscious simulation is paramount.

### **Treatment**

Pharmacological treatment: is administered in the acute phases, lasts for just a few days / weeks and consists of administering antidepressants (SSRI / SNRI) and/or benzodiazepines with a short/medium half-life.

Psychotherapeutic treatment: consists of consciousness-oriented psychotherapy, supportive psychotherapy, psycho-analysis, suggestion and hypnosis therapy.

### **Somatoform disorders**

The main traits of the somatoform disorders are somatic complaints, along with permanent soliciting of medical investigations, despite the repeated negative results and assurances from medical doctors that the symptoms have no somatic substrate. If there is a somatic illness present, it does not explain the ample symptomatic spectrum, nor the suffering or preoccupation of the patient.

The patient usually does not accept the possibility of a psychological cause, even though the onset of symptoms appears in a reactive context (stressful life events). Sometimes a behaviour meant to attract attention is also present, especially in patients that cannot convince their doctors to reassess them (to prove the existence of a somatic disorder).

### **Somatization disorder**

Consists of multiple, recurrent and frequently changing (regarding bodily location) somatic symptoms that have persisted several years before the first psychiatric contact. These patients have a history of multiple presentations to primary and specialised medical services, thus having many assessments (with negative results).

The symptoms include:

- Pain symptoms: headache, abdominal pain, back pain, thoracic, extremity, rectal and articular pains, pains during urination, sex and menstrual cycle.
- Gastro-intestinal symptoms: nausea, flatulence, vomit, diarrhea, intolerance to several food groups, irritable bowel syndrome.
- Sexual symptoms: sexual indifference, erectile or ejaculatory dysfunction, irregular menstrual cycles, excessive menstrual bleeding, vomit during the entire pregnancy.
- Pseudo-neurological symptoms: conversion symptoms, like balance or coordination dysfunctions, paralysis or localised decrease of motor function, difficulty swallowing, aphonia, urinal retention, hallucinations, loss of tactile or pain sensations, diplopia, blindness, epileptic seizures, dissociative symptoms like amnesia or a loss of consciousness (other than fainting).

After a thorough investigation, none of the aforementioned symptoms can be completely explained by a medical general known condition or by a direct effect of a psychoactive substance. When

there is a similar general medical condition, the somatic complaints or social/professional dysfunction are excessive to what one might expect from the patient history, somatic exam or lab results.

Often, the symptoms are “mobile”, they move from one part of the body to another.

Because of self-administering of medication (most frequently sedatives and analgesics) biological addiction to these substances may occur, and thus there is a risk for a uncomplicated/complicated withdrawal syndrome (when the medication is abruptly stopped).

**Differential diagnosis** is made with: somatic disorders (the stability in time of the somatic complaints), affective disorders (high intensity of depressive symptoms and a short persistence of somatic complaints), hypochondriac disorder (patients focus their attention on severe progressive disorders; patients are afraid of taking medication and their side effects), delusional disorders (bizarre beliefs, reduced amount of somatic symptoms and a longer persistency in time).

### **Hypochondriac disorder**

The essential trait is a persistent preoccupation regarding the possibility of having one or more serious or progressive somatic disorders. Patients present with persistent somatic complaints or preoccupations regarding somatic phenomena. Normal or basic sensations are often interpreted as abnormal. The patient is sometimes convinced that another somatic disorder or an additional one considered prominent may be present. Also characteristic is the conscious in acceptance of advices or assurances by doctors that a patient is not suffering from a somatic disorder.

During the evolution of the disorder comorbid depression or anxiety can appear. There are no differences regarding prevalence between sexes. The degree of associated dysfunctions is very variable – some patients manipulate their family or social network as a result of their symptoms in contrast of the minority who have almost normal functioning.

### **Differential diagnosis**

- Persistent delusional disorder with hypochondriac delusion (the patient has an absolute belief regarding the existence of a somatic disorder and can't be convinced, not even in the short time, through arguments, repeated reassurances and new reassessments).
- Somatisation disorder (the accent is on symptoms and not on the disorder itself or its future consequences)
- Depressive disorders (chronologically precede hypochondriac ideas)

- Generalized anxiety and panic disorder (patients accept the explanations about the psychological etiology of their problems; their belief about the existence of a somatic disorder goes away quickly).

#### **Somatoform disorders: outcome**

The evolution in somatoform disorders is chronic, with few remissions, still the severity of symptoms can fluctuate. In somatisation disorder complications include futile surgeries, substance addiction and adverse effects of unnecessarily prescribed medication.

#### **Somatoform disorders: treatment**

Pharmacological treatment in somatisation disorder is administering short-term antidepressants and/or anxiolytics. Administering any psychoactive substances in the long-term should be avoided to prevent psychological/biological towards these. In hypochondriac disorder one should administer SSRI antidepressants and benzodiazepines in the medium/long term.

Psychotherapeutic treatment includes long-term supportive psychotherapy (to overcome stressful-life events, to prevent psychoactive substance abuse, excessive medical reassessments and futile therapeutic procedures and diagnosis tests).

## CHAPTER VIII - EATING AND SEXUAL DISORDERS

In the International Classification of Diseases (WHO ICD 10), disorders of the feeding instinct within psychiatry are discussed in Chapter F5, along with those regarding sleep and sex. The main entities are anorexia and bulimia nervosa.

### ANOREXIA NERVOSA

Anorexia nervosa is a disorder characterized by deliberate weight loss or refusal of weight gain, when the subject deliberately stays underweight (below 85% of normal weight, BMI <17.5), and slim looking (thin).

#### Epidemiology

The epidemiology of this disorder raises multiple methodological issues, because the manifested intensity may be reduced, and the dependence on sociocultural factors is considered to be high.

- Lifetime prevalence is 3.7%.
- The onset is more common in women between 10-30 years. The disorder occurs mainly in young girls (girls/boys ratio is 10/1) around the first menarche, and is less frequent at other age groups or in boys.
- More frequently encountered in developed countries
- More common in women whose profession requires them to have a supple silhouette

#### Etiopathogenesis

Several factors are incriminated, starting with the hereditary component, educational dysfunctions, problematic relationships with parents, peculiarities of personality, endocrine and neurotransmission disruptions, or an aggregation of stressful life events.

##### 1. Genetic Factors

- The concordance rate in monozygotic twins is higher than in dizygotic twins.
- Increased family incidence of depressive and anxious disorders, alcohol misuse, eating disorders

## 2. Biological Factors

- Decline in Norepinephrine activity
- Hormonal changes: increased Cortisol, decreased Thyroid function, decreased levels of FSH and LH
- CT scans show enlargement of the Cerebral Ventricles
  - PET scans indicate an increased metabolism in the Caudate Nucleus

## 3. Psychological factors: some of the first theories have tried to explain anorexia by:

- Phobic mechanisms: anorexia is an avoidance behavior toward food that occurs as a result of sexual and social tensions caused by numerous changes in puberty
- Psychodynamic formulation: people remain fixed in the oral stage of development, are unable to psychologically separate from the mother, or have repressed sexual and aggressive tendencies

The mother-daughter relationship is considered central, in terms of the development of the young girl's body image, due to the fact that the mother's opinion on the daughter's body development is very important to the latter. The father's role is less important. Studies of families in which a member is experiencing anorexia, regarding intra-familial relations, showed that these families experience the following issues: intrusiveness, psychological rigidity, overprotection, and unresolved marital conflicts. These studies have also looked to identify main personality traits, which occur in people with anorexia, and the following were observed to occur more frequently:

- obsessiveness
- rigidity
- introversion
- difficult interpersonal relationships
- excessive compliance to rules

Perfectionist traits represent a risk factor. Cognitive theory states that there is a distortion of body image, a perceptual dysfunction and a sense of inefficiency.

4. Socio-cultural factors: society places an emphasis on the silhouette, especially for certain professions.

#### Clinical presentation

Weight loss is self-imposed by refusal to eat, special diets, self-inflicted vomiting and purging, excessive exercise, use of weight-loss, catabolic or diuretic drugs.

Distortion of the body image occurs in the form of a specific psychopathology, with the fear of weight gain persisting as an overvalued idea, while the patient is self-imposing a low weight threshold. The patient fails to understand their exaggerated appearance and the abnormality of their behavior, and their appearance can become impervious to any logical argument.

If the onset is prepuberal, the normal commencement of puberty sequences is delayed or even halted. Girls may not develop mammary glands, with primary amenorrhea, and for boys, the genitals may remain undeveloped. If the disorder becomes addressed, puberty can be achieved with its normal stages, but the menarche remains late.

A global endocrine disorder, involving the hypothalamic-pituitary-gonadal axis, is often present, manifesting in women with amenorrhea, and in boys with loss of sexual interest and potency. There may be elevated levels of Growth Hormone and Cortisol, changes in the peripheral metabolism of Thyroid Hormones and abnormalities of Insulin secretion.

Depressed mood is common, with social withdrawal, irritability, insomnia, and disinterest in sex. Moreover, obsessive and ritualistic traits may become manifest. Patients repeatedly check their appearance in a mirror, are weighing and measuring themselves several times daily. Social initiative and assertiveness can be reduced. Relationships with the family can also be damaged, due to issues relating to food control.

Self-inflicted vomiting and other interventions on the body, can create electrolyte imbalance, can reduce immunological resistance and favor various somatic diseases. Renal and hematological complications, along with osteoporosis and myopathy can occur. Therefore, the cases should benefit from a full somatic testing. The anorectic behavior can be combined with bouts of bulimia.

The intensity of symptoms may be reduced, and some cases may not represent a direct mental health problem. Anorexic tendencies can also be marked by repeated lent periods.

### Complications

#### A. Related to weight loss:

1. Cachexia: reduced muscle mass, intolerance to cold, difficulty maintaining body temperature
2. Hormonal disorders: decreased T3, amenorrhea (low levels of FSH and LH)
3. Digestive disorders: abdominal pain, bloating, constipation
4. Cardiac disorders: arrhythmias (long QT), VES, AES, bradycardia, ventricular tachycardia, sudden death
5. Dermatological disorders: lanugo, eczema
6. Blood disorders: leukopenia, anemia, thrombocytopenia
7. Skeletal disorders: osteoporosis
8. Neurological disorders: decreased taste sensation, apathy, mild cognitive impairment

#### B. Related to purging behaviors:

1. Metabolic disorders: metabolic alkalosis, metabolic acidosis, fluid and electrolyte disorders
2. Digestive disorders: inflammation of the salivary and pancreatic glands, gastroesophageal erosion (Mallory-Weiss syndrome), bowel dysfunction, tooth erosion (due to the acidity of the vomitus fluid)
3. Mental disorders: fatigue, weakness sensation, mild cognitive impairment

- 5-10% of patients with Anorexia Nervosa die in the first 10 years after onset, and 18-20% die after approx. 20 years, according to a US study.

- Only a proportion of 30-40% of patients will have a full recovery.

#### Laboratory tests:

1. FBC: pancytopenia
2. ECG: ST segment depression, inverted T wave
3. Low blood sugar
4. Hypokalemia, hypomagnesaemia
5. Low levels of FSH, LH



6. Low levels of T3, T4

7. Hypocalcaemia

Differential diagnosis

1. General medical conditions:

- Gastro-intestinal disorders, malabsorption syndrome, irritable bowel syndrome

- Diabetes mellitus

- Addison's disease (decreased Cortisol - satiety)

- Neoplasm

- HIV

2. Bulimia nervosa

3. Depressive Disorder

4. Obsessive-Compulsive Disorder related to eating

5. Body dysmorphic disorder

6. Social phobia

7. Specific phobias

8. Schizophrenia

Comorbidities

1. Major Depressive Disorder

2. Dysthymia

3. Suicide - more frequent in binge-purge anorexia

Course and prognosis

The course can be:

- With a spontaneous recovery, without treatment

- Recovery after treatment
- Fluctuating
- Gradual deterioration, and death through: malnutrition, electrolyte and fluid imbalances, inter-current infections, suicide

Adverse prognosis factors:

1. Denial
2. Low self-esteem
3. Parental conflicts in the family
4. Purging behavior
5. Psychiatric comorbidity

Minor anorectic events may be present, in those predisposed, even before puberty. Pathological reactions to stress and minor frustrations accompanied by lack of eating may represent a clue. Once the disorder is installed, with all its particularities, treatment will be long-term.

Treatment

Treatment is difficult, due to the patient's lack of motivation and delay in accessing services, through denial of illness. The goals of treatment are:

- Return to a normal weight
- Treatment of somatic complications
- Correcting cognitive distortions
- Improving mood
- Coping methods for associated psychological situations
- Relapse prevention

The treatment has two components: medication and psychotherapy. Admission is required when weight decreases by more than 30% of initial weight.

Treatment consists of:

- Correction of dehydration and electrolyte imbalances
- Restoration of adequate caloric intake. In view of this:

o The patient must be weighed daily.

- o Measurement of urine output and fluid intake
- o Daily food intake is fragmented into 6 meals per day (initially, in the first 5-7 days, liquid foods are preferred, followed by semi-solids, in the next 3-5 days).

Drug treatment consists of:

- Selective serotonin reuptake inhibitors
- Neuroleptics (if psychotic symptoms are present)
- Anxiolytics

Hospital admission offers behavioral programs, consisting of rigorous control of daily activities. Individual, group and family psychotherapy are practiced. The main difficulty is represented by the patient's ability to accept treatment. Cognitive-behavioral programs are highly recommended.

a. Cognitive-behavioral, individual or group therapy attempt to offer change for:

- The dysfunctional eating behavior
- Cognitive dysfunctions related to diet and body schema

b. Family Therapy attempts to change existing family interactions, with a view to reduce the intensity of symptoms.

## BULIMIA NERVOSA

Bulimia nervosa is characterized by repeated bouts of impulsive overeating, during which the person uncontrollably consumes large amounts of food, over a short period of time. That can lead to gastric distension, accompanied by pain and vomiting. During the crisis, the patient loses control and does anything to obtain the food. It consists of two key elements:

- paroxysmal excessive food consumption
- methods to prevent weight gain

## Epidemiology

- Lifetime prevalence is 2-4%.
- More common in women (female/male ratio = 10/1)
- Age of onset is 16-18 years.

Bulimia crises can coexist with anorexia nervosa and are generally correlated with a questioning of one's own weight and appearance. There is also a type of bulimic disorder accompanied by normal ingestion or weight. Bulimia can, sometimes, be triggered by diets, suggesting a psycho-cerebral reaction to the sudden change of body schema and image.

## Etiopathogenesis

It is considered that the anorexic and bulimic pathology belong to the same class, essentially having a common pathology, insufficiently clarified to date. A multidimensional model, involving several factors, has been proposed:

### 1. Genetic Factors

- The concordance rate in monozygotic twins is higher than in dizygotic twins.
- An increased family incidence for eating disorders

### 2. Biological Factors

- Studies show a low activity of NE and 5HT.
- Increased plasma endorphin levels (reinforce the behavior).

### 3. Psychological factors

- Generally, it was found that people with bulimia are mostly extroverts, more impulsive and angry.
- Family studies have noted that in families where one member has bulimia, there may be high levels of hostility, chaos, lack of empathy.
- Psychodynamic hypothesis - a young girl fighting against the maternal figure, a fight that plays out in the nature of eating.

### 4. Sociocultural factors

- Current society places an emphasis on body image.

Bulimic disorder also occurs more frequently in women, but, more often, it has an onset after puberty. Normal weight Bulimia is characterized by repeated diets that are followed by bulimic periods, in which the weight is gained back.

It is considered that Bulimia is also partially influenced by cultural factors, dietary habits and body image promoted by mass media culture. The prevalence in young women is considered to be 1-3%. Evolution is fluctuating.

Because Bulimia represents an impulsive behaviour, it can be frequently associated with other impulsive behaviors, or manifested in borderline, emotionally unstable, personality disorders.

#### Complications

Complications can be noted in a large number of cases, and are related to purging behaviors:

- Fluid/electrolyte imbalance
- Metabolic acidosis
- Erosion of tooth enamel
- Inflammation of the parotid glands
- Abdominal pain, dilation of the esophagus, gastric distention, esophagitis, gastric rupture
- Cardiovascular disorders: tachyarrhythmia, hypotension, ECG changes
- Endocrine disorders
- Hematological disorders

#### Laboratory tests

1. FBC: pancytopenia
2. ECG: depression of ST segment, inverted T wave
3. Low glycaemia
4. Hypokalemia, hypomagnesaemia

5. Low levels of FSH, LH
6. Low levels of T3, T4
7. Hypocalcaemia

#### Differential diagnosis

1. Neurological disorders:

- Kleine-Levin Syndrome: hypersomnia, hyperphagia, obesity, intellectual disability, hypogonadism
- Kluver-Bucy syndrome: visual agnosia, hypersexuality, hyperphagia
- CNS Tumors

2. Adjustment disorders, where bulimia can occur as a reaction

3. Borderline Personality Disorder

4. Depressive Disorder

#### Comorbidities

1. Loss of appetite with weight loss, and hyperphagia with weight gain may be symptoms that are part of the depressive syndrome.
2. Anxiety - social phobia
3. Substance abuse - alcohol
4. Impulsive disorder - cluster B
5. Sexual dysfunction

Vomiting can also be conditioned psychogenically. Besides self-inflicted vomiting in anorexia nervosa, it can also occur in dissociative-conversion disorders, in hypochondriacal states, as well as in certain reactive and adjustment disorders, when experiencing feelings of revulsion.

#### Course and prognosis

Evolution is chronic, but not fatal, unless complicated by severe fluid and electrolyte imbalances and metabolic alkalosis. Recovery with treatment is of 60%. The relapse rate at 5 years is 50%.

## Treatment

Treatment of bulimia nervosa consists of two essential components: medication and psychotherapy. Hospitalization is required when there is fluid and electrolyte imbalance, metabolic alkalosis or suicide risk. Attention given to somatic complications is imperative.

With regards to psychotropic medication, first-line treatment is with drugs in the class of selective serotonin reuptake inhibitors (fluoxetine). Other classes of antidepressants can also be used (imipramine, trazodone, amitriptyline).

Cognitive behavioral therapy (first line) can address the following issues:

- Breaking the vicious binge-purge cycle
- Correcting cognitive dysfunctions related to food consumption, weight, body image, self-esteem

Family therapy is applied, mainly, in cases with an onset in adolescence.

Interpersonal therapy is applied frequently, because people suffering with bulimia have interpersonal problems. This therapy focuses on interpersonal relationships, rather than on eating disorders, relying on the idea that, once interpersonal relationships are improved, eating disorders will decrease in intensity.

## Hyperphagia

Excessive eating, in the form of hyperphagia, may be associated with other pathological and existential disorders: mourning, special emotional events, accidents, surgery – they may be followed by excessive consumption of food, which is, however, not in the form of the Bulimia crisis, but that can lead to REACTIVE OBESITY, especially in people that are genetically predisposed to obesity. Hyperphagia may also occur in situations of anxiety or retained aggressive tension, subsequent to frustration, or in manic episodes. That is an important fact, when analyzing states of obesity and their treatment planning. In turn, obesity can cause secondary problems of psychological distress, regarding body image. Egodystonic obesity treatment is required to be undertaken with psychological supervision, so as not to extend to secondary bulimia or anorexia.

## SEXUAL DISORDERS

Sexual behavior is diverse and determined by a complexity of interacting factors: relationships, living conditions, cultural factors, personality, and perception of the self. The notion of abnormal sexuality means engaging in a behavior that is harmful to the individual and to other people, which cannot be directed towards a partner, which excludes genital stimulation or which is improperly associated with feelings of guilt and anxiety.

Sexual and gender identity disorders are classified into

- A. SEXUAL DYSFUNCTION
- B. PARAPHILIAS
- C. GENDER IDENTITY DISORDERS

Sexual dysfunctions will have a broader approach, due to a higher frequency in the general population, compared with paraphilias and gender identity disorders. They represent disturbances of the psycho-physiological changes characteristic of the sexual response cycle.

The prevalence of sexual dysfunctions is evaluated, by a study in the American population, at 1.3% under the age of 35, 6.7% under the age of 50, and 18.4% for those under 60. In this regard, the most common reason why men seek specialized treatment is erectile dysfunction, while women often have complaints regarding a decrease in sexual interest and orgasmic dysfunction.

The first step in the diagnosis of sexual dysfunction is to eliminate somatic health problems.

### DYSFUNCTIONS OF SEXUAL DESIRE

A decrease in sexual desire occurs more frequently in women and is centered by a decrease or complete absence of desire for sexual activity or sexual fantasies. The presence of such dysfunctions often reflects general problems in the couple's relationship or may mask another type of sexual dysfunction. It occurs frequently in depressive disorder.

Sexual aversion may be the result of traumatic sexual experiences (rape or sexual abuse in childhood), of repeated painful sexual experiences or can represent a psychological reaction within a relationship with interpersonal difficulties.

These disorders may be present since puberty, may be acquired, generalized or occasional.



## SEXUAL AROUSAL DISORDERS

Women's sexual arousal disorder is the persistent or recurrent inability to attain or maintain, pending sexual activity, an adequate genital response.

Female sexual inhibition is associated with:

- Psychological factors
- Menopause and changes in hormonal levels
- Atrophic vaginitis
- Diabetes mellitus
- Diminished lubrication (lactation, hypotensive treatment, antihistamines)
  
- Psychiatric disorders
- Various medication

Erectile disorder represents an episodic or persistent inability of a man to achieve or maintain, pending realization of sexual activity, an adequate erection. This disorder is also called erectile dysfunction or impotence. The disorder is caused by various medical conditions (cardiovascular, renal, hepatic, pulmonary, genetic factors, nutrition diseases, endocrine diseases, infectious and parasitic diseases, neurological diseases, surgical procedures), some medicines.

### Orgasm disorders

They are characterized by the delay, or recurrent or persistent absence of orgasm after a normal sexual arousal phase.

There are some drugs that exert inhibition of orgasmic function: tricyclic antidepressants, SSRIs, benzodiazepines, neuroleptics, hypotensive, narcotic.

Premature ejaculation is a persistent and repeated dysfunction, manifested by ejaculation after minimal sexual activity, before, during or shortly after penetration and before the person wants to. It is estimated that 30% of the male population have this dysfunction. Premature ejaculation is associated with anxiety about initiating a new sexual act, which may lead to social isolation for vulnerable persons.

Delayed ejaculation is achieved by gaining experience as a sexual being, and is controlled more easily in stable, long-lasting relationships.

### Painful sexual disorders

Dyspareunia consists of genital pain associated with intercourse. It can be found in both men and women, and can have different intensities, from the presence of a slight feeling of discomfort and embarrassment, to acute pain. The true incidence of dyspareunia is not known. It is estimated that 30% of female genitalia surgeries may result in a temporary disorder of this type.

Vaginismus is a persistent or recurrent involuntary contraction of the perineal muscles surrounding the external third part of the vagina, when penetration is attempted. It occurs more frequently as a result of painful scars (episiotomy after birth). Sometimes it can represent a phobic manifestation, regarding the fear of penetration. It also occurs more frequently in young women, in those with a history of sexual trauma or in women who have negative attitudes towards sex.

Sexual dysfunctions due to general medical condition

These are clinically significant sexual dysfunctions, due to medical conditions: neurological, endocrine, vascular, genitourinary. Treatment is performed by specific sexual therapy applied to both partners: behavioral psychotherapy, hypnotherapy, pharmacotherapy, hormone treatment, possibly surgery.

To avoid confusion about sexual identity, it should be noted that the concept of sex refers only to anatomic and physiological phenomena. The components of sexual identity are: gender identity, orientation and intention. According to them, the major forms of pathology are classified as follows:

- Gender Identity Disorder: trans-sexuality - a disorder characterized by the presence of intense and persistent preference to live as a person of the opposite sex (according to DSM-IV-TR)
- Disorders of the erotic-sexual orientation: homosexuality – a sexual attraction to persons of the same sex
- Disorders of the erotic-sexual intent: paraphilia

The currently accepted classification, according to the DSM-IV (American Psychiatric Association), includes the following categories:

- a. Exhibitionism
- b. Fetishism
- c. Frotteurism
- d. Pedophilia

e. Sexual masochism

f. Sexual sadism

g. Voyeurism

An accurate assessment of the prevalence of paraphilias in the general population is not possible, but, clinically, it is an accepted fact that the percentage is small.

## Chapter IX - PSYCHIATRIC DISORDERS DURING PREGNANCY AND POSTPARTUM PERIOD

Lately, the awareness of mental health issues that are particularly associated with different critical physiological stages of sexual active women's life has increased. These stages are mainly represented by menstrual cycle, pregnancy, postpartum period and perimenopause period. In this chapter, the psychiatric disorders that occur in perinatal period will be presented.

Besides significant hormonal changes that characterize pregnancy and postpartum period, a number of individual psychological factors as well as other socio-cultural factors should be undoubtedly taken into consideration. Only this way we can understand the complex and multifactorial mechanism that have a significant role in the occurrence of psychiatric disorders which are more frequently associated with these distinct physiological stages of the women's life. On the other hand, it is possible that some background vulnerability for a certain psychiatric disorder preceded the pregnancy (sometimes argued by the positive familial history for that disorder) and pregnancy and birth are only a triggering factor for that psychiatric condition. Moreover, there are situations where the mother has herself a positive personal history of mental illness, and the pregnancy and the postnatal period may just trigger a recurrence of that psychiatric disorder. This may be due to either the psychosocial stressors associated with this period (e.g. assuming the new parent status, financial difficulties, etc.) or by reducing or even interrupting the psychotropic maintenance medication administered for the pre-pregnancy psychiatric illness.

### A. MENTAL DISORDERS DURING PREGNANCY

Despite the previous prejudgment that the pregnancy has a protective role against mental disorders, recent research has shown that depression and anxiety are frequently spread in pregnant women. For this reason, we will particularly address the major depressive episode of clinical intensity as well as the anxiety disorders that may occur during pregnancy, and we will point out the issues of psychotic disorders that also may occur during the same period.

Before mentioning mental disorders of clinical intensity, according to some French authors, minor and transient psychopathological disorders during pregnancy should be also mentioned, such as: emotional lability, anxiety at the beginning of pregnancy (which subsequently alleviates and increases again just before the delivery), short-term dysphoria,

affective dependency, possible eating and sleeping disorders, nausea and vomiting in the first trimester that disappear subsequently.

Another problem that may arise during pregnancy and after birth is that of pregnancy denial, which may have the following causes: a preexisting psychiatric condition, lack of obstetrical monitoring, ambivalent attitude towards the own child before delivery, increased number of preterm deliveries, obstetrical complications, increased rate of perinatal death, disorders of mother-child interaction.

a. Anxiety disorders during pregnancy

- Agoraphobia
- Generalized anxiety disorder
- Panic disorder with a point prevalence ranging between 1.3 to 2.0% of pregnant women
- Obsessive-compulsive disorder that might get worse during pregnancy, with a point prevalence ranging between 0.2 – 3.5%.
- Posttraumatic stress disorder (after delivery) in a woman who had either a previous traumatizing pregnancy or a difficult delivery

b. Major depressive episode of clinical intensity during pregnancy

According to literature data, the incidence of depressive episodes during pregnancy is 12 to 20 percent, depending on the study, and is therefore similar to that found in non-pregnant women.

The presence of depression during pregnancy affects in a negative way the ability of self-care of the mother, lack of adequate food intake and subsequent weight decrease.

At the same time, the presence of depressive symptoms may favor the occurrence of preeclampsia in pregnant women. Regarding the risks for a newborn coming from a mother with depression, they are represented by premature birth, low birth weight and head perimeter smaller than normal. In the following period after birth, babies whose mothers had depressive symptoms or anxiety during pregnancy cry more and are more difficult to calm down by them and along the way they present insufficient psychomotor development and lack of adaptation to environmental factors.

### c. Psychotic disorders occurring during pregnancy

They are less common during pregnancy, despite the fact that pregnancy is considered to have a protective role. The delusional episode usually has an onset and an acute evolution, with all the clinical features of this type of psychiatric disorders (presence of delusions with various themes and / or hallucinations). Later, some of these cases evolve into a schizophrenic psychosis type.

### THE MANAGEMENT OF PREGNANT WOMEN WITH PSYCHIATRIC DISORDERS

One of the problems is the one of contraception in women with mental disorders. Voluntary interruption of an unwanted pregnancy is possible but under the conditions of the law. In this respect, in certain situations, a psychiatric expertise could be necessary.

Hospitalization of pregnant women with mental disorders should be considered if in the clinical picture are present delusions or suicidal risk.

Where possible, whether mental disorder is not severe, initially a psychotherapeutic treatment and psychological counseling of the pregnant women is attempted.

In case that medication is needed, some clinical aspects should be considered:

In order to support clinical practice, FDA organization (Food and Drugs Administration) from the U.S.A. made a classification of the medication which are prescribed to pregnant women, based on the teratogenic risk that they might have on the fetus. We show this classification in the following table:

Table 1. Teratogenic risk categories for pregnancy of various medications according to the FDA

FDA category	Category description
A	Adequate and well controlled studies in pregnant women have not shown an increased risk for fetal abnormalities.
B	Animal studies have shown no harmful effect on the fetus, but there are no adequate studies or well-controlled on pregnant women or animal studies have demonstrated the presence of adverse effects, but adequate and well controlled pregnant women demonstrated no risk to the fetus.
C	Animal studies have shown harm to the fetus, but there are no studies on pregnant women or animal studies and no adequate and well-controlled studies in pregnant women.
D	Adequate and well-controlled trials or observational studies in pregnant women or animals have demonstrated fetal abnormalities, but the benefits of treatment may outweigh the potential risk.
X	Adequate and well-controlled trials or observational studies in pregnant women or animals have demonstrated fetal abnormalities and use of these substances is contraindicated in pregnant women or those who want to conceive.

In any case of prescribed psychotropic drugs, close supervision is necessary for mother and child at birth because these drugs cross the blood-placental barrier. Sometimes neonatal withdrawal phenomena have been described for certain medications taken by the mother during pregnancy.

Researches to date have indicated that the use of paroxetine in the first trimester of pregnancy is associated with the risk of congenital heart defects in newborns, which made this compound to be classified as D risk according to the FDA, unlike the other compounds of the same class belonging to category C. Selective serotonin reuptake inhibitors administration in the third trimester of pregnancy increased the risk of Persistent Pulmonary Hypertension of the newborn associating a mortality of 10-20%. Thus, the choice of antidepressants in pregnant women with antenatal depression will be made after balancing the risk - benefit ratio.

Mood stabilizers such as lithium, carbamazepine, valproic acid and lamotrigine increased teratogenic risk causing various cardiac and neural tube defects and perinatal complications, especially if they are administered in the first trimester of pregnancy. This is why it is recommended that their prescription should be avoided especially during the first trimester of pregnancy.

Conventional high potency antipsychotics such as haloperidol and perphenazine, and have been shown to be safe in pregnancy having low teratogenic risk compared to classical antipsychotics with decreased potency. The risk of atypical antipsychotics in pregnancy is insufficiently documented. Clozapine is considered the safest new generation atypical antipsychotic in pregnancy being assigned in risk B category according to the FDA.

Use of benzodiazepines in pregnancy increase malformations of the labial cleft palate. Also, the use of benzodiazepines in pregnancy was associated with temperature adjustment disorders, apnea, low Apgar score, hypotonia and poor feeding of the newborn. As with other psychotropic must be taken into consideration the risk - benefit ratio because both depression and severe anxiety untreated can themselves, affect neurological-motor development of the fetus repercussions postnatal both proximal and distal during early childhood and even adolescence.

In most severe cases that do not respond to any pharmacological treatment, research has shown that electroconvulsive therapy can be effective and certainly satisfactory under general anesthesia, although it is much less used.

## B. MENTAL DISORDERS ASSOCIATED WITH POSTPARTUM PERIOD

### a. Postpartum blues

It is a syndrome consisting of sad mood, which can be accompanied or not by affective lability, anxiety, insomnia, decreased appetite and irritability. It usually occurs, within the first week after birth (often between 3 and 5 days after birth, along with the emergence of lactation) it is an quasi-constant sub-clinical entity found in about 70% of new mothers.

The clinical importance of postpartum blue should be viewed from the perspective of its vulnerability which results in an increased likelihood for a depressive episode of clinical intensity which occurs during postpartum period. there were studies that showed that women with postnatal blues have a probability 4 times more likely to develop further in the coming



weeks or months post-partum depression and that the last one includes in the clinical picture symptoms with more severe intensity compared to women who were euthymic in the first week after birth. The duration is usually between 1-7 days with complete and spontaneous regression of the symptoms. Rarely, it evolves towards postpartum depression or even puerperal psychosis (after 1 or 2 weeks).

Taking into account its lesser degree of severity, it is sufficient that immediate after delivery women to receive strict psychological intervention, which can vary from simple psychological measures and also psycho-education, to the brief cognitive-behavioral psychotherapeutic intervention administered in a few sessions.

#### b. Postpartum depression

It usually occurs in 2 to 8 weeks after birth, and may be in the extension of post-partum blues. It appears in 10-15% of women who give birth.

Among the etiopathogenic factors of postpartum depression could be mentioned the following:

- **Biological factors:** genetic, hormonal changes post-partum thyroid dysfunction, changes in cortisol, GABAergic dysfunction, decreased levels of beta-endorphins, decrease insulinemia etc.
- **Psychosocial factors:** personality traits, difficulties in social support, attributional styles and dysfunctional coping styles unwanted pregnancy, problems within the couple, if the mother suffered abuses in childhood, etc.

The constitutive elements of the clinical picture are the following:

- Sad and / or irritable mood
- Asthenia
- Crying easily
- Sometimes suicidal ideation (hospitalization is required)

- Phobic impulse obsessions (fear of harm to the child) conducting to various compulsions in response to obsessions.
- Other depressive symptoms

The most commonly used tool for assessing depression in the postnatal period is the Edinburgh Postnatal Depression Scale which is a self-assessment scale. The maximum obtainable score is 30. A threshold score over 10 indicates a potential depression and one above 13 suggests a moderate to severe depression.

From the evolutive point of view, it lasts on average between 3 to 12 months (with a shorter duration under treatment) and presents a recurrence in 30 to 50 percent of the total cases. It may evolve towards chronic depression. It affects the early relationship between mother and child with negative consequences in subsequent psychological development of the child and then of the adolescent.

#### THE MANAGEMENT OF THE CASES WITH POSTPARTUM DEPRESSION

Therapeutic intervention in mothers with postpartum depression is a medical decision which raises certain problems, especially in mothers who breast feed, because the majority of psychotropic drugs are eliminated through maternal milk. In order to prevent the new born from any risk it is preferable to stop natural feeding and switch to artificial feeding. If the mother does not agree with this decision, she must be extensively and clearly informed about the negative consequences which might appear in the new-born due to the drug release in the maternal milk.

Most psychotropic drugs are alkaline and therefore have increased liposolubility, making these drugs to diffuse quickly into breast milk.

This is one of the reasons why a Selective Serotonin Reuptake Inhibitor should be prescribed at the lowest possible dose in breastfeeding mothers. However, even a minimal dose does not guarantee that the infant is unaffected by the medicine because newborns younger than two months may have an insufficiently matured liver and kidney function as well as an immature blood-brain barrier that will increase the passage of SSRIs to the central nervous

system. We consider that the final decision on whether or not to administer antidepressant medication to a mother should be done solely on the basis of the risk-benefit balance.

A therapeutic alternative with fewer risks to breastfeeding women is the psychotherapeutic intervention. Interpersonal psychotherapy is effective in post-partum depression, relieving depressive symptoms and improving social adaptation, and is therefore an alternative to pharmacotherapy, especially for women who want to continue breastfeeding for newborns. The psychological intervention of non-directive psychological counseling type, the cognitive-behavioral therapy and the psychodynamic therapy have differential efficacy in mothers with postpartum depression.

In rare cases, where depression is severe having associated melancholic features and where suicidal risk is increased, electroconvulsive therapy may need to be administered under general anesthesia.

#### c. Postpartum psychosis

According to data from previous studies, the prevalence of postpartum psychosis (including bipolar episodes with psychotic symptoms) was approximately 1 to 2 cases of 1,000 postpartum women, and this seems not to be significantly different from one culture to another. Although the prevalence is significantly lower compared to that of perinatal depression, its exceptional severity is due to the increased risk of both suicide and infanticide.

The onset usually occurs after the first 2-4 weeks after birth.

Among the risk factors associated with postpartum psychosis were noted:

- Personal and family psychiatric history,
- Primiparous
- Obstetric and perinatal complications

During the prodromal period, nonspecific symptoms may occur, such as: insomnia, nightmares, anxiety, bizarre behavior, depressive symptoms during the last weeks of pregnancy.

Within the clinical picture we may meet:

- installed acute delusions, unorganized themed child-centered

- it can develop topics such as paranoid delusions of reference, persecution, jealousy and grandeur
- rapid emotional mood oscillation
- sometimes a picture subconfusional prevails especially situational disorientation
- sometimes hallucinatory experiences may be present
- marked disorganized behavior

Differential diagnosis is made with:

- infections
- cerebral thrombophlebitis
- placental retention
- other psychiatric causes (mania, postpartum major depressive episode)

Evolution may sometimes be favorable, some other times with relapses in the subsequent period in over 50% of cases or in 30% of subsequent pregnancies. It may also evolve into a bipolar affective disorder or even in a schizophrenia.

#### THE MANAGEMENT OF CASES WITH POSTPARTUM PSYCHOSIS

Firstly, due to the risk of infanticide the newborn must be promptly separated from his/her mother.

In order to have a close monitoring of the evolution and treatment administration, voluntary or involuntary hospitalization of the mother is necessary

First-line medication is antipsychotic and new generation antipsychotics are preferred, but also sedative drugs could be associated during periods of psychomotor agitation.

In severe cases presenting resistance to antipsychotic medication, electroconvulsive therapy should be used under general anesthesia.

After a satisfactory remission of psychotic symptoms, counseling techniques, psycho- education and even individual psychotherapeutic intervention, can be initiated.

d. Postpartum mania

It can occur within the first 15 days after birth.

The clinical features can be polymorphic with child-centered grandiosity theme but sometimes incongruent paranoid theme and even hallucinatory experiences.

Depending on the severity of the clinical features, hospitalization of the patient and the appropriate regimen treatment is decided.

## Chapter X - SCHIZOPHRENIA AND OTHER PSYCHOSES

Throughout the twentieth century, psychiatric nosology was divided into two parts, in what is called "psychosis" and "neurosis". Definition of psychosis is not clear at present, but there is a consensus in the sense that this term refers to the presence of delusions, hallucinations, a lack of awareness of the illness, and that these symptoms alter the relationing of the person to reality, and require specialized care.

In recent years, there are three directions of approach to what we call psychosis:

1. The concept of psychotic spectrum
2. The first episode of psychosis
3. The issue of psychotic continuum

Classification of psychosis

Functional psychoses:

- Schizophrenia
- Schizoaffective disorder
- Affective disorders
- Delusional disorder
- Acute psychotic disorders

Schizophrenia

Schizophrenia is central to psychiatry, representing alongside depression, a much debated disorder.

## Historical highlights

At the beginning of the twentieth century, Kraepelin synthesized the clinical presentation of this mental disorder, presenting it as "dementia praecox", by considering that it is a mental illness that occurs in the young (praecox) and leads to progressive and irreversible cognitive impairment (dementia), at the same time separating it from manic – depressive psychosis and melancholy. In 1911, Bleuler introduced the term "schizophrenic psychoses" for the same clinical entity, considering that the clinical picture of the disease is a deficiency of the association of ideas (including, decision and social-emotional networking), and secondarily noting the appearance of 'positive' symptoms (delusions, hallucinations). He believed that there are also mild forms of schizophrenia, which he called "non-dementia".

Over time, research effort focused towards clarifying the operational diagnostic criteria that would be based on symptoms, age of onset, duration of episode, evolutionary model and therapeutic response. After 1980, the focus was on the difference between positive and negative schizophrenia, and after 1990, research was oriented towards cognitive disorders that occur in schizophrenia, by considering that they lead to a decrease in personal functioning. Currently, great importance is attached to social functioning subsequent to an episode of schizophrenia, by trying to identify the factors that influence it.

## Epidemiological and demographic aspects

The lifetime prevalence is of about 1% and is higher in urban and industrialized areas, than it is in rural areas (as is the severity of evolution). By being a chronic disorder that tends to progress, the incidence is lower (approx.1 per 10.000 inhabitants/year).

The sex ratio is considered equal, but with an onset in adult women and one at a younger age in men.

Socioeconomic status: Prevalence is higher in people with lower socioeconomic status. At onset, performance, in terms of professional and marital status, is low, and is further reduced along evolution. Statistically, many people with this diagnosis have not attended/ completed higher education, and they did not/will not exercise performance/high rank professional functions.

1. Prenatal factors: genetics and maternal neuroinfections during pregnancy.
2. Perinatal factors: traumatic birth (hypoxia) and infections.

3. Postnatal factors: increased emotional expression (EE), urban life, drug abuse, immigration.

Statistically, people with a diagnosis of schizophrenia tend to be unmarried. When they achieve marriage, they can not maintain it or have significant difficulties.

The incidence is higher in people who were born in winter and early spring (January to April months in the northern hemisphere and July-September, in the southern hemisphere).

Until the first decades of the twentieth century, the majority of people with schizophrenia had to spend their lives in chronic hospitals. Currently, due to neuroleptic medication and community attitude of psycho-social rehabilitation and anti-stigma programmes, most people are able to live in the community with us.

### Etiopathogenesis

This is plurifactorial and involves the following factors:

1. Biological factors: genetic, biochemical and anatomopathological
2. Social factors: families with increased Expressed Emotion, schizophrenogenic mother and contradictory messages in the family
3. Psychological factors: schizoid personality model

When including the period in which these factors act, they can be further classified into:

1. Prenatal factors: genetic and maternal neuroinfections during pregnancy
2. Perinatal factors: birth trauma (hypoxia) and infections.
3. Postnatal factors: high Expressed Emotion, urban living, use of illegal psychoactive substances, immigration.

From the genetic point of view, the concordance rate is higher in monozygotic twins (50%) compared with dizygotic twins (10-15%). Also, the existence of a parent affected by the same disease determines a risk of 10-15%, and the presence of two parents with the same diagnosis increases the risk to over 40%. Children born to parents without schizophrenia, but adopted by parents suffering with the illness, have a minimal risk, compared to the general population, to develop the illness.



Predisposition for disease transmission is conditioned polygenically, and involves chromosomes 5, 10, 13, 18, 22 (among others), which is correlated to dopamine and serotonin neurotransmission

The vulnerability of the person can also be influenced by the following:

- Second trimester maternal viral infections: it was found that a significant part of persons who later develop schizophrenia are born during the months January to April (northern hemisphere); this fact correlates with greater frequency of viral infections during this period, and other factors (eg. nutrients);

- Perinatal trauma

These correlated factors intervene by perturbation of the neurodevelopmental process, and especially that of neuronal migration. This is achieved slowly, as not all the neurons reach the site they should occupy according to genetic programming, which translates into practically not reaching the corresponding cortical layer, leading to an inability to realize the necessary connections. This neurodevelopmental connection most often involves the following areas: limbic (and hippocampus) and prefrontal (especially in the dorso-lateral cortex).

As a consequence of the neurodevelopmental disorder, cerebral alterations occur, which are characterised by:

- a decrease in the overall volume of the frontal cortex (especially of the left dorsolateral prefrontal cortex);
- reduction in the volume of the left superior temporal gyrus, hippocampus and amygdala;
- the absence of normal asymmetry between the hemispheres;
- ventriculomegaly.

An overall and non-specific decrease in gray matter, unaccompanied by white matter involvement, and with alteration of the cytoarchitecture, smaller, compact and low arborization neurons has also been found. The changes precede the development of the disease, become amplified, and are only slightly modified through evolution, also being present in monozygotic twins, which do not suffer with the illness.

These neuro-morphological dysfunctions constitute neurovulnerability elements, underlying deficits of certain mental abilities, that precede illness onset, such as:

- perceptual inability, regarding signals reception and their integration in a cognitive system;
  - disorders of selective attention and hierarchy of information, as well as their categorization;
  - Deficiencies of "working memory" and executive functions (through prefrontal lobe dysfunction)
- 
- Language difficulties, dysfunctions in the construction of logical-semantic-syntactic expression;
  - Decreased ability of establishing interpersonal relationships;
  - Deficiencies in initiative, motivation and executive functions (abstract thinking, anticipation, planning).

Neurotransmission disorders are a partial consequence of the neuro-developmental deviations and are evident during episodes of illness and in residual states.

- Disturbances in the dopaminergic transmission: this represents mainly a hypersensitivity of the dopamine receptors in the limbic area (especially, postsynaptic D2 and D4), responsible for the positive symptoms; simultaneously, a hyposensitivity (hypofunction) of the D1, D3 dopamine receptors is also occurring in the prefrontal region - responsible for negative symptoms. Generally, there is an imbalance of neurotransmitters in the cortico-striatal-hypothalamic-cortical circuit, in the sense of an increase of dopamine and glutamate decrease. This causes the removal of thalamic neurons from the inhibitory process, and, practically, the thalamus ceases to be an efficient information filter.
- Disturbances in serotonergic transmission: the serotonin system is a cyclical process, with hypoactivity and hyperactivity, and, therefore, disturbs the serotonin/dopamine balance:
  - Hypoactivity determines dopaminergic hyperactivation that is responsible for positive symptoms.
  - Hyperactivity determines dopaminergic hypoactivation that is responsible for negative symptoms.
- Acetylcholine and glutamate transmission disorders: are responsible for cognitive dysfunction and for some cases in which "apoptosis" occurs (innate process by which cells inactivate their own structural and functional components to achieve their own death).

The implicated psychosocial factors are:

- Apathetic, non-stimulating mother during the first year of life.
- Hyperprotective mother (also apathetic), with a tendency to continuously monitor the baby, during the first 3-4 years of life and beyond.
- Disturbances in the clarity of interpersonal communication, and especially in verbal and nonverbal communication with the child (the theory of "double connection").
- confusion regarding roles and decisions in the family of origin; the child has no one to identify with clearly, in order to create one's own individuality.

All these factors contribute to the child's insufficient development of independence, of the boundaries between the self (I), the world and others, leading to dependent conduct and/or social withdrawal, and a reduction in interpersonal communication. In general, interpersonal skills and social insertion of self-abilities are deficient in many of those who develop schizophrenia.

Negative psychosocial factors are also important (so-called stress factors), which may play a role in triggering this disorder. For anyone, the following are important:

- The level of vulnerability they present, a level determined not only by genetic, neuro-developmental and psychosocial conditioning, but also through special periods of life cycles, in respect of puberty, young adulthood or life changes.
- The level of reality testing: that is, the relationship between one's expectations (which may be unrealistic) and negative psychosocial aspects, felt with a painful intensity, in the conditions of a reduced level of protective factors.
- An important role is given to the social support network, which is usually reduced: these people have fewer friends, often lacking a stable partner. The family of origin can play an ambiguous role: on one hand, it can be protective (even, negatively, overprotective), and on the other hand, it may be uninvolved (families with high Expressed Emotion).

- Psychoactive substance use: cannabis.

Currently, there is no clear hypothesis to fully explain the pathogenesis of schizophrenia, but there are several hypotheses, each accounting for a certain side of the schizophrenic pathology.

#### Clinical presentation

The onset of schizophrenia is most often insidious, progressive, considering that, in many cases, actual onset is preceded by a prodromal phase that can last months or years. This period, called prodrome, consists of decreased cognitive and professional performance, a tendency to social withdrawal, apragmatism, abstract concerns (eg. philosophy, astrology).

Because of these rather nonspecific symptoms, family and friends get used to them, being often interpreted as "oddities" of the person, and diagnosis and initiation of treatment will be delayed. This aspect later reflects on the evolution and prognosis of the disorder.

The onset can also be relatively sudden, therefore acute (days, weeks), when it is usually dominated by positive symptoms (hallucinations, delusions, bizarre behavior, psychomotor agitation), and sometimes precipitated by life events.

Another type of onset is the subacute (weeks), accompanied by: depersonalisation, derealisation, delusional disposition with secondary anxiety.

The clinical presentation of schizophrenia consists of a combination, of varying degrees, of four macro-syndromes: positive, negative, disorganized, catatonic.

The Positive macro-syndrome consists of:

- Delusions: one or more, usually bizarre, delusional themes may be present. The most common theme is paranoid, with an interpretation of others' attitudes as hostile and against the subject. It can occur as a "primary delusion" (initially, there is a delusional disposition, and the shift toward delusional beliefs is realized suddenly, through a perception, memory and delusional intuition). The paranoid delusion is

preceded by the delusional belief of being put under surveillance (specifically stared at by others, eavesdropped on, recorded, photographed, studied in intimate details, supervised by people with false identities - Fregoli illusions, doppelgangers). Paranoid delusions are usually accompanied by secondary anxiety. Other delusional topics may be: mystical, of grandeur, of demonic possession.

- The syndrome of transparency-influence is usually interpreted as delusional. Clinically, it's represented by: thought reading, thought echoes, or thought broadcasting, thought theft, thought withdrawal and thought insertion, delusions of xenopathic control of behavior and feelings, the external induction of unusual bodily sensations, etc.

- Hallucinations: the most characteristic are auditory and commenting hallucinations, as well as imperative or appellative hallucinations. With a lesser frequency, olfactory, gustatory, kinesthetic, sexual or visual (rarely) hallucinations can be encountered.

The Negative macro-syndrome consists of:

- avolition – represented by impoverishment of impulses, tendencies, curiosity, interests and, overall, intentionality. There is a deficiency in the spontaneity of initiatives, expressions and behavior.

The planification of actions and their actual realization is severely disrupted, executive functions are ineffective, with the subject being apragmatic.

- Emotionality is also altered by: indifference and lack of interest. The expression of emotions is minimized: subjectively, the patient lives an affective "coldness" or "obliteration". Anhedonia is also present (they can not enjoy anything), as is a disinterest in the operation and manifestation of one's own corporality.

- The thought process is poor, restricted, stereotyped. A restriction may be present in the quantity and spontaneity of speech (poverty of speech) or speech may be quantitatively adequate, but very little information is communicated (poverty of content of speech).

- Social relationships are significantly reduced, until reaching levels of social withdrawal and isolation.

The Disorganized macro-syndrome consists of:

- Ideo-verbal disorganization:

- The thought process and speech manifest through formal disorders, as circumstantiality, derailment, incoherence, elliptical or allusive speech, mental block, mentism.

- Disorders of logic, syntax and semantics can also be present: unusual meanings in the use of common words and phrases; creating symbols, expressions and new words, with an idiosyncratic meaning (neologisms). There is a tendency to unintelligibly cultivate abstractions or to use hyperconcrete phrases.

- Difficulties of abstractisation and comparison are present (noted by using the Interpretation of Proverbs test).

- Behavioral disorganization:

- behavioral manifestations are not sufficiently and logically motivated, sometimes have bizarre reasons or completely lack purpose. The subject can laugh without reason or in sad circumstances, they can undress in public or hit another without cause, have bizzare arguments or use bizarre facial expressions and nonsensical mannerisms etc.

- the entire behavior of the patient is strange, bizarre, and incomprehensible.

The Catatonic macro-syndrome consists of:

- Hypertonia with waxy flexibility
- Stereotypies
- Suggestibility
- Verbal and food-intake negativity
- Psychomotor retardation, sometimes with a sudden shift to psychomotor agitation

Some diagnostic systems, such as the DSM-IV TR, require for a diagnosis of schizophrenia, a first episode duration of at least six months (of which, at least 1 month of obvious florid symptoms). The ICD-10 diagnosis system requires a duration of a minimum of only 1 month of florid symptoms.

#### The clinical forms of schizophrenia

- Paranoid: predominantly, positive symptoms: unorganized paranoid delusions, auditory hallucinations, and phenomena of thought transparency – influence. This is currently the most common form.
- Disorganized (hebephrenic): predominance of ideo-verbal and behavioral disorganization, and has an onset at a young age.
- Catatonic: the catatonia syndrome is predominant; currently, it is rare.
- Undifferentiated: in this type, there are symptoms from all areas mentioned previously.
- Residual form: it is required that the patient presented, at one point during the course of illness, at least one productive episode with positive symptoms (delusions, hallucinations, etc.), but currently there are only negative symptoms in the clinical presentation (schizo-deficient)
- The simple form: characterized only by negative symptoms, without a history of positive symptoms.

#### Differential diagnosis

1. Psychotic disorders of a schizophrenic pattern, induced by the consumption of substances (psychoactive substances, alcohol) - based on history and toxicological examination.
2. Psychotic disorders of a schizophrenic pattern, induced through organic pathology (brain tumors, stroke) - based on history, clinical examination and imaging investigations.
3. Acute and transient psychotic disorders - may present with clinical symptoms of schizophrenia, but do not meet the time criterion, because symptoms resolve in a month.
4. Schizoaffective disorder – also has affective symptoms in the clinical presentation: manic, depressive or mixed.
5. Persistent delusional disorder – the clinical presentation is based on systematized delusions, usually monothematic.

## Evolution and prognosis

From an evolutionary standpoint, without treatment, after the first five years of evolution, the following may occur:

- Single episode (22%);
- Recurrent episodes, without deficit (35%);
- Recurrent episodes, with deficit (8%).
- Continuous evolution (progressive) from the first episode (35%).

In schizophrenia, after one or more episodes, the patient can often reach a defective state: clinically and socially, manifested by the persistence of some clinical features from the acute phase or through a decrease in the capacity to fulfill social roles.

The following are negative prognosis factors:

- An significant familial and genetic load;
- Problems during pregnancy or childbirth;
- Reduced social support network;
- Schizoid personality (schizotypal);
- Onset at a young age;
- Long prodromal period;
- Long duration of first episode (over 6 months, from onset until remission)



- The predominance of negative symptoms;
- The presence of a sizeable deficit in terms of energy, relationships and pragmatic performance (possibly, alongside residual symptoms) after the first episode;
- Family members with high EE (expressed emotion = e.e.) or other relational distortions (= rejection, indifference, lack of understanding and poor support capacity);
- Poor premorbid functioning;
- Non-compliance to treatment;

The following are positive prognosis factors:

- Onset at an older age;
- Acute onset type;
- Paranoid clinical type;
- Affective elements;
- Good premorbid functioning;
- Absence of genetic load;
- Adequate social support network;
- A short duration of the first episode.

## Treatment

In recent decades there have been major advances in treating schizophrenia through the discovery and use of neuroleptics and implementation of psychosocial rehabilitation programs. The treatment of schizophrenia is applied in accordance with the clinical presentation and is divided into two phases: the acute phase and the maintenance phase. It involves psychotropic medication and psychotherapy, and takes place in hospitals, outpatient settings, special units and the community.

## Psychopharmacological treatment

This can be used both in the acute phase, and in the maintenance phase. In order to control clinical symptoms, hospitalization is usually required. Initially, a clinical evaluation is performed (psychopathological, biographic, psychosocial, somatic) and afterwards neuroleptics can be administered.

## Neuroleptics

These are drugs that have proven to be effective for psychosis in the mid twentieth century, and are still used today. The first neuroleptic was chlorpromazine, long considered the standard in evaluating "neuroleptic power" of drugs of this class. The product belongs to the class of neuroleptics, which have been traditionally called "sedatives", due to side effects, consisting of: sedation (and anxiolysis), somnolence, orthostatic hypotension, dryness of mucous membranes. A presentation, in terms of years of development of neuroleptics, is shown in the figure below.

### Classification of neuroleptics:

- Sedatives: chlorpromazine, levomepromazine and thioridazine
- Incisive: haloperidol, trifluoperazine
- Bimodal: amisulpiride, sulpiride
- Atypical: olanzapine, risperidone, quetiapine, aripiprazole, ziprasidone and clozapine

Classical neuroleptics block dopamine neurotransmission by blocking D1 and D2 receptors. New generation neuroleptics only block D2 and serotonin 5HT 2a receptors. Blocking dopamine receptors has different effects, depending on the location:

1. Mesolimbic pathway: antipsychotic effect
2. Mesocortical pathway: intensification of negative symptoms and cognitive impairment
3. Nigro-infundibular pathway: amenorrhea-galactorrhea syndrome
4. Nigro-striatal pathway: extrapyramidal syndrome

Side effects are many, the most important being:

1. Anticholinergic effects: dryness of mucous membranes, midriasis, constipation, and urinary retention
2. Antihistaminic effects: sedation, weight gain
3. Antiadrenergic effects: hypotension, ejaculatory dysfunction
4. Amenorrhea-galactorrhea syndrome
5. Cognitive dysfunction with emphasis on negative symptoms
6. Extrapyrimal effects: acute dystonia, akathisia, parkinsonian syndrome and tardive dyskinesia
7. Neuroleptic malignant syndrome, which may lead to death

Advantages of atypical neuroleptics:

- They act on the schizo-negative symptomatology of schizophrenia and on depression.
- They act, positively, on cognitive impairment, improving social adjustment and quality of life.
- They have minimal extrapyramidal effects, however less intense compared to classical neuroleptics.

Classical neuroleptics (incisive):

Haloperidol - effects on positive symptoms

Levomepromazine – sedative effects

Bimodal neuroleptics (antidepressant effect at low doses, and antipsychotic effect at high doses):

Amisulprid - side effects: amenorrhea-galactorrhea Sulpiride - side effects: amenorrhea-galactorrhea

New generation neuroleptics (atypical):

Risperidone - possible side effects: galactorrhea, extrapyramidal symptoms

Olanzapine – possible metabolic side effects

Quetiapine - possible sedative side effects

Ziprasidone - side effects: cardiac function - can increase QTc interval

Aripiprazole - side effects: extrapyramidal symptoms Clozapine - side effects: neutropenia

Depot neuroleptics (slow release of the drug in the body):

Haloperidol decanoate: 1 ampoule/2 weeks

Flupentixol: 1 ampoule/2 weeks

Risperidone (25 mg, 37.5 mg, 50 mg): 1 ampoule/2 weeks

Olanzapine (210 mg, 300 mg, 405 mg): 1 ampoule/2 weeks, 1 ampoule/month

Acute phase treatment

In schizophrenia, a single neuroleptic in adequate doses is commonly used. If it is not effective after a few weeks, another may replace it. A combination of two neuroleptics can be used (a "sedative" with an "incisive"). The choice of neuroleptic is based on clinical symptoms:

1. Positive symptoms: incisive, bimodal or atypical neuroleptics
2. Negative symptoms: atypical or bimodal neuroleptics (low dose)
3. Disorganization symptoms: incisive or atypical neuroleptics
4. Catatonic symptoms: incisive or atypical neuroleptics (administered by injection)

Depending on the case, the following may be used, along with neuroleptics: anxiolytics (benzodiazepines), antidepressants, hypnotics and mood stabilizers. Medication must take account of somatic comorbidity.

In severe cases of catatonic schizophrenia, ECT may be applied, carried out with appropriate medical supervision.

## Maintenance phase treatment

After the acute phase of the treatment, a maintenance therapy is required. This phase is managed by the outpatient psychiatrist and comprises of administering the same treatment, which was used to obtain remission. The duration of treatment depends on several factors, but generally, after a first episode of schizophrenia, it is required for two years, after two episodes of schizophrenia it is required for 5 years, and after three episodes, treatment will be life-long. The decision to stop or continue the maintenance treatment is shared by the psychiatrist and the patient.

## Psychotherapy treatment

Psychotherapy requires to be initiated early, due to the tendency of the patient toward isolation and non-communication (some neuroleptics may even exacerbate these tendencies), and is considered complementary to medication. Interpersonal and social contact is favoured, and patients' attendance in club activities, gymnastics and sports, occupational therapy and cultural and artistic activities is stimulated. There are several psychotherapeutic interventions that can be applied: cognitive behavioral therapy, family therapy, psycho-education.

Cognitive-behavioral therapy can be applied as symptoms improve, and consists of: techniques of problem-solving, increase of social networking techniques. Patients then may be included in the cognitive – behavioural group, which currently runs in our Mental Health Center.

Because communication within the family is usually disturbed and this may result in high levels of EE, the reshaping of families is attempted, in the sense of increasing tolerance levels, but without determining hyperprotection or rejection.

One of the most important factors that determine relapse is noncompliance. Therefore, psycho-education programs are used to help patients and their families by learning about their meaning:

1. What is the disease?
- 2 What is the most useful treatment?
3. What are the possible side effects?
4. What are the symptoms of an imminent relapse that require re-evaluation of treatment?

The patient and their family must become "co-therapists" working with the medical – psychiatric system in maintaining the wellbeing of the patient.

In some cases, cognitive psychotherapy treatments can be used to reduce the intensity of hallucinations and delusions.

Schizophrenia treatment is usually lengthy, sometimes life-long, which requires continuous monitoring thereof. From the perspective of community psychiatry, patients suffering with schizophrenia (and others with the same evolutionary model) are supported by a therapeutic team, in a territorial center, comprising: a psychiatrist, social worker, nurse, psychologist, and occupational therapist.

For cases with a long evolution, marked by periodic relapses and tendencies toward a social defect, there is a whole institutional network oriented toward relapse prevention, psychosocial rehabilitation, and maintenance in the society. In case of relapse, hospitalization should be short, and, if possible, done in Day Centers or Psychiatric wards of General Hospitals.

For people who lack social support, there is protected housing in

"Hostels". Here, people suffering with schizophrenia, which retain partial self-care abilities, live under the supervision of the therapeutic team, can participate in clubs, sheltered workshops and

other activities. This avoids prolonged hospital admissions through lack of social support or rejection.

Community psychiatric support for people with schizophrenia should be in the direction of "antistigma" action, in the sense of shaping community attitudes, in order for them to accept patients as part of the community.

## Persistent delusional disorders

These are a group of psychoses with a chronic course, where the main symptoms are, as evident from their name, systematized delusions. They include old concepts, such as "Paranoia" and "paraphrenia".

They are considered rare illnesses, although it is generally accepted that the actual number in the population is much higher than that of those who come in contact with psychiatric services.

Their onset usually takes place in adulthood, usually after the age of 35.

## Paranoia

It can be considered the basic prototype of persistent delusional disorders. In the current international diagnostic classifications, it is identified with "delusional disorder."

Emil Kraepelin, who described paranoia as a themed and consistent delusion, in particular relating to persecution, carried out the basic description of paranoia. He differentiated paranoid disorders from dementia praecox, by saying that patients with paranoia do not have a formal thought disruption, with the exception of delusions, and thus, the main deficiency is found in the judgment process. Personality is also well preserved, even after a long duration of illness, the only changes being noted in terms of the behavior that occurs as secondary to one's delusional beliefs.

Paranoia is more common in those who have a premorbid paranoid personality. The clinical picture is characterized by the presence of a systematic delusion, apparently logical and well organized, which is at the center of the patient's existence and their behavior. Hallucinations, transparency-influence phenomena, schizo-negative or disorganized symptoms are never present.

The diagnosis is made after at least three months of presence of a systematized delusion. Delusional themes found within this pathology are:

- The theme of persecution. Persecutory delusion is the archetype of "Paranoia" and represents the most common theme. The patient lives with a feeling of hostility from others, who are considered to have an unfavourable attitude, an antagonistic, aggressive tendency toward the patient. One's psychological mask becomes suspicion. Their beliefs are very stable and usually, over time, their development increases. People involved in the persecutory system may be relatives, neighbors, doctors, police, government officials, security organizations and others.

- The litigious version of the theme of persecution. For these these individuals, there is a deep and persistent feeling that they were wronged in one way or another, and they constantly seek compensation, either by personal or legal means. The starting point can be a genuine loss or unsatisfactory reward, but the subsequent behavior of the subject is obviously exaggerated and endless. Therefore, complaints and secondary behavior may seem coherent and reasonable at first. These people generate a lot of publicity in the media.

- The somatic theme. The main theme is delusional dysmorphophobia or hypochondriasis. In these cases, we find four major thematic areas:

1. Delusions relating to the skin (infestation by microorganisms, parasites, etc.)
2. Delusions relating to ugliness and deformity (dysmorphic delusions);
3. Delusions relating to bodily smells and halitosis;
4. Various (dental, sexual and non-sexual transmission diseases).

- The erotomania theme. The subject is convinced that another person of the opposite sex (who they may not even personally know) is in love with them and they are about to be united in marriage; intense socially disruptive behaviors follow. This theme is more common in women.

- The theme of megalomaniac invention. The subject, after years of concern, is convinced that they have found the "cure for cancer", the "elixir of immortality", the "perpetuum mobile", the "essence of matter", and so on. They require the official recognition of their discoveries (which, as a scientific objective, can not be justified in any way), and thereby become socially disruptive. Themes of illustrious lineage, with broader social relations (often confabulatory, in nature) may occur. The expansive, mystic delusion of special divine mission, which even manages to recruit others (due to long preservation of logic and persuasiveness), may occur.



- The theme of jealousy. The subject is convinced that their partner is cheating (with hundreds of people, children, elderly, women, etc.), although the arguments to others are considered unreasonable. The theme is more common in men.

- The theme of reference. The subject experiences sensitively the fact that others are concerned with critical attention toward themselves. They are in a continuous state of alert, with suspicious hypervigilance regarding the behavior and expressions of others, with distorted, overvalued, hyperanalytical interpretations of this behavior, which is no longer considered normal or ordinary. They feel looked at in a particular way (possibly, with others turning their heads after them), they believe they are being the subject of discussions, they are maligned, commented on negatively, that others laugh and joke about them, trying to publicly embarrass and dishonor them. The subject tends to exaggerate trivial or ordinary incidents along the course of life, by giving them an exaggerated interpretation, as having an aggressive significance against the self, appearing as a delusion of reference. Sometimes, trivial verbal expressions are interpreted as alluding to them. In a more advanced form of delusion, they are convinced that television programmes mention them, as do the newspapers, with information that refers to them.

There are two forms of pathology described in paranoia:

- Active paranoia (of combat): with delusions of persecution or prejudice, when the person fights for their rights, writes memoirs, complaints, lawsuits, becoming, from persecuted, a persecutor;

- Passive paranoia (sensitive): with delusions of persecution or reference, when the person lacks energy, is self-conscious, and places the blame for failure on others.

### Paraphrenia

This was described by Kraepelin, who considered it as a functional psychosis, distinct from paranoia and dementia praecox. It is characterised by a later onset than dementia praecox and is similar to the current concept of paranoid schizophrenia: with fantasy delusions and hallucinations, but with fewer thought disorders, with better affective preservation, with less damage to the personality and a better maintenance of motivation. Kraepelin saw paraphrenia as an intermediate disease between dementia praecox and paranoia. (9)

He identified four types:

- a) Systematic: with insidious development of a delusional system of persecution, excitement, and the predominance of the transparency-influence (control) syndrome;
- b) Elation: ideas of grandiosity and euphoric mood;
- c) Confabulatory: counterfeit memories, delusions are embellished by imagination, memories, literature;
- d) Fictional: extraordinary, incoherent and changeable delusions.

In general, the defining elements of paraphrenia are considered to be represented by:

- A fantastic character of delusional themes, with a predominance of the imaginary;
- The juxtaposition of an imaginary world alongside reality, where the patient continues to adapt well;
- A long-term maintenance of the personality core;
- Dominance of language over action.

In the clinical presentation, in addition to the systematized clinical delusion, the transparency-influence syndrome is also described, along with, predominantly, visual and auditory hallucinations.

Another characteristic of paraphrenia is the presence of double accounting (the patient is able to distinguish between the real and the imaginary world). If decompensation occurs, there will be an intricacy between the real and the imaginary, as the patient loses double accounting.

The evolution of persistent delusional disorders is typically chronic, but non-deteriorating (compared to the progressing course of schizophrenia), and after several years the delusion is placed in the background, and there is a decrease in the affective resonance to the delusional themes. In terms of prognosis, unlike schizophrenia, there is a better preservation of mental functions and of overall personality, with better functionality in all areas of life of the individual.

Neuroleptics are the first line of treatment (see the Treatment of schizophrenia section). As appropriate, antidepressants, anxiolytics or mood stabilizers may be added.

## **Acute and transient psychotic disorders**

Their presence in the general population is considered to be rare, but their incidence and prevalence is not known.

Acute and transient psychotic disorders may occur at any age, with a peak frequency considered to be around the 3rd decade, with a lower age of onset in women than in men. Most studies mention their preponderance in females.

The onset is acute, from a few days to 1-2 weeks, preceded or not by stressful life events.

During the state, delusions with multiple themes (persecution, poisoning, possession, influence, sexual transformation, reference, mystical, richness or fabulous powers, guilt) are characteristic, and changeable from day to day. There may be various and oscillating hallucinatory experiences. The most common are auditory hallucinations, but very vivid visual hallucinations can also be present, as well as haptic, kinesthetic or pseudohallucinations.

The emotional state will also oscillate between anxiety, euphoria, ecstasy, irritability, depression, behavioral inhibition (up to stupor) and social withdrawal (up to nonresponding and negativity), and may alternate with agitation. Feelings of depersonalization-derealisation, transparency-influence (short duration), and even confusional type symptoms (with denivelation of conscious vigility) may be present.

Insomnia is a common symptom, as are attention disorders and hypomnesia for recent events.

The behavior is inappropriate, bizarre, delusionally motivated, inhibited, bewildered, agitated with aggression, aimless travelling, or sometimes accompanied by suicide attempts or forensic acts.

Sometimes, the clinical presentation is not as complex and polymorphic as described above, and can be reduced to paranoid delusions, accompanied by hallucinations, anxiety, restlessness, depression (but sometimes also by euphoria, elation); it can be reduced even to reference delusions, coupled with a depressed-anxious state (rarely, euphoric).

As regards the duration of these psychotic episodes, in the presence of typical symptoms of schizophrenia (commenting auditory hallucinations, transparency-influence syndrome, bizarre delusions, etc.), this should not be longer than 1 month, in which case the diagnosis should be changed the schizophrenia. If typical symptoms of schizophrenia are not present, such episodes can last up to 3 months, after which time the diagnosis will change to that of persistent delusional disorder or other non-organic psychotic disorder.

The main diagnosis subgroups of acute and transient psychotic disorders are:

1) Acute polymorphic disorder without symptoms of schizophrenia;

2) Acute polymorphic disorder with symptoms of schizophrenia;

These diagnostic subgroups have as common feature the polymorphism of clinical symptoms with the variability and rapid change of symptoms from day to day or even during the same day. The presence or absence of schizophrenia symptoms distinguishes them into the above diagnoses.

3) Schizophrenia-like acute psychotic disorder. In it, the symptoms are relatively stable and meet the criteria for schizophrenia, but the episode duration is less than one month. Persistence of symptoms of schizophrenia for more than one month requires a change in the diagnosis to that of schizophrenia.

4) Other acute, predominantly delusional, psychotic disorders. The main characteristic is the presence of delusions and hallucinations, which are quite stable, but which do not meet the symptomatic criteria for schizophrenia. The main delusional themes are those of persecution or reference. If the delusions persist for more than three months, the diagnosis should be changed to that of persistent delusional disorder.

Their differentiation is made with:

- Schizophrenia (or schizophreniform psychosis, according to the DSM-IV), wherein the productive psychotic disorder is complex and bizarre, with the existence of negative semiological elements (prodromal, during the episode and thereafter), as well as of disorganized symptoms;

- Mood disorder, where manic or depressive symptoms are predominant, while psychotic elements are secondary.

The short-term evolution of acute and transient psychotic disorders is toward a complete remission of psychotic symptoms, with a return to the previous level of functioning of the individual, aspects that are also part of the diagnostic criteria. The persistence of symptoms over the specified time intervals for the diagnosis subcategories requires a change of diagnosis. In case of remission, there is a tendency for recurrence, conditioned or not by stressors.

In the long-term, specialty literature refers to the following progression option: single episode, recurrent acute psychotic episodes

and an evolution toward chronic psychoses (affective disorders, especially bipolar type, schizoaffective disorder and schizophrenia).

Psychotropic treatment is, essentially, neuroleptic (see Treatment of schizophrenia). Based on clinical symptoms, anxiolytic and mood stabilizers can be administered.

## **Schizoaffective disorder**

This represents a controversial psychosis, which would be placed in an intermediate zone between the pathology of schizophrenia and mood disorders. The intermediate position in psychoses is supported by clinical aspects, ie overlapping elements of schizophrenia with affective symptoms (depressive, manic and mixed) in the same episode of illness.

The lifetime prevalence is below 1%, with a women/men ratio slightly in favor of women.

The psychopathological picture contains approximately equal proportions of the number of schizophrenic symptoms (eg. commenting auditory hallucinations, ideo-verbal and/or behavioral disorganization, transparency-influence syndrome, etc.), and dispositional symptoms (depressed mood, euphoria and/or irritability, mixed state). In order to differentiate schizoaffective disorder from mood disorders, it is necessary (according to diagnostics criteria) that, for a minimum of two weeks during its development, affective symptoms are not prominent.

Thus, according to eventualities that may result from the combination of the two psychopathological entities, we can have: schizodepressive, schizomanic, schizohypomanic episodes etc. Schizoaffective episodes can occur in an isolated context, in the development of other psychotic disorders, therefore the distinct nosological entity quality of this disorder is questionable in the minds of certain authors.

Similar to schizophrenia and to the pathology of mood disorders, the most frequent evolutionary model of this disorder is episodic, with complete or partial remission with defective states that can remain constant or may increase, as they advance in illness.

Evolution is heterogeneous and polymorphic, with the appearance of at least two different episodes: schizoaffective episodes, affective episodes, and purely schizophrenic episodes. Schizoaffective episodes have been noted to be the most common, followed by the purely affective, and the simple schizophrenic types.

The treatment consists, essentially, in administering neuroleptics (preferably new generation, administered both during episodes, and also in the maintenance phase), antidepressants (for schizodepressive episodes) and mood stabilizers (both during episodes of illness, and as maintenance therapy). In periods of remission, it is useful to associate psychosocial interventions, such as psychotherapy, psychoeducation etc.

## Chapter XI – PERSISTENT DELUSIONAL DISORDERS

They represent a group of chronic evolutionary psychoses in which the main symptom is, as it is also apparent from their name, the systematized delusion. They include the old concept of "Paranoia" and "Paraphrenia".

They are considered rare illnesses, although it is generally accepted that the actual number is much higher than that of those who come into contact with psychiatric services.

Their onset generally occurs in adulthood, usually after 35 years of age.

### Paranoia

It can be considered the basic prototype of persistent delusional disorders. In the current international classifications of diagnosis, it is confused with "delusional disorder".

The basic description of paranoia was made by Emil Kraepelin, who described it as a themed and consistent delusion, with most themes of persecution. He distinguished the paranoid disorders from dementia praecox, by the fact that patients with paranoia have no formal disturbance in the thought process, except for delusions, and thus the principal defect is found in the area of judgment. The personality is well preserved, even after a long period of illness, the only changes being the behavior secondary to delusional beliefs.

Paranoia is more common in people with a premorbid paranoid personality. The clinical picture is characterized by the presence of a well-organized, seemingly logical, systematized delusion that is at the center of the patient's existence and behavior. There are no hallucinations, thought transparency-influence phenomena, schizo-negative series or disorganizing disorders.

The diagnosis is made after at least 3 months of systematized delusion. The delusional themes encountered within it are:

- The theme of persecution. The delusion of persecution is the archetype of "paranoia", this type of delusion being the most common. The patient experiences a feeling of hostility on the part of other people considered to have an unfavorable attitude, a hostile, aggressive tendency towards the subject. His psychological mask is suspicion. Beliefs are extremely stable and usually, over time, they develop more. Persons involved in the

system of persecution may range from relatives, neighbors, doctors, police, government diplomats, intelligence organizations, and others.

- The litigation variant of persecutory delusions. These people have a deep and persistent feeling that they have been wronged in one way or another, permanently claiming damages, either personally or legally. The starting point can be a genuine damage or an unsatisfactory reward, but the subsequent behavior of the subject becomes obviously exaggerated and endless. Thus, complaints and secondary behavior may seem coherent and reasonable at first. These people generate a lot of publicity in the media.

- The somatic theme. The main theme is delusional dysmorphophobia or hypochondria. Within it we find four major thematic areas:

1. Delusions involving the skin (infestation with microorganisms, parasites etc.);
2. Delusions involving ugliness and deformity (dysmorphic delusions);
3. Delusions involving body odor and halitosis;
4. Miscellaneous (dental, sexually transmitted and non-sexually transmitted diseases).

- Erotomania theme. The subject is convinced that another person of the opposite sex (who might, possibly, not even know them) is in love with them and they are about to unite in marriage; significantly socially disruptive behaviors will ensue. This theme is more common in women.

- The megalomaniac theme of invention. The subject, after years of concern, is convinced that he has discovered the "cancer cure", "the elixir of immortality", the "perpetuum mobile", the "essence of matter", and so on. He claims the official recognition of his discoveries (this scientific objective can in no way be justified) and becomes socially disruptive. Illustrious descent themes, with extended social relationships (often confabulatory) may also emerge. The mystical delusion of a special, expansive, divine mission should also be mentioned, which can sometimes manage to also convince devotees (due to the long-term preservation of logic and persuasion power).

- The theme of jealousy. The subject is convinced that the partner is unfaithful to them (cheating with hundreds of people, with children, elders and women, etc.), although arguments for others are considered unreasonable. The theme is more common in men.

- The theme of reference. The subject experiences sensitively that others are concerned and critical of their own person. He presents a state of continuous alert, with suspicious hyper-vigilance over the behavior and expressions of others, with distorted, over-evaluated, hyper-analytic interpretations of this behavior, which is no longer considered to be natural or trivial.

He feels looked at in a special manner (maybe others turn their heads after him), they talk about him, they gossip about him, he is commented on negatively, some laugh at him and joke about him, they try to publicly embarrass him, to dishonor him. The subject exaggerates ordinary or common incidents of life, giving them an exaggerated interpretation, as having an aggressive meaning against him personally, which constitutes a reference delusion. Sometimes banal verbal expressions are interpreted as allusions to oneself. In a more advanced form of the delusion, he is convinced that on television they are talking about him, that there are information about him in the newspapers.

There are two forms of illness described in paranoia:

- Active (fight) paranoia: with a delusion of persecution or harm, the person will be fighting for his rights, writing memoirs, complaints, trials, becoming a persecutor himself;
- Passive (sensitive) paranoia: with a delusion of persecution or reference, in which the person is devoid of energy, self-conscious, blaming his failures on others.

### Paraphrenia

This was described by Kraepelin as a functional psychosis, distinct from paranoia and dementia praecox. It develops later than dementia praecox and was similar to today's paranoid schizophrenia: with a fantastic delusion and hallucinations, but with fewer thought disorders, with better preservation of affectivity, with less impairment of personality and with a better preservation of volition. He interpreted paraphrenia as an intermediate disease between dementia praecox and paranoia. (9)



He identified four forms:

A) Systematic: with the insidious development of a delusional system of persecution and exaltation, and the predominance of the thought transparency-influence syndrome;

B) Expansive: ideas of grandiosity and euphoric mood;

C) Confabulatory: fake memories, the delusions are enriched by imagination, memories, literature;

D) Fantastic: extraordinary, incoherent and changing delusions.

In general, the defining elements for paraphrenia are represented by:

- The fantastic character of the delusional themes, with a major contribution from the imaginary;
- The juxtaposition of an imaginary world to the real one, in which the patient continues to adapt well;
- Long-term preservation of the core of personality;
- The predominance of language over action.

Within the clinical picture, besides the systemic clinical delusion, there can also be a thought transparency-influence syndrome and, predominantly, visual and auditory hallucinations.

Another feature of paraphrenia is the presence of double accounting (the patient distinguishes between the real world and the imaginary world). In the case of decompensation, there is confusion between the real world and the imaginary one, and the patient loses the double accounting.

The evolution of persistent delusional disorders is usually chronic, but non-deteriorative (compared to the evolutionary situation of schizophrenia), and after several years of evolution, the delusion is placed on a secondary plane, along with a diminishment of the emotional resonance to delusional themes. From a prognostic point of view, unlike schizophrenia, there is a better preservation of mental functions, as well as of personality, as a whole, with better functionality in all areas of existence of the individual.

The treatment is primarily neuroleptic (see the section on schizophrenia). Depending on the condition, antidepressant, anxiolytic, and mood stabilizers can be added.

## ACUTE AND TRANSIENT PSYCHOTIC DISORDERS

Their presence in the general population is considered to be rare, but their incidence and prevalence is not known.

Acute and transient psychotic disorders may begin at any age, the peak being considered around the 3rd decade, with a lower age of onset in women. Most studies mention their predominance in women compared to men.

The onset is acute, from a few days to 1-2 weeks, preceded or not by stressful life events.

In the characteristic illness period there are multiple delusional themes (persecution, poisoning, possession, influence, sexual transformation, reference, mystical, wealth or fabulous powers, guilt), which change from day to day. There may be different and oscillating hallucinatory experiences. The most common are auditory hallucinations, but extremely vivid visual, haptic, kinesthetic hallucinations and pseudo-hallucinations may also present.

The affective state can also oscillate, between anxiety, euphoria, ecstasy, irritability, depression, behavioral inhibition (to stupor), and social withdrawal (to lack of response and negativity), which can alternate with agitation. There may also be experiences of the depersonalization-derealization series, transparency-influence phenomena (of short duration) and even confusional symptoms (with an uneven conscious vigilance).

Insomnia is a common symptom, as are the disturbances of attention and hypomnesia for recent events.

The behavior is inappropriate, bizarre, delusionally motivated, such as inhibited behavior, perplexed, agitation with aggression, aimless travel, sometimes suicide attempts and forensic acts.

Sometimes, the clinical picture is not so complex and polymorphic as previously described, and can consist of only paranoid delusions, accompanied by hallucinations, anxiety, restlessness, depression (but sometimes even euphoria, expansiveness); it can be summed up even as a sensitive-reference delusion, doubled by a depressed-anxious state (rarely, euphoric).

Regarding the duration of these psychotic episodes, in case of the presence of typical symptoms of schizophrenia (commenting auditory hallucinations, transparency-influence syndrome, bizarre delusions, etc.), this should not exceed one month, in which case the diagnosis should be changed that of schizophrenia. If the typical symptoms of schizophrenia are not present, these episodes may last up to 3

months, after which the diagnosis will change to that of persistent delusional disorder or other non-organic psychotic disorder.

The main diagnostic subgroups of acute and transient psychotic disorders are, as follows:

- 1) Acute polymorphic disorder without symptoms of schizophrenia;
- 2) Acute polymorphic disorder with symptoms of schizophrenia;

These diagnostic subgroups have as a common feature the polymorphism of the clinical picture with the variability and rapid change of the symptomatology,

from day to day or even during the same day. The presence or absence of symptoms of schizophrenia differentiates them in the abovementioned diagnoses.

1) Acute schizophrenia-like psychotic disorder. Within it, the symptoms are relatively stable and meet the criteria for schizophrenia, but the duration of the episode is less than one month. The persistence of schizophrenia symptoms over 1 month requires a change of diagnosis to that of schizophrenia.

2) Other predominantly delusional acute psychotic disorders. Its main feature is the presence of delusions and hallucinations that are somewhat stable, but do not meet the symptomatic criteria for schizophrenia. The main delusional theme is that of persecution or reference. If the delusions persist for more than 3 months, the diagnosis must be changed to that of persistent delusional disorder.

Their differential diagnosis is made with:

- Schizophrenia (or schizophreniform psychosis, after DSM-IV), in which the productive psychotic disorder is more complex and bizarre, and there are also semiological elements from the negative series (prodromal, during the episode and subsequently), as well as from the disorganized series;
- Mood disorders, where the manic or depressive symptomatology is predominant, and the psychotic elements are secondary.

The short-term progression of acute and transient psychotic disorders is towards a complete remission of the psychotic symptomatology, with a return to the person's previous level of functioning, aspects that are

part of the diagnostic criteria. The persistence of symptoms over the above-mentioned time intervals for diagnostic subcategories requires a change of diagnosis. In case of remission, however, there is a tendency towards recurrence, whether or not conditioned by stressors.

In the long term, the data in literature mentions the following evolutionary variants: single episode, recurrent acute psychotic episodes and an evolution towards chronic psychoses (affective disorders, especially bipolar type, schizoaffective disorder and schizophrenia).

The treatment is essentially neuroleptic (see the treatment of schizophrenia). Anxiolytic and mood stabilizers can be administered, depending on the clinical picture.

#### SCHIZOAFFECTIVE DISORDER

This represents a controversial psychosis that would be placed in an intermediate area between schizophrenia and the pathology of mood. The intermediate position in psychoses is supported by clinical aspects, i.e. the overlapping of elements of schizophrenia with affective ones (depressive, manic and mixed) in the same episode of illness.

Lifetime prevalence is less than 1%, with a women/men ratio slightly in favor of women.

The psychopathological picture contains approximately equal proportions of both schizophrenic symptoms (e.g., commenting auditory hallucinations, ideo-verbal and/or behavioral disorganization, transparency-influence syndrome, etc.), as well as mood symptoms (depression, euphoric and/or irritable, mixed mood). In order to distinguish schizoaffective disorder from mood disorders, it is necessary (according to the diagnostic criteria) to have a minimum of 2 weeks during its evolution in which the affective series symptoms are not prominent. Thus, according to the potentialities that may result from the combination of the two psychopathological entities, we will have: schizodepressive episodes, schizomanic episodes, schizohypomanic episodes, etc. Schizoaffective episodes may also occur in an isolated context in the evolution of other psychotic disorders, thus questioning the quality of a distinct nosologic entity of this disorder, in the view of certain authors.

Similar to schizophrenia, as well as to mood disorders, the most common evolutionary pattern in this disorder is episodic, with complete or partial remissions with defective states that may remain constant or may increase as the disorder progresses.

Evolution is polymorphic heterogeneous with the occurrence of at least two different types of episodes: schizoaffective episodes, affective episodes, and purely schizophrenic episodes. The number of schizoaffective episodes has proven to be the most common, followed by purely affective and simple schizophrenic episodes.

The treatment consists, essentially, of the administration of neuroleptic drugs (preferably of new generation, administered during episodes, as well as an underlying treatment), antidepressants (in the case of schizodepressive episodes) and mood stabilizers (both during the episodes of illness, but also as maintenance treatment). In times of remission it is useful to associate psychosocial interventions, such as psychotherapy, psycho-education, etc.

## Chapter XII - PERIODIC AND PERSISTENT MOOD DISORDERS

### INTRODUCTION AND SHORT HISTORY

The generic label of mood disorders reunites a wider group of psychiatric disorders, which all have a quantitative mood change in common (in variable degrees), consequently being considered hyperthymic states. This mood change of clinical intensity, can either be in the sense of pathological sadness, or in the sense of elevated mood with the occurrence of euphoric feelings. In both situations, these states can be mixed with a variable degree of irritability. Depressive and manic symptoms can occur simultaneously, this situation being called a mixed episode. In some cases, the clinical manifestations of depression can alternate, more or less rapidly, with mania symptoms, a situation called rapid cycling (at least 4 episodes of abnormal changed mood within a year). These symptoms can alternate more rapidly, a situation described as ultra-rapid cycling.

Mood episodes have a few other clinical characteristics in common: mood changes are unreactive to external events (except for atypical depression, where patients experience hypersensitivity to situations where interpersonal rejection is perceived); the persistence of a modified mood for at least 2 weeks in case of a depressive episode, at least 7 days in case of a manic episode or 4 days for a hypomanic episode (time criterion); the mood change has a pervasive or noticeable character as it affects all functional levels of the psyche; the mood change is not directly caused by a primary medical condition or by a condition with secondary effects upon the central nervous system, by psychoactive substance use or by another major psychiatric disorder (e.g. Schizoaffective disorder). The mood changes interfere with the individual's global functioning, to a variable degree, according to their severity, thus justifying the need for therapeutic intervention.

Concerns about understanding and finding a remedy for depression have been raised since ancient Egyptian medicine, as it is recorded in Eber's papyrus (approximately 1552 BC).

The story of King Saul from the Old Testament describes a depressive syndrome, as well as the story of Ajax' suicide from Homer's Iliad. The Hippocratic corpus (460-377 BC) states the humorous theory of melancholy, which was considered a trait rather than a state, and was believed to reflect an excess of black bile.

In 1621, Robert Burton was the first author to publish a more systematic approach to depression, entitled "Anatomy of Melancholy."

During the 19th and 20th century psychiatry and psychopathology have made the biggest progress regarding semiology, nosology and therapeutic intervention in mental illness. In 1854 Jules Falret described a condition called "folie circulaire" where patients experienced alternating manic and depressive moods. During the approximately same period Jules G.F. Baillarger, another French psychiatrist, described a condition named "folie à double forme", where patients became profoundly depressed and fell into a stuporous state from which they eventually recovered.

At the end of the 19th century it was the German psychiatrist Emil Kraepelin who first clearly differentiated manic-depressive psychosis (currently known as bipolar disorder) from schizophrenia, which he called dementia praecox.

In 1917, Sigmund Freud approached the matter of depression, from a psychoanalytic perspective, in his work "Mourning and Melancholia", making an analogy between the two states. In 1920, Kurt Schneider created the concepts of reactive and endogenous depression. In 1957 the German psychiatrist Karl Leonhard was the first to introduce the concept of a dichotomous classification of mood disorders in bipolar disorder (where depressive episodes alternate with manic episodes) and unipolar disorder (a succession of only depressive episodes).

In 1967, the British psychiatrist Aaron Beck described the cognitive triad in depression, stating that the person suffering from depression has a negative perception of the future, the present and of one's own self.

#### EPIDEMIOLOGICAL AND SOCIODEMOGRAPHIC DATA

The National Comorbidity Survey Replication indicated a lifetime prevalence of major depressive disorder of 16,6% in the United States, occupying the first place as the widest spread psychiatric disorder in the general population. The DEPRES Study, an Europewide study, found a prevalence of approximately 6,9% for any kind of depressive disorder over a time span of 6 months. The lifetime prevalence of a major depressive episode in Romania, is according to a study carried out by the Romanian League for Mental Health, 21%. The female:male ratio for recurrent depressive disorder is approximately 2:1. The age of onset for recurrent depressive disorder is mostly around 40 years.

According to a study carried out by the WHO and the World Bank, unipolar depression is estimated to occupy the second place as a cause of disability out of a list of 135 somatic and psychiatric disorders, with only ischemic heart disease surpassing it. This estimation turns depression into a priority for health policies and a public health issue.

In terms of geographic distribution, depression occurs more frequently in the northern hemisphere, the closer it gets to the polar circle, possibly due to the cumulative effect of seasonal mood disorders.

The lifetime prevalence of mood disorders in the United States is, according to the National Comorbidity Survey, approximately 4%, with a female:male ratio of 3:2. The male:female ratio for bipolar disorder is classically believed to be 1:1. The National Comorbidity Survey Replication found a prevalence of 2,6% for both bipolar I and bipolar II disorder over a time span of 12 months in the general population, with 82.9% suffering from a severe form of the disorder. The mean age of onset for bipolar disorder is 25 years, with an earlier onset in male patients in comparison to females.

## ETIOPATHOGENIC FACTORS

In this section the etiopathogenic factors that interfere both in the onset of recurrent depressive disorder and bipolar disorder will be approached in parallel , taking into account that some of them are common for both disorders. Both bipolar disorder and recurrent depressive disorder are believed to have a complex multifactorial etiology, with these factors being active over a long period of time (starting during early childhood, or even before birth) at all levels of the human being – biological, psychological and social.

## BIOLOGICAL FACTORS

### 1. Genetic factors

While trying to determine the genetic component of a disorder, besides fundamental genetic studies regarding changes on genomic level correlated with the risk of developing the disease, genealogical studies upon I grade relatives of the subjects, adoption studies used to establish whether it is the biological parent (whom the patient had not been in contact with since birth) or the adoptive parent, as well as twin studies comparing concordance rates in monozygotic twins (who have a mostly identical genome) to dizygotic twins hold an at least equally high value. The table below offers a comparison between a few genetic studies carried out for recurrent depressive disorder and bipolar disorder respectively.

Type of study	Recurrent depressive disorder or unipolar depression	Bipolar disorder
Linkage and candidate gene studies	The short allele of the gene encoding the serotonin transporter, genes encoding the synthesis of tyrosine hydroxylase (chromosome 11) and tryptophan hydroxylase, the gene encoding the synthesis of COMT and other genes encoding serotonin and dopamine receptors (chromosome 5)	Linkage studies have shown that genes situated on chromosomes 5, 11 and X are most frequently associated with mood disorders.  More recent studies have found bipolar disorder to be more frequently associated with genes situated on chromosomes 4p,4q,8q,10q,12q,13q,13p,18p,18q,21q and 22q



Genealogical and family studies	First degree relatives have a 3 times higher risk of developing the disorder than the general population	First degree relatives of people with bipolar I disorder are 8 to 18 times more likely to develop bipolar I disorder in comparison to subjects who don't have a family member with the disorder.  50% of the ones with bipolar I disorder have at least one parent with a mood disorder, most often major depressive disorder
Concordance rates in monozygotic twins compared to dizygotic twins	Approximately 50% in monozygotic twins compared to 10-25% in dizygotic twins	Concordance rates between 60-80% in monozygotic twins compared to 20-30% in dizygotic twins
Adoption studies	Biological parents, as well as adoptive parents conferred the risk of suffering from a major depressive episode, without significant differences between them.	The biological parent conferred a significantly greater risk than the adoptive one.

## 2. Epigenetic factors

Epigenetic research explains the disorder as a result of the genome interacting with various environmental factors: food, drugs, etc. Among the best-known epigenetic mechanisms are: DNA methylation in promoter regions of genes, thus preventing the gene's expression; microRNA dysfunctions and histone alterations at chromatin level. These epigenetic mechanisms explain how one monozygotic twin can develop a certain disorder, while the other doesn't.

### 3. Changes in cerebral neurotransmission

The monoaminergic theory was launched as the first etiopathogenic hypothesis, and suggested the quantitative dysfunction of serotonin and noradrenaline, and to a lesser degree dopamine, as the mechanism causing depression. According to this theory, depression is linked to a deficit of these neurotransmitters in the synaptic cleft during nerve impulse transmission. Monoaminergic dysfunction occurs in certain cerebral circuits that connect various brain regions. In reverse, according to the monoaminergic theory, during a manic episode, a quantitative and/or functional excess of dopamine (also confirmed by the antimanic effect of haloperidol, which is a dopamine antagonist) and noradrenaline can be observed.

### 4. The theory of receptor dysplasticity

Considering the inability of the monoaminergic theory to explain the delayed onset of therapeutic effect in antidepressants, as well as the lack of antidepressant effect by simply supplementing intake of the essential aminoacids which are precursors to the mentioned neurotransmitters. Thus, the theory of receptor dysplasticity appeared, which shifted the focus from neurotransmitters to their respective receptors, stating that prolonged lack of certain neurotransmitters at synaptic level leads to a compensatory hyper-activation of the receptors, consisting of an increased number of receptors on the postsynaptic neural membrane, along with a change in their activation threshold. Antidepressant effect appears not after quantitatively reestablishing these neurotransmitters but only after the return to a normal number and function of their receptors. This theory is supported by postmortem studies which showed a significantly larger number of serotonergic receptors in the prefrontal cortex of subjects who committed suicide.

### 5. The theory of secondary messengers

This more recent theory further places the cause of the appearance of affective symptoms at the level of the secondary messengers system involved in mediating gene expression. More specifically, the AMPc pathway is meant, which is over-activated in a several stages under the action of antidepressants: stimulation of G protein coupling with adenylyl- cyclase, induction of high levels of AMPc proteinkinase and CREB proteins, especially in the hippocampus and prefrontal cortex. The secondary messenger system of Inositol triphosphate has also been invoked, especially in relation to bipolar disorder, as it appears to mediate the therapeutic.

### 6. Neuroendocrine factors

The most studied neuroendocrine axis, which links childhood trauma, due to its vulnerability, with depression at adult age, is the hypothalamo-pituitary-adrenal axis.

This neuroendocrine axis is hyperactive in patients with depression, leading to a hypercortisolemia which is unresponsive to dexamethasone suppression therapy. The origin of this neuroendocrine dysfunction lies in the hypothalamus. The prolonged effect of cortisol as a chronic stress hormone becomes neurotoxic, leading to atrophy of the hippocampus. This explains the cognitive impairment on the level of fixation memory found in depression. Another neuroendocrine axis that is proven to be dysfunctional in patients with mood disorders is the hypothalamo-pituitary-thyroid axis, which is unresponsive to TRH stimulation. The endocrine dysfunction associated with affective symptoms is mostly subclinical and is found in approximately 10-15% of mood disorders cases. Besides thyroid hypofunction, most often associated with depressive symptoms, some studies revealed situations of subclinical hyperthyroidism. This neuroendocrine axis is particularly important to bipolar disorder, based on the clinical observation that oral administration of Thyroxine (T4) hormones in high doses can lead to remission in individuals with rapid cycling, where standard pharmacological treatment had proven itself ineffective.

#### 7. The kindling phenomenon

According to this theory, which bears an analogy to the mechanism of developing epileptic seizures, stressful life events have an important role in triggering the first mood episodes. Subsequently, as the disease progresses, the significance of these stressful life events in triggering mood episodes becomes more and more insignificant, with mood episodes occurring spontaneously, without a triggering event, due to the gradual sensibilization of the limbic system.

#### 8. The role of neuropeptides and neurotrophic factors

Substance P has been the most studied neuropeptide. Its principal role is believed to be the inhibition of the gene responsible for suppressing BDNF (Brain-derived neurotrophic factor). This neurotrophic factor has a key role in maintaining neuronal viability, and its absence or depletion, under unspecific stress conditions, presumably determines grey brain matter atrophy, especially in the hippocampus, or even brain cell death through apoptosis. This theory might as well provide an explanation for the recurring character of depression and the cognitive deficit in depression, secondary to hippocampal hypotrophy. On the other hand, antidepressants stimulate the expression of the gene responsible for BDNF synthesis, through CREB proteins (transcription factors). Thus neurogenesis at hippocampal level is stimulated, a fact proven in vivo through animal studies, as well as in vitro through longitudinal neuroimaging studies.

## 9. Neuroanatomic factors

Animal and structural neuroimaging studies carried out in depression have shown the predilect involvement of certain brain areas such as the hippocampus, prefrontal cortex, anterior cingulate gyrus, thalamus, caudate nucleus, nucleus accumbens and amygdala. Hypothrophy of the hippocampus, as well as reduction of its surface have been found. In some cases of psychotic depression an unspecific enlargement of the lateral brain ventricles has been found. Functional neuroimaging studies have shown a decrease in blood flow and brain cell metabolism in areas located mostly in the right brain hemisphere. The dysfunction of dopaminergic pathways in the nucleus accumbens is clinically translated into loss of interest, lack of pleasure, fatigability and low energy. In the case of manic episodes, the brain areas involved are close to the ones involved in depression, but usually those are hyperactive.

## 10. Sleep phase related disorders

The most constant sleep architecture changes found in unipolar depression consist of: decreased latency of the first REM sleep cycle to 60 or even 40 minutes, disturbed sleep continuity with frequent awakenings, reduced non-REM sleep ratio in favour to REM sleep. The total duration of sleep is also reduced in depression, with awakening insomnia. In bipolar depression as compared to unipolar depression, although changes in sleep architecture were largely similar, research consistently identified early morning awakenings and a higher REM sleep density over the total sleep duration as being more frequent.

## 11. Neurocognitive factors associated with bipolar disorder

In the case of bipolar disorder, as opposed to recurrent depressive disorder, there are certain markers or cognitive dysfunctions that were proven to be persistent including throughout periods of remission or euthymia. Impairments in attention persistence, working memory, verbal memory, visuospatial memory, declarative memory, problem solving, verbal learning, the speed of information processing and executive functions were among the most constant cognitive dysfunctions. These cognitive deficits are correlated with a more negative outcome of the bipolar disorder and, although to different extents, are common for both mood disorders.

## PSYCHOLOGICAL FACTORS

### Stressful life events

As mentioned while discussing the "kindling" phenomenon, stressful life events may have a triggering role in the appearance of mood episodes during the early stages of the mood disorder.

At the same time, it is considered that stressful life events, especially those representing a loss, can play a determining role in developing vulnerability for depression, whether the loss is real (eg death, divorce) or symbolic (eg loss of confidence in a confidant or in a life partner).

A loss event with a high predictability for depression in adulthood is the death of a parent around the age of 9, as children become aware of the irreversible character of the death process around this age.

As mentioned before, physical and emotional abuse during childhood can leave the neuroendocrine hypothalamo-pituitary-adrenal axis vulnerable for the rest of the person's life, which will contribute to developing depression when new stressful life events occur in adulthood.

On the other hand, resolutive events that counter the effects of prolonged negative circumstances, such as re-employment after a prolonged period of unemployment, may favor remission of the depressive episode.

#### Factors associated with personality

Personality, as a vulnerability factor for mood disorders, can be approached from several perspectives. The first perspective is the intensity of changes associated with personality, which progressively goes from a personality profile with the predominance of certain features (harmonic personality) → to accentuated personality traits with rigid and persistent, but adaptive features → to a personality disorder with rigid, persistent, pervasive and disadaptive features, the risk of developing a psychiatric condition often being directly correlated with this severity. A second perspective is the categorical one, which has shown that the predominance of emotionally unstable personality traits most frequently increases the risk for bipolar disorder, while the predominance of anankastic (perfectionistic) traits increases the risk for depression. On the other hand, although they are no longer considered personality disorders but persistent mood disorders, and thus evolutive, classically cyclothymia was considered a risk factor for bipolar affective disorder and dysthymia was a risk factor for clinically manifest depression. Moreover, in 1961 Tellenbach described the depressive personality characterized mainly by conscientiousness, meticulousness and excessive attachment to order. From the dimensional perspective on personality expressed through the 5-factor model, the dimension of neuroticism was directly correlated with the risk of depression, and those related to extraversion and openness correlated with bipolar disorder. German psychiatrist Ernst Kretschmer has correlated morphotypes with the specific risk for a certain type of mental illness, so the picnic type (short height and tendency towards excessive weight) is thought to be prone to what we call bipolar disorder today.

#### The behavioural theory

Of all the behavioral theories focusing on depression, the theory of learned helplessness, which originated in experiments carried out in psychology research laboratories, remains the reference. More specifically, it is Martin Seligman and Steve Maier (1967) who subjected dogs to painful stimuli - electric shocks - thus having an aversive character and from which they were not been able to escape, have developed behaviors similar to those encountered in human beings with

depression. Just like the cognitive theory and the one of social modeling, which will be discussed later, the behavioral theory is based on the principle of pathological learning.

#### The cognitive theory

According to the cognitive theory, each individual has a certain perception of the world and, more precisely, the events that are profoundly influenced by their own sets of fundamental beliefs. Developed by Aaron Beck (1979), it involves the cognitive triad consisting of cognitive distortions with negative interpretation / appreciation of one's own person, the present and the future, which increase vulnerability for depression and are latent in asymptomatic individuals. At the core of these thought distortions, there are dysfunctional cognitive schemes characterized by rigidity and persistency. The most profound level is represented by fundamental beliefs, acquired during the development period and usually under the influence of educational factors, which in those vulnerable to depression comprises the fact that they are unloved and worthless.

#### The social modeling theory

This theory was developed by Albert Bandura and states that both normal, adaptive and pathological, maladaptive behaviours are learned through imitation of adults' behaviour. Bandura started from the observation that those children whose parents displayed a high level of aggressivity reflected this in their way of playing.

#### The psychodynamic theory

Sigmund Freud pointed out the analogy between mourning and depression, the withdrawal of emotional attachment to the beloved person that ceases to exist (death, separation, etc.) and towards which there is a mixture of ambivalent feelings of love, anger and even hate → defensive mechanism with the introjection of aggression and its redirection against the EGO or Self → DEPRESSION.

#### The interpersonal theory

Developed by Klerman et al. (1984), it focuses on the existing difficulties in the current interpersonal functioning. This involves a formal diagnostic assessment, an inventory of current and past interpersonal relationships, and the circumscription of the current problematic area. According to the interpersonal theory, depression could be caused by one or more difficulties involving the following functional areas: disputes regarding interpersonal roles, role transitions, and interpersonal deficits.

## SOCIO-DEMOGRAPHIC FACTORS

### The social support system

For a start, it should be noted that there is a wider social network which includes all acquaintances and even people who can be contacted through their intermediation in order to support the person in distress. The social support network is usually a more restrained one and is made up of relatives or people intimately linked to the subject. Social relations have been shown to exert their beneficial effects on mental health through two psychological mechanisms: 1) their support has a direct effect on the general state of health and 2) the buffer effect hypothesis, where the social support cushions the impact of stressors upon the risk of depression. On the other hand, there are two types of support usually offered by those close to the subject: instrumental support consisting of providing material support to meet the needs or wishes of the subject, and emotional support manifested by love, empathy, affection displayed by those close to the subject and which, in the etiopathogenesis of mood disorders, play a key role in developing resilience towards these disorders (exceeding instrumental support).

### Gender

As indicated in the epidemiology section, women are more prone to depression than men. This could be the result of the more important biological changes, especially those associated with the reproductive system, that women go through during their life (eg, menstrual cycle, pregnancy and birth, climax) compared to men. From another perspective, women in traditional societies, including our country, is pressured by family and society, to fill multiple and more burdensome roles than men, such as mothers, housewives, and even financial support for the family through active engagement in different jobs. In addition, women are more exposed and more receptive than men to childhood trauma, including sexual abuse, with long-term consequences on their mental health.

### Marital status

Studies indicate that celibate, divorced or widowed people are more prone to depression than those who have a love life. At the same time, there are data that support the selection theory according to which health affects marital status: as a result, depressed women are less likely to get involved in marriage.

### Socioeconomic status

The predominance of a disease among people with a low socioeconomic status can be explained by two alternative theories: one of social selection and the other of the social cause. For example, in schizophrenia, either during the early stages of the disease or in a more advanced stage where

various disabilities appear, the person tends to descend the social ladder by losing their working capacity and inability to maintain social relationships. In this case the social decline is secondary to mental illness. On the other hand, in the case of depression, it seems that social factors are in part causing it and consequently the exposure to various aspects of a low socioeconomic status, such as poverty and unfavorable living conditions, contribute to the social cause of depression.

#### CLINICAL PRESENTATION, CLASSIFICATION AND DIAGNOSTIC CRITERIA

The clinical presentation of depression is an extremely polymorphic one. Fulfilling the time criterion of having depressive symptoms for a minimum of 2 weeks, during most of the time, is mandatory in order to diagnose a depressive episode. According to the diagnostic manuals, the three essential symptoms for diagnosing depression are: depressed mood, loss of interests and pleasure, and increased fatigability. Out of these, at least 2 essential symptoms must be present. Depressive symptoms can be synthesized as follows:

- Symptoms on the affective level: depressed mood or pathological sadness, unreactive to external situations or events, inappropriate in terms of severity and persistence, which is one of the major criteria for the diagnosis of a depressive episode; anhedonia or lack of pleasure regarding things or activities that the person previously enjoyed; variable degrees of associated irritability; due to the overlapping neurobiologic substrate represented by serotonergic dysfunction, it is very common in depression to also encounter associated anxiety symptoms that can have various clinical expressions in the form of phobias, panic attacks, generalized anxiety, etc.
- Symptoms on the instinctual level: the diminishing of all instinctual urges with changes in the behaviors motivated by them: diminished appetite, sexual desire, social withdrawal, alteration of the self-preservation instinct with the emergence of suicidal risk that can progress from suicidal ideation to plans and ultimately to a suicide attempt (finalized or not); in the case of postpartum depression, there might be an alteration of the maternal instinct, which may determine a high risk of infanticide in postpartum depression with psychotic symptoms.
- Symptoms on the cognitive level: bradypsychia, decreased thought volume, thought content disorders consisting of: hopelessness, low self-esteem, ideas of guilt that can reach the intensity of delusions, ideas of self-devaluation and uselessness, delusions of ruin, especially in elderly people, ruminations focusing on existential problems or the disease; sometimes ideas of reference, persecution and injury can appear, which may evolve to mood-incongruent paranoid delusions. As mentioned before, there might be a significant suicidal risk. There are also important memory impairments, with hypomnesia secondary to concentration and persistence hypoprosexia, with the depressed patient focusing more on the "painful" past and less interest in the present; However, some authors describe a selective hyperprosexia for the negative aspects of the patient's current life, along with a selective evocation hypermnesia for the negative events experienced by the patient in their lifetime; on the perceptual level, there is on one hand, a decreased



perception regarding environmental details and chromatics, and on the other hand, associated cenestopathies or dyscenesesthesias can occur, along with a decrease of the pain threshold; also in the sphere of perception, in the case of depression with psychotic features, hallucinations can occur – auditory hallucinations (e.g, voices ordering the patient to kill himself) or olfactory hallucinations with rotting content associated with negation delusions (the patient has the delusional belief that body parts, usually internal organs, or the whole body is devitalized and enters a process of rotting) .

- Symptoms on the conative and motivational level: decrease/loss of curiosity and interests, spontaneity, hypobulia to abulia, hyperdeliberation, indecision with difficulty in acting, and decreased persistence in action especially in clinical forms of inhibited depression; however, the psychiatrist must be extremely careful, especially during the first days of antidepressant treatment, as behavioral symptoms begin to improve, but due to the persistence of suicidal ideation, he develops the necessary energy to implement his suicide plan.
- Somatic and Behavioral Symptoms: Psychomotor retardation that can evolve to melancholic stupor when the patient becomes akinetic with negativity, mutism, refusal of food and water, representing a psychiatric emergency that may require electroconvulsive therapy; if depression is associated with a significant level of anxiety symptoms, the patient may experience psychomotor restlessness, or even agitation; low vital energy with increased fatigability; the patient may also experience a series of somatic symptoms such as: constipation, dry mouth, abdominal discomfort, chest discomfort with tightness and/or pressure in the chest area etc .; the speech is bradylalic, with a low voice tone, slow frequency and a content concordant with the abnormal thought content; the facial and gestic expressivity is reduced, the patient may adopt a depressive posture with little eye contact with the interlocutor, a wrinkled brow forming a depressive omega at the level of the glabella, fallen shoulders, the mouthcorners facing down, the hands on the midline, sometimes spontaneous crying.
- Sleep-wake cycle disturbances with dysomnia, mostly awakening insomnia, when the highest frequency of suicidal behavior occurs. Parasomnia consists of night-time nightmares with crucifixes, cemeteries, etc.
- People with depression will neglect their clothing, but will preserve their personal hygiene, and dark colors will prevail, although women will lack accessories or makeup.

#### CLINICAL EVOLUTIVE CRITERIA THAT DIFFERENTIATE BIPOLAR DEPRESSION FROM MONOPOLAR DEPRESSION

The importance of distinguishing monopolar depression from bipolar depression lies not only in the importance of an accurate diagnosis of the mood disorder which it is part of, but also in the perspective of establishing a therapeutic strategy. To this end, it is important to try to obtain

information from the patient's relatives, considering that the possible presence of manic symptoms in the history of illness tends to be undervalued or even unrecognized by the patient.

	Bipolar depression versus unipolar depression
Age of onset	Onset at an earlier age, often before the age of 30
Clinical picture	More frequently symptoms as hypersomnia, hyperphagia, comorbid anxiety, psychomotor retardation, emotional lability, psychotic features, suicidal thoughts
Behavioural markers	More frequent disturbing behavior, aggressivity, impulsivity
Family history of bipolar disorder or finalized suicide	Often present
In rapport with previous therapeutic response	History of lacking therapeutic response to antidepressants, or very fast remission, more frequent adverse effects to antidepressants, such as insomnia, agitation, anxiety
Evolution	A larger number of depressive episodes over time and of relatively shorter duration, frequently with an acute onset

#### CLINICAL SUBTYPES OF DEPRESSION

##### A. Melancholic Depression

Anhedonia, diurnal mood swings, awakening insomnia, fatigability, significant psychomotor symptoms are most constantly present.

##### B. Inhibited Depression

The clinical picture is dominated by a psychomotor syndrome that is marked by psychomotor retardation which may worsen to the state of stupor when the patient becomes akinetic, displays

non-selective mutism and behavioral negativity involving, among other things, the refusal of food and/or water intake. This is the reason why this clinical situation is considered a psychiatric emergency. On the cognitive level, patients display bradypsychia with markedly decreased cognitive performances.

### C. Seasonal depression

More frequent during the autumn / winter months and in the northern hemisphere, due to short daylight duration and low luminosity, its symptoms are often atypical. It is presumed that melatonin dysfunction plays a leading role in this form of depression.

### D. Depression in adolescents

The mood is more often irritable than sad, and the teenager develops oppositional defiant behavior towards parents and teachers, becomes uninterested in school with a drop in school performance, which is why he is often diagnosed with school failure. Moreover, depressed adolescents are more likely to engage in substance use, which is why another misdiagnosis is that of behavioral disorder.

### E. Depression in the elderly

The elderly often deny depressive mood while somatoform complaints are at the forefront of the clinical picture, which corroborated with weight loss and low appetite are often a source of diagnostic error, most often being mistaken for a neoplastic disease. In addition, hypochondriac ideation, that can reach delusional intensity, is more frequent in elderly depressed patients. Delusions of negation or Cotard's syndrome (delusions of negation plus delusions of enormity plus delusions of immortality) may also occur. Suicidal behavior is more common compared to young people with depression, and it is encouraged by the reduction the social support network, in particular through the death of the life partner, and the reduction of the social network through retirement. Another particular feature is the presence of a significant number of somatic comorbidities, which raises important clinical management problems in these cases.

### F. Atypical depression

It is characterized by increased appetite and weight, hypersomnia, leaden paralysis, a durable pattern of sensitivity to interpersonal rejection. It should be noted that in classic literature, the term atypical had another meaning and referred to the presence of psychotic symptoms in the clinical picture, often with a bizarre character.

### G. The depressive episode with postpartum onset

In order to receive the additional postpartum diagnostic label, the depressive episode of clinical intensity should begin within the first 4 weeks after giving birth.

H. In terms of intensity, the depressive episode can be classified as:

- Mild
- Moderate
- Severe, with or without psychotic symptoms

The manic episode should last at least 1 week and be severe enough to negatively interfere with the patient's professional and/or social activity. The clinical symptomatology is complex and can be summed up as follows:

- Symptoms on the affective level: elevated and / or irritable mood, unreactive to external situations or events, inappropriate in terms of severity and persistence;

Symptoms on the instinctive level: heightening of all instinctive urges with behavioural changes motivated by them: increased appetite, sexual desire, hypersociability, but a superficial one marked by oscillations in interpersonal relationships, increased familiarity, hypererotism.

- Symptoms on the cognitive level: accelerated thought stream up to flight of ideas, which make the thought process appear incoherent, pressure of thought, thought content disorders consisting of: ideas of grandeur, either related to the subject's identity or his abilities; as it is the case with depression, ideas of reference, persecution and prejudice can sometimes appear, which may evolve to mood incongruous paranoid delusions. Attention persistence disturbances also occur with increased distractibility and secondary fixation hypomnesia. There is a selective evocation hypermnesia for positive events in the patient's biography. There is an accentuated perception of environmental details and colours. In the case of mania with psychotic features, hallucinations may appear, most often auditory hallucinations (for example, voices that compliment him).
- Symptoms on the conative and motivational level: an increased awareness of the tendency to act with many actions, accentuated spontaneity but with short deliberation, hasty decisions and rapid passage to the act, without persisting in the action until its completion due to the multitude of actions that the patient plans to engage in. There is also an increase in hedonically motivated behaviors and expansive behavior with excessive expenses.
- Behavioral symptoms: psychomotor unrest that can evolve to psychomotor agitation, a situation that might require pharmacological and / or mechanical restraint; unlike catatonic agitation, in manic agitation the patient uses all available space and his behaviors are purposeful; accelerated verbal flow up to logorrhea, with a high tone and

frequency and a content concordant with the abnormal thought content; the facial expressiveness is accentuated, the gestures are broad, the patient is very cheerful and transmits his good mood to those around him.

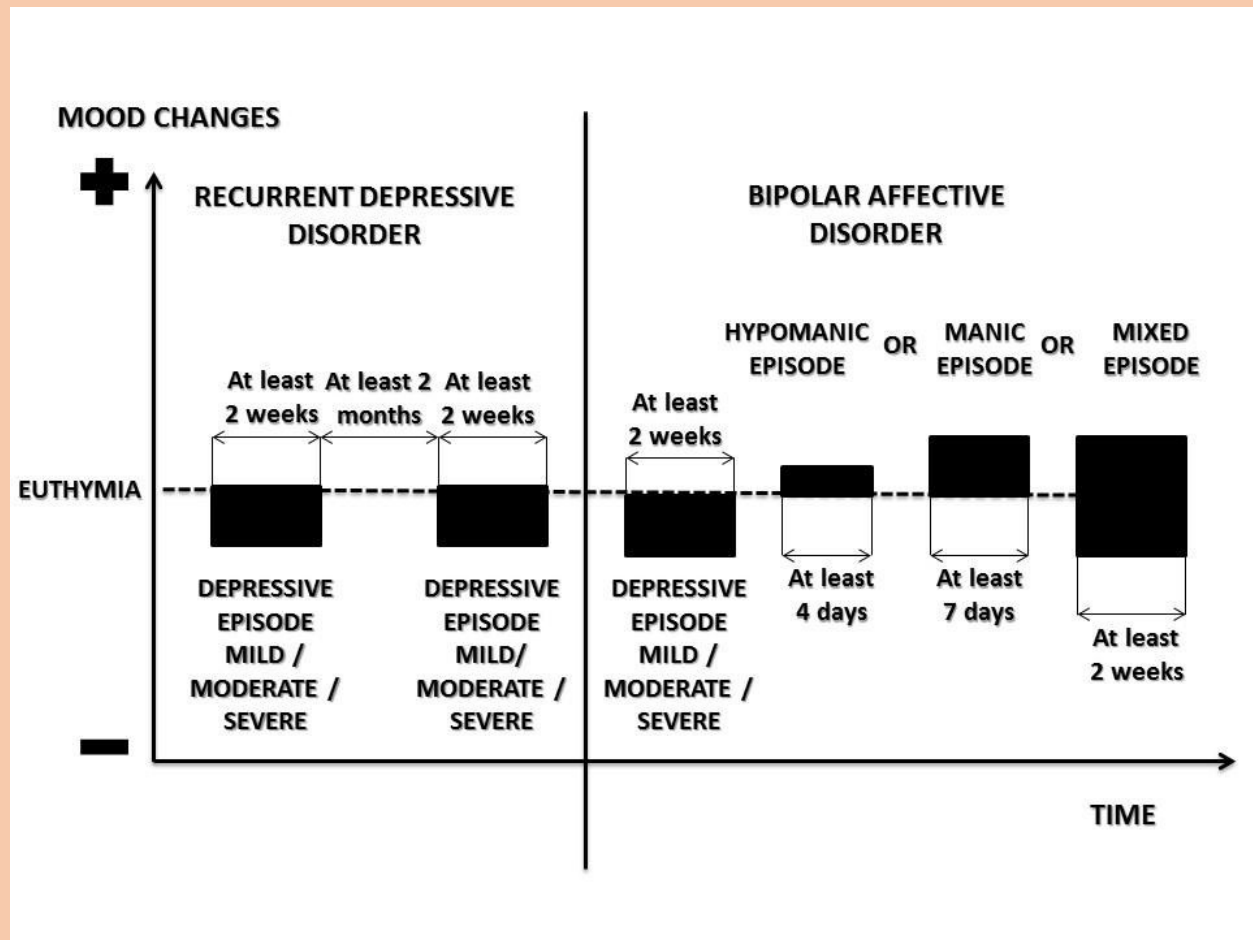
- Disorders of the sleep-wake cycle: reduced sleep duration, however the patient does not feel tired during the day and has a high energy level.
- The clothing style is characterized by warm and bright colors, although personal hygiene may be deficient and women there may wear excessive makeup and accessories with the use of a wide colour palette.

In terms of severity, according to the diagnostic criteria, the manic episode may be with or without psychotic symptoms.

Hypomania is a milder form of mania, and changes in mood and behavior are too persistent and noticeable to qualify as cyclothymia but are never associated with delusions or hallucinations. Interference with social and professional abilities is significant but usually the patient can adapt to the requirements assigned to these existential roles (this distinguishes him from the maniacal patient).

For a diagnosis of recurrent depressive disorder, at least 2 depressive episodes throughout the history of the disorder are required (see Figure 1). The current depressive episode should be specified in terms of severity, which may be mild with or without somatic symptoms, moderate with or without somatic symptoms or severe with or without psychotic symptoms. In order to talk about a recurrence or a new depressive episode, a minimum of 2 months must have passed from the previous depressive episode, during which the patient either had a complete remission or had a minimal number of mild depressive symptoms, though insufficient for a diagnosis of a depressive episode of clinical intensity. Depressive episodes that last for more than 12 months require the additional specifier of chronic depressive episode.

Figure 1. Schematic representation of periodic mood disorders



For the diagnosis of bipolar disorder, we must have at least 2 episodes of abnormal mood throughout the history of illness, one of which must be a hypomanic, manic or mixed one (see Figure 1).

The bipolar disorder can be:

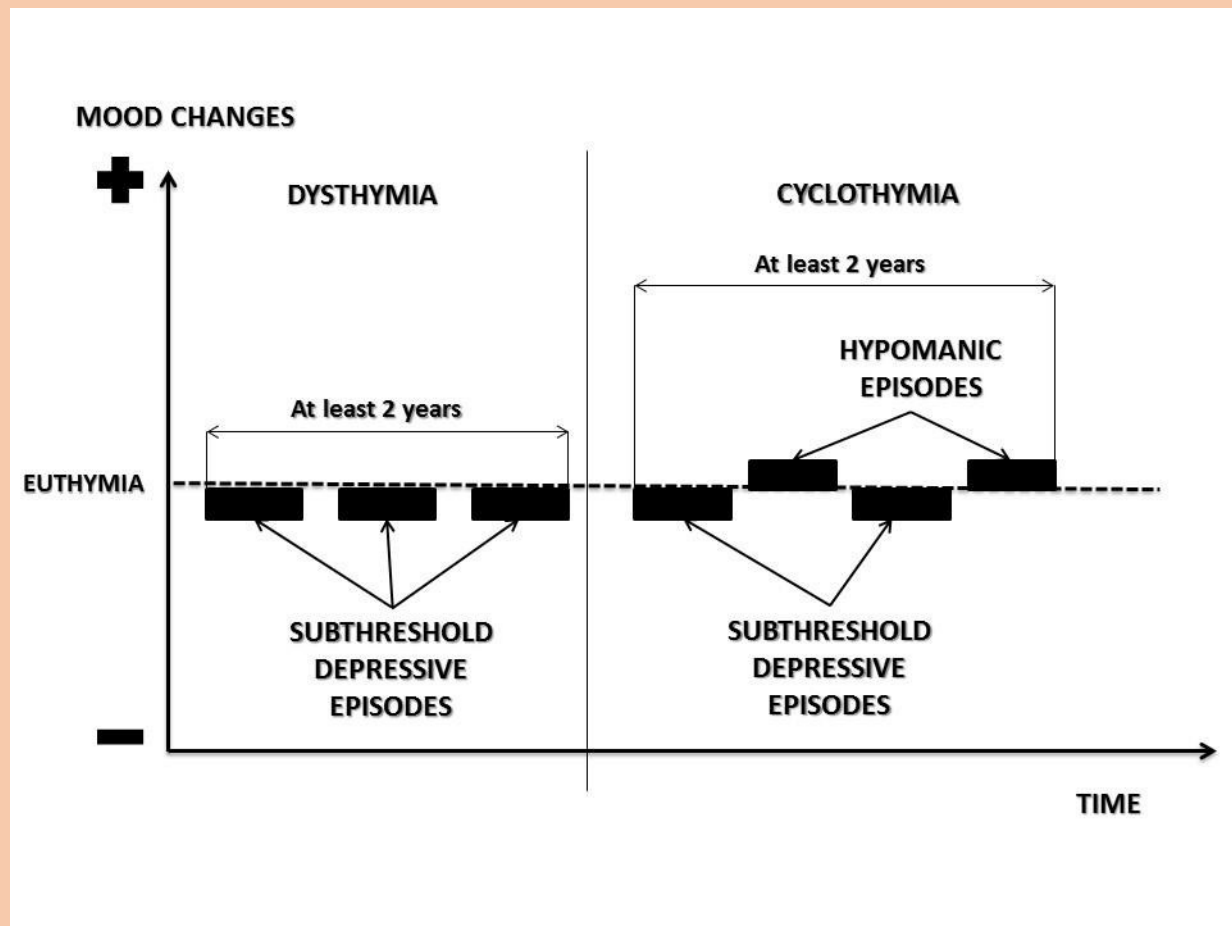
- Type I bipolar disorder, characterized by an alternation of major depressive episodes of clinical severity throughout the history of illness and at least one manic or mixed episode
- Type II bipolar disorder, characterized by an alternation of major depressive episodes of clinical intensity and at least one hypomanic episode throughout the history of the disorder. The occurrence of manic or mixed episodes during the history of illness is excluded.
- During the 2-year period considered for the diagnosis, there is no more than 2 months asymptomatic periods in terms of affective disposition.

## PERSISTENT MOOD DISORDERS

Cyclothymia consists of a history of at least 2 years of altered/abnormal mood swings, with the alternation of periods of hypomanic symptoms (insufficient in terms of number, severity, persistence or duration to diagnose a manic episode) with periods of depressive symptoms that do not meet the criteria for a major depressive episode of clinical intensity (see Figure 2). During the 2-year period considered for establishing the diagnosis, there are no more than 2 months free of affective symptoms.

Dysthymia comprises a history of at least 2 years of persistent mild depressive symptoms, which are insufficient to meet the criteria for a major depressive episode of clinical intensity. If over time these symptoms overlap with a major depressive episode, this situation is labeled as a double depression. During the 2-year period considered for the diagnosis of dysthymia, there should be no more than 2 months free of any affective symptoms.

Figure 2. Schematic representation of persistent mood disorders



## DIFFERENTIAL DIAGNOSIS

### A. Differential diagnosis of the recurrent depressive disorder

1. Bipolar disorder - we need to identify at least one hypomanic, manic or mixed episode during the history of the illness.
2. Dysthymic disorder – the depressive symptoms have an evolution of at least 2 years and their intensity should not meet the criteria for a major depressive episode of clinical intensity.
3. Anxiety disorders with associated depressive symptoms - diagnostic criteria for an anxiety disorder must be met and depressive symptoms usually occur after a certain period of time after the onset of the anxiety symptoms.
4. Depressive symptoms associated with somatoform disorders - the diagnostic criteria for a somatoform disorder must be met and depressive symptoms are directly related to the suffering generated by the first psychiatric condition.
5. Schizo-affective disorder – the clinical picture must simultaneously comprise both depressive symptoms and symptoms of schizophrenia (for example, auditory hallucinations, thought broadcasting and xenopathic influence, etc.)
6. Adjustment disorder – the brief depressive reaction (up to 1 month), the prolonged depressive reaction (up to 2 years) or the grief reaction that obviously arise as a direct consequence of a stressful life event (eg the death of a family member) or a significant change in life, and the clinical symptomatology is of mild, or at most moderate intensity. It should be noted that grief may also be a triggering factor for a major depressive episode that can gradually increase in severity and even involve a certain suicidal risk.
7. Depression secondary to a persistent delusional disorder – it implies the presence of one or several delusional themes with a duration of at least 3 months, which must precede the appearance of depressive symptoms, the latter being a direct consequence of the delusional experiences.
8. Depressive disorders induced by a brain dysfunction (temporal lobe pathology, Alzheimer's disease, Parkinson's disease) and those induced by a general medical condition (eg Cushing's syndrome) - careful clinical examination and all appropriate paraclinical investigations should confirm a neurological disease as the supposed cause of depression. The issue of pseudo dementia must also be discussed here. This refers to the occurrence of a severe depressive episode usually in an elderly person and in which cognitive disorders prevail in the clinical picture.
9. Depression induced by the use of psychoactive substances - we must have a positive history of the use of licit substances (alcohol, drugs) or illicit substances (such as drugs) that, either in the case of intoxication or in the situation of complications caused by dependence, can explain the occurrence of depressive symptoms. In the situation of abstinence from the psychoactive substance, theoretically the remission of the depressive symptoms should occur after a certain period of time (usually a few weeks).



10. Drug-induced depression - depressive symptoms are a direct consequence of the administration of certain medications prescribed for various medical conditions (eg interferon alpha, corticosteroids, beta-blockers or oral contraceptives).

11. Post-schizophrenic depression - the diagnostic criteria for schizophrenia must have been met in the period preceding the onset of the depressive symptoms and they may still be present to some extent in the clinical picture.

12. Simple schizophrenia - is a clinical form of schizophrenia with the manifestation of only the negative symptoms of disease, this being a hypothyria (including flattening/blunting of affect) in which bizarre thoughts and behaviour also arise.

#### B. The differential diagnosis of bipolar disorder

The differential diagnosis of bipolar disorder will be made with mood disorders induced by a brain dysfunction, psychoactive substance use, secondary to drug administration, schizoaffective disorder and other psychotic disorders, in the same manner as the recurrent depressive disorder. In particular, the differential diagnosis of the bipolar affective disorder will be done with:

1. Cyclothymia – it is to be distinguished from type II bipolar disorder in which depressive symptoms reach the clinical intensity required for a major depressive episode diagnosis.

2. Emotionally unstable personality disorder of the borderline type - although both have instability as a common clinical feature, especially in relation to others, the diagnostic criteria for a major depressive episode, hypomanic episode, manic episode, or mixed episode are not met. Moreover, the borderline personality disorder appears at a fairly early age and is marked by a persistent and pervasive pattern of social interaction difficulties that will lead to a number of maladaptive behaviors.

#### COMORBIDITIES

The concept of comorbidity refers to the clinical situation in which a distinct additional clinical entity occurs during the clinical course of another previously diagnosed disease, without a causal relationship between the two.

##### A. OTHER PSYCHIATRIC DISORDERS

- Anxiety disorders
- Harmful use or substance dependence
- Personality disorders
- Dysthymia, which if associated with a major depressive episode, is called double depression
- Pathological gambling

- Attention deficit hyperactivity disorder, more commonly comorbid with bipolar affective disorder

**B. WITH MEDICAL CONDITIONS**

- Cardiovascular conditions
- Endocrine diseases and Type II diabetes
- Neurological diseases: migraine, epilepsy, cerebrovascular disease, Parkinson's disease, multiple sclerosis
- Diseases of the locomotor system
- Neoplasms
- Digestive diseases: ulcerative disease, Chron disease, ulcerative colitis

**COMPLICATIONS**

**I. PSYCHIATRIC COMPLICATIONS Suicide**

- 15% of those with monopolar depression, end up completing suicide; About two-thirds of all completed suicide cases are caused by monopolar depression;
- Every case should be analyzed from the suicide versus parasuicide perspective, although both clinical situations require equal attention! (with parasuicide - "the principle of the Russian roulette")

**CHARACTERISTICS THAT DIFFERENTIATE SUICIDE FROM THE PARASUICIDE**

<b>SUICIDE</b>	<b>PARASUICIDE</b>
More frequent in males	More frequent in females
More frequent at older ages	More frequent in younger people
Preceded by a longer period of time during which the suicide risk increases progressively: suicidal ideas → plans → attempt	Usually carried out impulsively and triggered by an interpersonal conflict, with a demonstrative character

There is a strong desire to die, death is regarded as the only way to end the problematic situation, takes cautions in order not to be saved	There is no real desire to die, usually with the purpose of `emotional blackmail` as a means of resolving the conflict, takes cautions in order to be saved and chooses less dangerous methods
Usually leaves a letter assuming this behavior and taking direct responsibility while absolving the others from any blame for this gesture	If the person leaves a letter, it usually plays the victim and blames the others for the gesture
More frequent in major depression with comorbidities (depression+anxiety+addiction = major suicide risk!)	More frequent in individuals with accentuated or pathological personality features of histrionic type

B. Alcohol and other psychoactive substance abuse / dependence

Approximately one-third of those with recurrent depression and half of those with bipolar disorder have substance abuse as a psychiatric comorbidity.

C. Association of anxiety symptoms over time

D. Premature death due to other chronic medical conditions by decreasing adherence to treatment for the disease or by developing unhealthy behaviors such as smoking.

II. SOCIAL COMPLICATIONS

A. Decreased quality of life

B. Intrafamilial conflicts that may lead to separation or divorce

C. Social withdrawal especially in those with depressive episodes

D. Difficulties regarding social interaction skills

E. School or work difficulties that may result in expulsion or dismissal.

## EVOLUTION AND PROGNOSTIC

The natural evolution of mood disorders tends to be a long-lasting one, with mood episodes intertwined with periods of remission that are initially usually complete. With the progression of the disease, the duration of the episodes tends to increase and that of the remissions decreases.

Depressive episodes may last between 6 months and sometimes up to 1 year, and manic episodes last for an average of 4 months. As a rule, the onset of the manic episode tends to be sudden, and in depression it is often insidious. Naturally, both manic and depressive episodes tend to be shorter under specific treatment.

The rate of chronification in those with recurrent depressive disorder is quite high at around 7% 10 years after its onset. Between one-quarter and one-third of patients hospitalized for bipolar disorder will subsequently develop a chronic evolutive pattern of the psychiatric condition.

20% of those with bipolar disorder have rapid cycles, meaning at least 4 distinct affective episodes in one year. Also, rapid cycling is considered a mark of an unfavorable evolution of the bipolar disorder, which may sometimes announce the progression towards chronification.

The prognosis of mood disorders is better than that of schizophrenia, with the mention that the recurrent depressive disorder tends to have a better prognosis than bipolar disorder.

For the recurrent depressive disorder, the short-term prognosis is relatively good in the sense that a remission occurs in approximately 50% of those with a first clinical depressive episode during which treatment was initiated. Also, therapeutic response (a 50% reduction in clinical symptomatology) is achieved in 2/3 of those undergoing treatment compared to the same reduction in symptomatology in only one-third of untreated patients. In the long run, however, the prognosis of recurrent depressive disorder is unfavorable, so recurrence rates are over 40% in the first 2 years, over 60% after 5 years, and over 75% 10 years after the first episode of depression of clinical intensity.

## TREATMENT TREATMENT

### SETTING

The need for hospitalization in patients with mood episodes is dictated by the following situations:

- Presence of suicidal ideation and / or plans; also the presence of homicidal ideas
- Lack of any social support network
- The patient is unable to undergo outpatient treatment
- The patient presents psychiatric or medical complications / comorbidities that would make the ambulatory treatment unsafe

- The patient did not achieve a therapeutic response during outpatient treatment

PSYCHOPHARMACOLOGICAL TREATMENT OF RECURRENT DEPRESSIVE DISORDER AND BIPOLAR

1. Antidepressant medication

It is administered at all stages of treatment in both the first depressive episode and recurrent depressive disorder. The three phases of antidepressant treatment are:

- The acute phase of treatment (6 to 12 weeks): its goal is the remission of the clinical symptomatology of the current depressive episode.
- The continuation phase of antidepressant treatment (4 to 9 months): it aims at strengthening the clinical and functional remission obtained in the previous phase and preventing relapse.
- The maintenance phase of antidepressant treatment (lasting 1 year or more depending on the number of previous depressive episodes): aims to prevent recurrence (new distinct episodes of major depression). In the opinion of some authors, given the increased chronicity and recurrence rates of depression, patients with more than 2 major depressive episodes should be advised to continue their long-term antidepressant treatment. If it is decided to discontinue antidepressant treatment, it should not be done abruptly but by gradual dose reduction.

In the table below we will present the main classes of antidepressants and their representatives used in the treatment of depression along with the main mechanism of action, recommended daily doses and their adverse effects:

<b>Classes of antidepressants</b>	<b>Representatives</b>	<b>Mechanism of action</b>	<b>Therapeutic dose</b>	<b>Most frequent adverse effects</b>
Selective serotonin reuptake inhibitors	Paroxetine Escitalopram	Inhibition of 5-HT reuptake	20 – 60 mg/day 10 – 20 mg/day	Nausea, vomiting, sexual dysfunction, insomnia
Selective norepinephrine reuptake inhibitors	Reboxetine	Inhibition of norepinephrine reuptake	8 – 12 mg/day	Xerostomia, constipation, heavy sweating, insomnia
Selective norepinephrine and dopamine reuptake	Bupropion	DA and NA reuptake	200 – 300 mg/day	Xerostomia, headache, agitation,

inhibitors		inhibition		nausea, vertigo, constipation
Serotonin modulators	Trazodone	5-HT <sub>2A</sub> 5-HT reuptake inhibition	200 – 600 mg/day	Drowsiness, xerostomia, headache, vertigo
Monoamine oxidase inhibitors	Moclobemide	Selective MAO A inhibition	300 – 600 mg/day	Insomnia, vertigo, headache
Noradrenergic and specific serotonergic antidepressants	Mirtazapine	$\alpha$ <sub>2</sub> antagonism, 5-HT <sub>2,3</sub> antagonism	30 – 90 mg/day	Drowsiness, xerostomia, vertigo, high appetite
Melatonergic antidepressants	Agomelatine	Melatonin M <sub>1</sub> /M <sub>2</sub> receptor agonist, selective 5-HT <sub>2C</sub> antagonist	25 – 50 mg/day	Headache, vertigo, drowsiness, insomnia
Glutamate modulators	Tianeptine	Glutamate modulation	25 – 37,5 mg/day	Abdominal pain, nausea, vomiting, constipation, xerostomia
Tricyclic antidepressants	Amitriptyline Clomipramine	Non-selective 5-HT and NA inhibition	150 – 300 mg/day	Xerostomia, vertigo, constipation, visual accommodation difficulties, urine retention, excessive sweating, cardiotoxicity!!!
Tetracyclic antidepressants	Mianserine, Maprotiline	5-HT reuptake inhibition and	60 -120 mg/day	Xerostomia, constipation,

		NA reuptake inhibition	150 – 225 mg/day	headache, less than with tricyclics
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Legend: 5-HT = 5-hydroxytryptamine or serotonin; DA = dopamine; NA = norepinephrine; 5-HT<sub>2A</sub>, 5-HT<sub>2,3</sub>, 5-HT<sub>2C</sub> = subtypes of serotonergic receptors;  $\alpha_2$  = subtype of noradrenergic receptors; M1 and M2 = melatonin receptors; MAO A = monoamine oxidase subtype A

#### CONTRAINDICATIONS OF ANTIDEPRESSANT MEDICATION:

##### A. Relative contraindications:

- closed-angle glaucoma;
- epilepsy;
- cardiac ischemic and rhythm disorders;
- prostate adenoma;
- Diabetes.

##### B. Absolute contraindications:

- comatose states;
- agranulocytosis;
- severe history of hepatic insufficiency;
- association with MAO inhibitors.

We would like to mention that in the case of bipolar depression, the therapeutic guidelines recommend avoiding the use of antidepressant medication in favor of mood regulating medication.

#### Treatment-resistant depression

The WHO defines treatment-resistant depression by two formulas representing two incremental degrees of severity: relative resistance - lack of response to inadequate treatment and absolute resistance - lack of response to 4-week treatment with imipramine at a dose of 150mg / day.

Marinescu defines treatment-resistant depression as "a major depressive disorder that does not respond positively to two families of antidepressants administered sequentially and for an

appropriate period of time - at least 6 weeks for an antidepressant - in a sufficient dose and with good treatment compliance".

## 2. Mood stabilizing medication

The label mood stabilizing medications is currently used for two categories of psychotropic drugs. The first refers to classical and new generation anticonvulsants along with lithium salts. The second refers to atypical antipsychotics that have also been approved for their mood regulating clinical action and will be presented in the chapter about antipsychotic medication.

Mood stabilizers are administered during all phases of treatment of bipolar disorder, regardless of the type of current or previous mood episode (depressive, hypomanic, manic, or mixed).

Pharmacologic class	Representatives	Mechanisms of action	Therapeutic doses	Most frequent adverse effects
Lithium salts	Lithium carbonate	Inositol monophosphate inhibition, G protein modulation, regulating the gene expression of neuronal growth factors	900 – 1800 mg/day	Tremor, nephrogenic diabetes insipidus, thyroid goiter, ataxia, dysarthria
Classic anticonvulsants	Carbamazepine	Inhibition of voltage-gated sodium channels, glutamate release inhibition	400 – 1600 mg/day	Vertigo, drowsiness, balance disorders, ataxia, agranulocytosis, hepatotoxicity



	Valproic acid	Inhibition of voltage-gated sodium channels,  GABA agonism, stimulates neuroplasticity	300 – 2400  mg/day	Sedation, tremor, vertigo, ataxia, hepatotoxicity, aplastic anemia, thrombocytopenia, transitory alopecia
New generation anticonvulsants	Lamotrigine	Reduces glutamate release, inhibits voltage-gated sodium channels	50 – 200  mg/day	Vertigo, headache,  diplopia, ataxia, skin rash
	Gabapentin	inhibits voltage-gated sodium channels, modulates  glutamate release	900 – 1800  mg/day	Vertigo, drowsiness, ataxia, nystagmus, nausea, peripheral edema
	Topiramate	Blocks voltage-gated sodium channels, glutamate receptor antagonist, inhibits carbonic anhydrase	50 – 300  mg/day	Metabolic acidosis, paresthesia, drowsiness, weight loss

It has to be mentioned that for lithium salts the weekly measuring of lithemia is mandatory at the beginning of treatment, with a therapeutic window of 0.8 - 1.2 mEq / L. Under these limits, medication is clinically ineffective and above the upper limit it is toxic, since the therapeutic window is very narrow. It should be noted that both lithium salts, valproic acid and

carbamazepine have a significant teratogenic risk, which is why either pharmacological classes should be avoided during pregnancy, or the risk-benefit balance should be considered.

### 3. Antipsychotic medication

Atypical antipsychotics may be used on a short-term basis during episodes of recurrent depressive disorder while psychotic symptoms are also present. Recently, due to its proven antidepressant effect, quetiapine was approved for the treatment of recurrent depressive episodes. In the treatment of bipolar disorder some of the atypical antipsychotics have been approved for their mood stabilizing clinical action and are administered during all phases of treatment regardless of the type of the current or previous affective episodes.

Our clinic also has experience with haloperidol, which can be given over a limited period of time, due to its high anti-manic potency. To prevent a potential neuroleptic induced extrapyramidal syndrome, in this situation, trihexyphenidyl (commercially available as Romparkin) will also be combined in doses ranging from 4 to 14 mg / day.

The table below shows the antipsychotics currently used in the treatment of bipolar affective disorder.

Class of antipsychotic /main mechanism of action	Representative	Therapeutic dose	Adverse effects
D2 dopamine receptor and 5-HT <sub>2A</sub> serotonin receptor antagonists (atypical antipsychotics or new generation antipsychotics)	Olanzapine	5 – 20 mg/day	Weight gain, drowsiness, hyperlipidemia, increases the risk for type II diabetes mellitus and dyslipidemia
	Quetiapine	400 – 800 mg/day	drowsiness, xerostomia, orthostatic hypotension, vertigo, increases the risk for type II diabetes mellitus and dyslipidemia

	Risperidone	4 – 16 mg/day	Drowsiness, extrapyramidal syndrome, hyperprolactinemia, might increase the risk for type II diabetes
	Ziprasidone	80 – 160 mg/day	Vertigo, sedation, extrapyramidal syndrome, nausea, xerostomia
D2 dopamine receptor antagonists (classic antipsychotics)	Haloperidol	5 – 20 mg/day	Extrapyramidal syndrome, sedation, vertigo, hyperprolactinemia

Legend: 5-HT<sub>2A</sub> = subtype of serotonergic receptors; D<sub>2</sub> = subtype of dopaminergic receptors

#### 4. Psychotropic medication aimed at other associated psychiatric symptoms

##### A. Benzodiazepines

In the case of associated anxiety symptoms and psychomotor restlessness during the acute depressive episode, alprazolam may be administered in therapeutic doses of 1 and 3 mg / day, preferably over a period of no more than 2 months,. Alprazolam has been shown to be a benzodiazepine with a slight antidepressant effect. Among the most common adverse effects while initiating treatment, there were: Drowsiness, fatigue, vertigo, ataxia, dysarthria, confusional state, attention and memory disturbances. Another problem is that of dependence, which is why it should be prescribed for as little time as possible, with a gradual dose reduction.

In bipolar disorder, especially in severe manic episodes, due to its mood regulating effect, clonazepam may be administered over a limited period of time. The therapeutic doses are between 0.5 - 4 mg / day. More frequent side effects, especially at the beginning of treatment, are: drowsiness, vertigo, ataxia, fatigue, confusional state, fixation amnesia. As a

benzodiazepine, the increased risk of addiction should be considered, which is why it will be prescribed for as little time as possible and then gradually reduced upon discontinuation.

## B. Hypnotics

It is preferable to use them in the case of sleep-onset insomnia and reduced sleep duration, and to administer them exclusively at night before bedtime. Hypnotics should not be administered for more than a month. Among the most commonly used hypnotics of the new generation, are zolpidem at a therapeutic dose of 5-10 mg / day and zopiclone at a therapeutic dose of 7.5 mg / day, both given in a single take in the evening at bedtime. Some of the more common side effects of this class are: headache, drowsiness, dizziness, vertigo, fatigue, ataxia, diplopia. With zopiclone administration, the persistence of a bitter taste has also been observed.

## PSYCHOTHERAPEUTIC TREATMENT

1. Cognitive Psychotherapy - is centered on identifying and modifying thought distortions that contribute to the maintenance of depressive symptoms; The patient is helped to understand the connection between distorted thoughts and depressed mood.
2. Behavioral psychotherapy - is based mainly on the reinforcement of pleasure-generating behaviors.
3. Interpersonal Therapy - focuses on identifying and correcting difficulties in the area of the patient's interpersonal relationships.
4. Family therapy - addresses dysfunctional relationships that occur within the family homeostasis and that generate depressive symptoms.
5. Psychodynamic oriented psychotherapy - addresses subconscious intrapsychic conflicts through psychoanalytic techniques such as: free association, defensive mechanism analysis and transfer interpretation.
6. Melotherapy

It should be noted that psychotherapy is also aimed at patients with bipolar disorder, which, depending on the type of their current mood episode, benefit from customized treatment approaches / protocols.

## OTHER TYPES OF THERAPEUTIC INTERVENTIONS IN DEPRESSION

1. Bright light therapy – depression with a seasonal pattern.
2. Transcranial magnetic stimulation therapy
3. Electroconvulsive therapy (ECT) – has a limited indication in severe forms of depression, with stupor or behavioral negativity, that endanger the patient's life through hydro-electrolytic

inbalances, severe malnutrition, etc. and which has been proven refractory to any of the pharmacological treatments. It is also used in acute manic episodes refractory to psychotropic medication. During ECT electrodes are applied unilaterally to a single hemisphere, usually the right one, while the patient is being given curare under general anesthesia guided by an anesthesiologist. The most common transient adverse effects reported by some authors are the inter- and post-operative confusional state and predominantly anterograde amnesia. ECT is contraindicated in the following situations: space occupying intracerebral lesions (tumors, hematomas, etc.), other causes of increased intracranial pressure, recent myocardial infarction, recent intracranial haemorrhage, aneurysm or any unstable vascular malformation, pheochromocytoma and increased anesthetic risk.

#### 4. Sleep deprivation

## Chapter XIII - ALCOHOLISM

### The definition of alcoholism

Alcoholism may occur at different ages and is a result of drinking alcoholic beverages. Clinical manifestations are varied and depend on the amount of alcohol consumed, the duration of consumption, the type of drink used, and other factors related to the person concerned.

### Epidemiology

It is quite difficult to estimate the amount of alcohol consumed in a specific population. Most commonly, this can be achieved by calculating the amount of alcohol that is produced in a country, but it does not accurately reflect alcohol consumption. We have to keep in mind that, on the one hand, not all of the alcohol that is produced is also consumed, and on the other hand, besides the legally reported production, there is also a significant quantity of alcoholic beverages that are produced illegally or in the domestic environment, which escape National statistics.

According to official statistics, the average alcohol consumption per capita ranges from 1.0 liters in Israel to 13.6 liters in France. In Romania average alcohol consumption per capita is about 7.7 liters, but it is in continuous growth. In the United Kingdom, average alcohol consumption in males is of 17 units of alcohol per day, and in women of 9 units of alcohol per day, under the condition that the permitted amount would be 4 units of alcohol/day for men, and of 2-3 units of alcohol/day for women.

In general, alcohol consumption is higher in males (10/1) and begins in adulthood. There is, currently, an increase in female alcoholism (in some countries the male/female ratio reaches 4/1) and a decrease in the age of onset of consumption (early onset in adolescence).

### Classifications of pathological consumption of alcoholic beverages

There are several classifications of alcoholism, depending on the evolutionary stage, type of consumption or on multidimensional aspects.

## Cloninger's classification

1. Type I alcoholism (environmental alcoholism) with a late onset, after the age of 20, a slow evolution, observed in both genders. The risk factors are represented by the environmental disorders in childhood - emotional deficiencies, early separation, family disruption, and, less, genetic factors. The basic personality is marked by the weakness of the Ego with feelings of guilt after the substance abuse. Psychological dependence is stronger than the physical dependence.

2. Type II or exclusively male (father-to-child) alcoholism, with an early onset before the age of 20 years, a rapid evolution toward addiction that will lead to serious somatic and social complications. It can be associated with the presence of antisocial behaviors and other drug addictions. Risk factors are genetic (alcohol dependence of fathers) and neuropsychological (hyperactivity syndrome and/or attention deficit in childhood). The role of environmental factors is limited. The presence of an antisocial personality would be an intermediate risk factor.

## Clinical classification

This is made from an evolutionary, prognostic and therapeutic perspective and divides alcoholism into:

1. Primary alcoholism - without any other psychiatric disorder that precedes or is associated with alcohol consumption;
2. Secondary alcoholism - in which we have at least one comorbid psychiatric disorder, most commonly: anxiety, depression, cyclothymia, personality disorders and psychotic defects. Some studies have indicated that alcoholism secondary to depression is more common in females.

## Etiology

The etiopathogenic approach to alcoholism is complex and multifactorial.

### Sociocultural factors

Consumption of alcoholic beverages is rooted in history, and currently alcohol is the psychoactive substance with the greatest potential for abuse, partly because of the large cultural acceptance, regardless of the ethnic or religious affiliation of the various social groups. A significant role is played by social prejudices, which thus consider that alcohol fortifies, stimulates social integration, and plays an important role in adulthood. Another important aspect is that alcoholism can be found in certain professions that require more difficult work (in construction) or those requiring contact with alcohol (waiters, businessmen, commercial representatives).

### Psychological factors

Various theories associate alcohol consumption with the reduction in tension, increasing the feeling of "coping" with the mitigation of psychological suffering. It should be underlined that many people with alcohol-induced problems say that alcohol intake reduces their nervousness and helps them cope more easily with daily stress. Also, in the opinion of many people with moderate/integrated alcohol consumption, it is considered that the daily ingestion of small alcohol quantities in a tense social environment or after a busy day of work would help to increase the feeling of "well-being" and to facilitate social interaction.

The role of personality in the emergence of alcoholism, though debatable, has revealed that alcoholism occurs more often in people with antisocial, passive-dependent, avoidant, anankastic and emotionally unstable personality disorders.

### Behavioral Factors

An important role is held by the effect of reward and behavior reinforcement after alcohol consumption and this aspect contributes to the decision to re-use after the first experience with alcohol. The neurobiological substrate of these factors is that of dopaminergic neurotransmission which, through the mesolimbic pathway, projects into the nucleus accumbens, which represents the pleasure center.

### Genetic factors

Family studies have shown that first-degree relatives of people with alcoholism have a 4 times higher risk of developing the disease than the general population. Genetic studies on adopted persons have indicated that the biological parent confers the risk to excessive alcohol consumption, which is 4 times higher than the risk in the general population. There is also a higher concordance rate of alcoholism among monozygotic twins compared to dizygotic twins.



The risk of developing alcoholism is also associated with the qualities of the acetaldehyde-dehydrogenase isoenzyme that causes a variable inborn tolerance (it seems that determinism is hereditary) in alcohol consumption. Practically, the low metabolic qualities of this enzyme determine, after alcohol consumption, the accumulation in the body of acetaldehyde that is responsible for the clinical symptomatology that occurs. This may explain the lower alcohol tolerance of women.

#### Biological factors

As alcohol enters the body, it begins to interact with the neurons. This interaction occurs through two neurotransmitters with different actions: glutamate (a neurotransmitter with a stimulating function) and GABA (a neurotransmitter with an inhibitory function). Practically, glutamate produces neuronal excitation, GABA inhibits the action of neurons and helps organize brain information. Alcohol acts on the two neurotransmitters by inhibiting the transmission of glutamate and increasing GABA transmission. Because glutamate is inhibited, the flow of information between neurons becomes slower and only stronger signals are perceived. This translates clinically by the fact that the individual will feel less, see less, notice less, and remember less.

Other mediators involved are catecholamines that interfere in the withdrawal syndrome by increasing the presynaptic norepinephrine release and norepinephrine receptor hypersensitivity.

The association between depression, alcoholism, alcohol-induced aggression, and suicidal behavior could be based on a dysfunction of the serotonergic system. A decrease in serotonin activity was associated with increased aggressiveness and impulsivity and with an early onset of alcoholism among men.

#### The circuit of alcohol in the body

After ingestion, absorption is predominantly at the duodenum and jejunum level. Carbonated drinks (champagne) are absorbed in the stomach. The maximum blood concentration is reached approximately 30-90 minutes after ingestion. Absorption is slower if the subject has eaten food or if the drink is highly concentrated in alcohol. If consumption is rapid or not associated with food, absorption increases and the duration until reaching peak blood levels decreases.

After passing into the blood, alcohol is:

- 10% excreted unaffected through the kidneys, lungs (the alcohol evaporates and is exhaled in the alveoli - the breath alcohol testing associated with the ampoule turning into the color green) or through sweat.

- 90% is metabolized in the liver by two pathways that result in the intermediate formation of acetaldehyde that is more toxic than alcohol when accumulated. The metabolized alcohol will subsequently be eliminated through feces.

The metabolic pathway of alcohol:

1. The alcohol-dehydrogenase pathway - the alcohol is converted to acetaldehyde under its action, which is subsequently converted to acetate by acetaldehyde dehydrogenase. Blocking acetaldehyde-dehydrogenase (via Disulfiram / Antalcol / Antabuse) causes accumulation of acetaldehyde in the body, which will lead to the release of increased amounts of histamine with the occurrence of facial flushing, tachycardia and nausea 20 minutes after ingestion of alcohol.
2. Microsomal oxidation - occurs in the presence of O<sub>2</sub>, and results in the production of water. This oxidation causes the proliferation of the endoplasmic reticulum. NAD is a cofactor and hydrogen acceptor when alcohol is converted to acetaldehyde and further to acetyl-CoA. The generated NADH penetrates the mitochondria and changes the NADH / NAD ratio and the liver redox status. The generated hydrogen replaces fatty acid as fuel and is followed by accumulation of triglycerides and fatty liver manifestation.

Alcohol disseminates throughout the body, in all tissues, including neurons. Blood alcohol content is an index of the level of alcohol in tissues. The rate of alcohol metabolism is 15 mg/dL/h with a variability of between 10 and 34 mg/dL/h, depending on several characteristics, such as: duration of consumption, gender, race, etc.

## Clinical presentation

From a clinical point of view, we can discuss the following:

### 1. Experimental consumption of alcohol

This represents a consumption that occurs at young ages generated by the desire to see what the effects are, and is influenced by the social aspects of that person.

### 1. Socially integrated alcohol consumption

Information from various studies or research shows that alcohol consumed in moderate amounts seems to actually have a beneficial effect on the human body. However, this affirmation must be made with caution, because it is very difficult, if not impossible, to set the limits of a "normal consumption" of alcohol. This is because there is a different alcohol tolerance from one person to another. What

may be beneficial for some, can be very damaging, even fatal, for others. There are people who have consumed large amounts of alcohol for 30-40 years without serious consequences, while others, after moderate chronic alcohol consumption for 10-15 years, have developed liver cirrhosis. This type of consumption basically involves alcohol use that is not harmful to health.

## 2. Harmful alcohol use

This is a pattern of alcohol consumption that affects the health of the person, either at the somatic level (hepatic or cardiac complications, etc.) or at a mental level (depressive episodes, anxiety states). Other people generally criticize this consumption, but the subject, in spite of these problems, does not suspend alcohol consumption.

## 3. Pathological drunkenness

When a small amount of alcohol is consumed, a twilight state (a state of restriction in the field of current awareness) is triggered, a state of aggressive potential, followed by the amnesia of the episode. These manifestations occur in people with cerebral micro-lesions (most commonly following trauma). It should be kept in mind that these cases might, at any time, become forensic cases.

## 4. Acute ethanol intoxication

It may occur in people who are not alcohol users (accidentally) or in habitual or addicted consumers. Clinical manifestations depend on the level of blood alcohol:

> 0.15 g ‰ - a prolongation of the reaction time;

0.8 g ‰ - decrease in lateral vision, decrease in performance, increase in the threshold of sensory and motor reflexes (which explains the obvious increase in reaction time);

1.5 g ‰ - mental disinhibition, boldness, logorrhea (often hypomanic); insufficiently controlled or coordinated movements, increase in the amplitude of movements;

2 g ‰ - diminished perception, poor orientation, confusion regarding others, difficult speech, difficult, inebriated gait, inadequate gestures;

2.5 g ‰ - extreme confusion, sopor, imperceptible speech, the person can no longer walk, they sustain falls, sleep or coma.

3-4 g ‰ - alcoholic coma, characterized by: hypotonia, cold sweats, mydriasis, progressive reduction of reflexes, bradypnea, respiratory inhibition, hypotension, hypothermia, death.

In addition to these manifestations, one can also see those of acute complications:

1. Hypothermia in people who have fallen in the rain or snow;

2. The possibility of developing a subarachnoid hematoma after a 1-2 day free interval, or of meningeal haemorrhage.

#### 4. Ethanol dependence

Consists of daily alcohol consumption, with a progressive increase in quantities in order to achieve the desired effect and followed by the occurrence of complications. In time, the subject begins to feel a strong desire to consume alcohol, a desire that they cannot control. The subject loses control over alcohol consumption, in terms of the dose consumed, the place or time of consumption, and they can no longer stop drinking because the mental and physical withdrawal reaction occurs, which can go up to delirium tremens. These individuals also neglect other activities in favor of alcohol consumption and do not suspend it, despite the occurrence of negative somatic or social consequences.

The dependence is analyzed, as follows:

1. The age of onset - the younger the age, the worse, because the prognosis is poorer if the patient comes from an alcoholic father and was raised in his family;

2. The mode of consumption in the initial phase:

- Intermittent (dipsomania, periodically abusive consumption) with gradual reduction of the free interval;
- Slowly progressive continuous consumption - isolated or social consumption, in the latter case the subject drinks in groups of consumers, thus maintaining pseudo-sociability.

3. Duration of consumption, taking into account that the subject with alcohol dependence usually attends for psychiatric assessment and treatment after several years of daily consumption. A dependent person may have periods of abstinence, especially in particular circumstances (travel, detention), but consumption resumes quickly and reaches high daily doses.

At first, tolerance increases, daily dosages increase, followed by a decrease in tolerance.

4. The quantity that is consumed daily is evaluated in units named "drinks", 1 drink = 12 grams of pure alcohol consisting of the equivalent of 330 ml of beer, 140 ml of regular wine and 40 ml of vodka or scotch.

Ethanol dependence may be primary (when there is no other psychiatric disorder) or secondary (when there is anxiety, depression or personality disorder).

- Clinical presentation of uncomplicated withdrawal

It usually starts within a few hours of cessation or reduction of massive alcohol consumption in a person who is already addicted to alcohol (a sign of physical dependence on alcohol). The manifestations are at the following levels:

- Mental: state of restlessness, anxiety, insomnia, subjective malaise, panic attacks, incapable of doing anything productive;
- Somatic: tremor of the extremities, sweating, blood pressure oscillations (frequent hypertensive crises), nausea, vomiting.
- It can be complicated by:
  - o Seizures, sometimes grand mal seizures - higher risk for subjects with a history of epilepsy or head trauma, crises are often in the morning, sometimes occurring in groups of two or three.
  - o Delirium tremens.
- Clinical presentation in delirium tremens

Delirium Tremens is a major psychiatric complication whose central component consists of mental confusion syndrome that occurs in withdrawal (48 to 72 hours after abrupt or sudden reduction in consumption) in a patient with malignant alcoholism. It is a medical emergency that occurs in 1-3% of alcohol addicts. The manifestations are at the following levels:

- Mental: delirium (confusional state) with reduced vigilance and temporo-spatial disorientation, false recognition, psychomotor restlessness or agitation, incoherent speech, predominantly visual and tactile hallucinations (zoomorphic - small animals climbing on the body) and scenery - panoramic, hypomnesia or amnesia of fixation, hypoprosexia or aprosexia of concentration and reversal of sleep-wake rhythm.
- Somatic: marked hyperactivity of the vegetative nervous system with generalized tremor, profuse sweating, tachycardia, hyper- or hypotension with a tendency to collapse, hyperpnoea, nausea, vomiting, sometimes central fever may occur due to metabolic and hydro-electrolyte imbalance.

#### Complications

##### Somatic

- Overall modified appearance, sometimes with weight gain (due to excess calorie intake through alcohol), facial flushing with telangiectasia; sometimes weight loss due to appetite disturbance;

- Gastrointestinal: gastritis, ulcer aggravation, liver steatosis, chronic alcoholic hepatitis, liver cirrhosis, esophageal varicose veins, esophageal and hepatic cancer, Mallory-Weiss syndrome, pancreatitis, enteritis, malabsorption syndromes;
- Cardio-circulatory: alcoholic dilative cardiomyopathy with severe rhythm and conduction disorders, hypertension (especially by drinking salty beverages, such as beer);
- ENT: laryngeal or pharyngeal cancer;
- Haematological: megaloblastic anemia through food deficiency and malabsorption syndrome leading to a deficiency of vitamin B12 and folic acid;
- Infectious complications (by immuno-depression): pneumonia, bronchopneumonia, TB;
- Metabolic complications: hypoglycaemia, hyperglycaemia (due to pancreatic involvement), ketoacidosis, hyperlipidemia, hyperuricemia;
- Fetal alcoholic syndrome (due to the direct harmful effect of alcohol and acetaldehyde on the development of the fetus - postnatal clinical presentation: severe mental retardation, microcephaly, stature deficits, facial abnormalities, etc.);
- Trauma: epidural, subdural and intracerebral hematomas, basal fractures, etc.

#### Neurological

- Ethanol tremor - is very ample in delirium tremens and in patients with chronic malignant alcoholism, it occurs at the level of the hands and fingers, with small amplitude and high frequency (8-10/second), occurring both in resting state and intentionally.
- Seizures
- Polyneuritis (vitamin B1 deficiency)
- Cerebellar symptoms (due to cerebellar atrophy)
- Persistent alcohol-induced amnesic disorder
- Wernicke encephalopathy (acute disorder - acute B1 vitamin deficiency)
- Korsakoff Syndrome (chronic disorder - chronic vitamin B1 deficiency)

- Cerebrovascular disease (increased arterial fragility due to direct toxic effect on the arterial wall) with possible strokes, especially during withdrawal

#### Psychiatric

- Confusional state - delirium tremens (presented above).
- Paranoid psychosis - Wernicke alcoholic hallucinosis - The clinical picture consists of: vivid, persistent (often visual and auditory) hallucinations, without delirium, following (usually within 2 days) the reduction of alcohol consumption in an alcohol dependent person, anxiety secondary to hallucinatory experiences that can cause psychomotor restlessness or psychomotor agitation. It may evolve into a clinically similar form of chronic schizophrenia. We should mention that it appears on a clear field of consciousness and after a period of abstinence.
- Systematic delusion of jealousy - occurs after long-term alcohol consumption, it is correlated with decreased sexual performance, and comprises a systemic paranoid delusion consisting in the belief of the patient that his partner is unfaithful.
- Anxiety disorders - many people use alcohol to help relieve anxiety. Phobic disorders and panic disorder are the most common comorbid diagnoses in these patients. On the one hand, alcohol may be used for "self-medication" to relieve symptoms of agoraphobia or social phobia, and on the other hand, an alcohol-induced disorder may precede the occurrence of panic disorder or generalized anxiety disorder. The complete remission of anxiety symptoms at several weeks after obtaining complete abstinence certifies the causal relationship associated with alcohol consumption.
- Depressive disorders – suicide - approximately 30 to 40% of people with an alcohol-related disorder meet the diagnostic criteria for depressive disorder at a certain point in time. People with alcohol-related disorders and major depressive disorder have the highest risk for suicidal behavior. It is important to note that the alcohol-depression relationship is bidirectional, in the sense that alcohol consumption can cause depression, but also vice versa, depression causing secondary alcohol consumption.
- Cognitive impairment of varying degrees, which ultimately leads to alcoholic dementia
- Alcohol-induced personality disorders - occurring in people with long-term alcohol consumption and consisting of: progressive disinterest towards the family, the profession, irritability, impulsivity, and unpredictable hetero-aggressive behaviour.

## Social

- Reduced social network, focused on drinking partners;
- Reduced participation in social life, outside of the home and job. However, drinking partners do not represent a real network of social support. The social network will progressively decrease through job loss, family rejection.
- Dissocial behavior, consisting of conflicts, physical aggression, crimes, accidents (labor, traffic), suicide, murder
- Decrease in professional performance, absenteeism - professional downgrading - change and loss of employment = loss of professional status;
- Disturbance of family life: family conflicts - rejection by relatives and spouse - divorce = loss of family status; sometimes the patient returns to the family of origin.
- Isolated existence with one or two supporters, concurrent with biological and psychological degradation, frequent admissions
- Loss of accommodation - homeless

## The prognosis

The prognosis of chronic alcoholism is reserved. Several negative prognostic factors are described: the presence of genetic load, young age of onset, long duration of consumption, the extent of complications, the low motivation of the subject to abandon consumption, the presence of a reduced social support network.

Alcoholism is a serious public health problem, because it disrupts both the state of biological health and the mental state and social behavior of people. It is also an important cause of reduction in life expectancy and quality of life.

## Treatment

The therapeutic intervention is complex and individualized and aims at the following: cessation of alcohol consumption, treatment of medical complications and support through psychotherapeutic interventions. In the first step, drug therapy is important, and later, psychotherapeutic interventions



are important for the stabilization and prevention of relapse. Individuals can be hospitalized for: acute intoxication, uncomplicated or complicated withdrawal (delirium tremens).

#### Treatment of acute ethanol intoxication

- Adequate thermic conditions;
- 5% glucose infusions at 3000-4000 ml/day plus physiological saline and potassium chloride;
- Vit. B1, B6, intramuscular administration;

#### Treatment of uncomplicated withdrawal

- Oral or parenteral hydroelectrolytic rehydration and re-balancing (in cases of gastric intolerance 2000-3000 ml/day);
- Multivitamin preparations (B1, B6, etc.);
- Sedative-anxiolytic medication: benzodiazepines (Diazepam, Lorazepam);
- Anticonvulsant medication: mood stabilizers (Carbamazepine) to reduce the risk of seizures.

#### Treatment of complicated withdrawal - delirium tremens

- Vital signs every 6 hours;
- Hydro-electrolytic rebalancing (0.9% physiological saline or 5% glucose in 2000-3000 ml/day);
- Sedative-anxiolytic medication: benzodiazepines (Diazepam, Lorazepam);
- Anticonvulsant medication: mood stabilizers (Carbamazepine) to reduce the risk of seizures;
- Antipsychotic medication: neuroleptics (incisive - Haloperidol) for psychomotor agitation and hallucinatory-delusional phenomena
- Multivitamin preparations (B1, B6) are administered intramuscularly.

#### Anti-alcohol treatment

There are substances that can stop the subject from consuming alcohol by producing unpleasant effects upon ingestion. Unpleasant effects include nausea, vomiting, dizziness, facial congestion, headache, drowsiness, and general malaise. The main drug used is disulfiram (Antalcol). The mechanism of action of disulfiram is given by the inhibition of the acetaldehyde-dehydrogenase enzyme, which is responsible for the oxidation of alcohol in the liver. By blocking this enzymatic pathway in the body, acetaldehyde accumulates, leading to the symptoms described above.

To administer it, the informed consent of the subject is required. There are other medicines that can be used: acamprosate (a glutamatergic antagonist and GABA agonist), naltrexone (a non-selective opioid antagonist that has an anti-craving effect).

#### Treatment of other complications

- Depression: antidepressant medication (tianeptine) not metabolised by the liver;
- Anxiety: anxiolytics (alprazolam);
- Psychosis: antipsychotics (olanzapine);
- Associated somatic pathology: the medication recommended for the specific pathology.

Psychotherapeutic interventions are applied in a later stage, after overcoming the acute phase and the most important objective for starting a therapeutic program is motivation. There are several techniques that try to increase motivation for change and especially for interruption of alcohol consumption. Most beneficial is individual psychotherapy for motivation, structure and lifestyle, for life satisfaction, as therapy options are very limited for the patient with severe alcohol dependence, where virtually all behaviors are subordinated to an irresistible desire to consume alcohol.

Family therapy is utilized to explain to family members about alcoholism, insisting that the subject should not be rejected, but supported. Attempts are also made to alleviate communication difficulties within the family and avoid symmetrical escalation of conflicts that exist between partners, conflicts that usually lead to physical aggression.

It is useful to reform the social network, most frequently by integrating into the social group of former alcoholics (Alcoholics Anonymous), and by attempting to reinstate the socio-professional status.

## Chapter XIV - PSYCHOACTIVE SUBSTANCE USE (TOXICOMANIAS)

### Generalities

Toxicomanias are mental disorders characterized by:

- Compulsive consumption of psychoactive substances (one or more)
- Inability to limit substance use;
- Occurrence of the withdrawal reaction when stopping the use of substances.

Either natural or synthetic, psychoactive substances are capable of inducing psychological or biological dependence. They generally act on the level of several systems, the most important being the motivational system where they produce lasting changes. All these substances induce a euphoric effect in first instance, associated with depressing, stimulating or hallucinogenic effects.

Classification according to their effects on the central nervous system:

1. Depressant: opioids, alcohol, cannabis, benzodiazepines, barbiturates and volatile substances.
  2. Stimulant: cocaine, amphetamines, caffeine, nicotine
3. Hallucinogenic: phencyclidine, MDMA (ecstasy), LSD, mescaline, psilocybin

In 50% of cases, consumption involves a combination of substances (poly-toxicomania). Initially, it starts with light substances (cannabis, LSD), which then pave the way for powerful drugs (opium, cocaine). The association of psychoactive substances is used to:

- amplify the euphoric feeling: a mixture of heroin and cocaine (double flash) is injected;
- combat some undesirable effects of stimulants, such as insomnia (a sedative substance is associated to the stimulant substance);
- combat the effects of withdrawal to the substance (two sedating substances are combined).

Initially, the consumption of psychoactive substances begins through EXPERIMENTAL CONSUMPTION, when the doses are controlled. With the passage of time, the consumption turns into:

- Abuse: The subject can control substance consumption in the absence of stimuli associated with consumption (syringe, pipe, joint, ritual), but in their presence there is a craving and compulsion to consume the substance;
- Addictive consumption: the subject loses control over consumption, tolerance to the effects of the substance develops, followed by addiction.

### Etiopathogenesis

Toxicomania represents an interrelation between the psychoactive substance, the person and the socio-cultural context.

A) Psychoactive substances have an effect on the central nervous system by favoring their abusive use:

- Euphoric effects that induce a good mood;
- Dynamic effects that are sought because they favor social relationships, they increase self-esteem and confidence in their own abilities, they reduce fatigue and hunger;
- Analgesic effects that are particularly sought by those suffering from chronic painful conditions;
- Anxiolytic and hypnotic effects that are sought by anxious or depressive persons.

Compared to other therapeutic alternatives, these substances provide a quick method to change the affective state or to suppress reality.

An important role is played by the availability of the drug, for example:

- Access to alcohol for bartenders, sailors;
- Access to morphine, fentanyl, ketamine for anesthetists;
- Access to barbiturates and anxiolytics for doctors.

A) Socio-cultural factors:

1. Religion plays a particularly important role in the prohibition or use of psychoactive substances (for example in Muslim countries, alcohol is forbidden).

2. Country legislation differs in terms of drug permissiveness.
3. Prohibition of alcohol (in the interwar period in the USA or imposing prohibitive prices in the Scandinavian countries. Both methods proved to be ineffective due to the development of alcohol smuggling).
4. Banning tobacco advertising, banning smoking in public places.
5. Regulating cannabis use in the Netherlands.
6. Family plays a particularly important role, often substance abuse can be learned in the family. Disorganized families are generally considered to favor consumption.

B) Individual factors (genetic, personality, age):

1. Genetic factors influence:

- The enzyme equipment of the individual has the role of eliminating the drug by metabolism.
- The number of dopamine D2 receptors. Neuroimaging studies conducted in people who do not consume psychoactive substances show that those individuals with a smaller number of D2 dopamine receptors experience a feeling of pleasure in the administration of methylphenidate, and are, therefore, more vulnerable to drug abuse than individuals with a higher number of type D2 dopamine receptors, which had unpleasant experiences when receiving methylphenidate.

2. Personality traits such as impulsivity (emotionally-unstable/borderline and dissocial/antisocial personalities) and shyness (anxious/avoidant personality) favor abusive drug use.

3. Age influences the consumption of substances, in the sense that there are certain age groups that favor consumption: adolescence, young age and the elderly.

4. An important role in the consumption of psychoactive substances is played by the motivational system that is based on several neural circuits. These circuits are cortical-striatal-thalamus-cortical type, they start from different cortical areas (anterior cingulate, orbital or dorsolateral prefrontal cortex) and project into specific regions of the basal ganglia and nucleus accumbens. The frontal cortex and corpus striatum are areas that control voluntary and involuntary motor behavior and are primary motivational structures. These structures receive information (exteroceptive or interoceptive mnemonic)

and affective sensorial information) from secondary motivational structures (association cortex, hypothalamus, hippocampus and amygdala). In the corpus striatum, the GABA-ergic neurons have the role of selecting, by collateral inhibitions, certain behaviours from a wider range of alternatives.

Motivational brain systems are of two types:

1. Facilitators, with dopamine as a neuro-mediator (the mesolimbic circuit in which the dopamine secreted by the ventral tegmental area of the mesencephalon reaches the nucleus accumbens and the limbic system's amygdala nucleus).
2. Inhibitory or of control, with serotonin as a neuromodulator (secreted from the mesencephalon level and acting on the nucleus accumbens and the amygdala nucleus, but also on the ventral tegmental area and the prefrontal cortex).

The release of dopamine in the nucleus accumbens is responsible for the euphoric state of psychoactive substances, in both, addicts and healthy people. The faster and more intense dopamine release from these neurons is, the more the euphoric state induced by the drug will be felt faster and more intense (high, rush). Any exteroceptive or interoceptive stimulus that is stored in the memory (the storage of information is done in the hippocampus) will have an affective (pleasant or unpleasant) significance attributed to it, through the function of the amygdala nucleus. The two formations (hippocampus and amygdala) modulate the corpus striatum response.

The massive and longer-lasting psychoactive release produced by psychoactive substances (compared to the shorter response time produced by natural motivational stimuli, such as food, water, or sexual activity), in the nucleus accumbens, will narrow the range of behavioral alternatives of the individual, paving the way for addiction. However, the facilitator motivational system is subject to control by the inhibitory motivational system. The prefrontal cortex plays an important role in the inhibition of impulsive or compulsive behaviors (orbitofrontal cortex). Anatomical or functional abnormalities of the prefrontal cortex (dementia, traumas, tumors, affective disorders, schizophrenia, obsessive-compulsive disorder, antisocial personality disorder) are accompanied by a decrease in impulse control. Combining these conditions with drug use will increase the risk of developing an addiction.

## Opioids

Are divided into two categories:

1. Opium alkaloids: morphine, codeine, papaverine;
2. Semisynthetic or synthetic products: diacetylmorphine (heroin), pentazocine (fortral), petidine (mialgin), methadone, fentanyl;

Administration method:

1. Opium: ingested, smoked;
2. Morphine: injected, ingested;
3. Heroin: injected, ingested, smoked.

Clinical manifestations:

Heroin intoxication:

- Psychiatric manifestations: euphoria with sedation (passive happiness), apathy and detachment from the outside world, distractibility, peaceful and detached sensation.
- Somatic manifestations: analgesia, bradycardia, respiratory depression, decreased cough reflex, constipation, vomiting, peripheral vasodilatation (sensations of warmth, tingling, sweating), miosis.
- Severe poisoning: obnubilation, coma, collapse, acute pulmonary edema.

Opioid withdrawal:

- These substances give tolerance, psychological and physical dependence;
- The duration of action of the substance is very important: heroin 3-4 hours, morphine 3-4 hours;

- Heroin withdrawal occurs 8 to 10 hours after the last injection and consists of: abdominal pain, limb myalgia, lacrimation, rhinorrhea, diarrhea, sweating, nausea, fever, mydriasis, piloerection, insomnia, anxiety, agitation, the need to consume drugs.

Complications:

- Overdose that can cause death, anaphylactic shock, nephropathy, TB, abscess, septicemia, endocarditis, HIV infection.

Treatment:

1. Pharmacological treatment:

- Acute Intoxication: antagonists, such as nalorphine, naloxone, naltrexone;
- Withdrawal: hydro-electrolytic rebalance, tranquilizers, possibly neuroleptics;

2. Substitution treatment - there are national methadone substitution programs;

3. Cognitive-behavioral psychotherapy, family therapy.

Cannabis

The active substance is delta 9 tetrahydrocannabinol (THC). Cannabis is of two types:

1. Cannabis indica is a plant that grows in the tall plateaus of Iran and North Africa.
2. Cannabis sativa grows in temperate regions.

Cannabis is found in several forms:

1. Leaves and flowers have low THC content and are consumed as marijuana, kif, bhang.
2. The resin of the plant is consumed as hash.
3. Cannabis oil is found as hash oil and has a high THC content.

Administration method:

1. Inhalation – the effect is quickly set, in minutes, and lasts for several hours; Inhaled as a cigarette or special pipe;



2. Ingestion - the effect is weaker and occurs later; it is ingested in the form of sweets or beverages.

It is considered a light drug, but can give slow onset psychological dependence; its effects are achieved through GABA neurons. It can be traced in the urine.

Clinical manifestations:

Acute intoxication:

- Somatic manifestations: injected conjunctival membranes, hypothermia, hypotension, tachycardia, hunger sensation, dry mouth.
- Mental status manifestations: anxiety, cannabis drunkenness, toxic delirium, toxic psychosis.

Chronic intoxication:

- Somatic manifestations: cerebral atrophy, COPD, changes in spermatogenesis, bronchopulmonary neoplasm;
- Mental status manifestations: amotivational syndrome manifested through apathy, disinterest, decrease of intellectual capacities, decrease of memory capacity.

Cannabis drunkenness

Clinical manifestations depend on the expectations of the person consuming it, the environment in which they consume it, and they consist of:

1. Euphoric excitement: logorrhea, euphoria, hypersociability;
2. Exaltation: sensory hyperesthesia, impulsivity, aggressiveness, hyper-emotionality;
3. The state of quiet ecstasy with distortions of time and space, hallucinations;
4. Sleep.

Treatment:

Cognitive-behavioral psychotherapy

## Cocaine

This substance is extracted from the coca bush. The mechanism of action consists of the blockade of dopamine re-uptake pumps, causing its levels to increase in the synaptic cleft.

### Forms of presentation:

1. Cocaine hydrochloride: the powder that can be snorted (the effect is quickly settled, in 15-60 minutes and lasts for 4-6 hours), it can be dissolved and administered as an energizing drink or it can be injected intravenously.
2. Cocaine alkaloid: smoked in the form of pipes or cigarettes.

### Clinical manifestations:

#### Acute intoxication

- Mental status manifestations: euphoria, insomnia, lack of appetite, increased energy, self-confidence, logorrhea, anxiety, and sometimes delirium;
- Somatic manifestations: mydriasis, hypertension, cardiac arrhythmias, fever, sweating, seizures, nausea, pruritus, grating lesions.

#### Chronic intoxication

- Mental status manifestations: apathy, violent states, toxic psychosis (visual and tactile hallucinations, delusional paranoid ideas).
- Somatic manifestations: perforations of the nasal mucosa, cachexia, pulmonary emphysema.

#### Withdrawal

- occurs 48-72 hours after cessation of consumption;
- mental manifestations: marked depressive mood (possibly suicidal ideation), insomnia, nightmares.
- somatic manifestations: asthenia, headache, sweating

### Treatment

1. Pharmacological, depending on clinical manifestations: neuroleptics, antidepressants, anxiolytics.
2. Cognitive-behavioral psychotherapy

## Amphetamines

These substances are divided into two categories:

- Classic amphetamines: levoamphetamine, dextroamphetamine, methamphetamine, methylphenidate.
- Designer amphetamines: MDMA (ecstasy), MDEA, MDA, DOM.

Mechanism of action:

- classic amphetamines stimulate dopamine release;
- the designer subtype combines the stimulation of the release of dopamine, norepinephrine and serotonin with the effects of hallucinogens.

Methods of administration: oral, i.v., i.m., inhalation and smoking.

Consumers:

- students before exams.
- business people to increase performance.
- athletes before competitions.
- long-distance drivers.
- women to lose weight.

We must mention that amphetamines are also used in medicine for:

- Nasal decongestion
- Narcolepsy
- Hyperkinetic syndrome
- Treatment-resistant depression

Clinical manifestations:

Acute intoxication

- psychiatric manifestations: euphoria, excitement, lack of fatigue, of hunger and of need for sleep, increased self-esteem, increased pain threshold, anxiety states, amphetamine psychosis (visual, tactile, auditory hallucinations, delusional paranoid ideas, delusions of infestation with parasites), irritable mania, paranoia.

- somatic manifestations: tachycardia, hypertension, polypnea, hyperthermia, weight loss, mydriasis, heat waves, in more severe cases ventricular fibrillation, heart failure, stroke, seizures (multiple cerebral infarctions), coma.

#### Withdrawal

- increased sleep time, nightmares, fatigue, increased appetite, depression with suicidal ideation and attempt, craving for the drug.

#### Withdrawal

- occurs 48-72 hours after cessation of consumption;
- mental manifestations: marked depressive mood (possibly suicidal ideation), insomnia, nightmares;
- somatic manifestations: asthenia, headache, sweating.

#### Other amphetamine-induced psychiatric disorders

- psychoses (paranoid elements, auditory, haptic hallucinations), mood disorders, aggressive homicidal or suicidal behavior.

#### Treatment:

1. pharmacological, depending on clinical manifestations: neuroleptics, antidepressants, anxiolytics.
2. cognitive-behavioral psychotherapy.

#### Hallucinogens

They are substances that produce the sensation of mind expansion, disrupt the mind, or mimic psychosis. They do not produce significant abstinence syndrome. Stopping consumption causes flashback.

This category includes the following:

- Amanita muscaria;
- Psilocybin;
- Mescaline;

- Atropa belladonna;

- LSD (lysergic acid of diethylamide);

-PCP (phenylcyclidine): intoxication causes violent behavior, hyperactivity, mutism, echolalia, nystagmus, ataxia, focal neurological signs, seizures, intracerebral haemorrhage, coma.

Clinical manifestations following ingestion are, as follows:

- Phase I: relaxation, euphoria, lucidity, sociability, sympathomimetic somatic effects;
- Phase II: perceptual distortions, such as visual illusions, synesthesia;
- Phase III: Distorted perception of time, feeling of doubling, depersonalization, feeling of increased personal capacity, mystical ecstasy, perception of internal organs, reliving of past events, paranoid psychosis or delirium (hallucinations).

Pharmacological treatment is recommended, according to the clinical symptomatology present.

Barbiturates and benzodiazepines

Doctors prescribe these substances for clinical anxiety symptoms or for their hypnotic effects, as they are drugs with a well-known potential to create addiction. An important aspect is that they can create dependence, even in therapeutic doses, if used over a longer period of time. This form of addiction does not occur during administration, but in the attempt to discontinue it.

Clinical manifestations:

Barbiturates intoxication: euphoria, psychomotor disinhibition, logorrhea, emotional lability, irritability, aggression, ataxia, dysarthria, disturbance of attention and memory. More serious cases can reach coma states with respiratory depression, bullous skin lesions, sweat glands necrosis. After a prolonged use, a deficient syndrome with apathy, asthenia, intellectual slowness and feebleness may occur.

Barbiturates withdrawal: anxiety, irritability, blood pressure oscillations, orthostatic hypotension, tachycardia, sweating, nausea, delirium, myoclonus or even grand mal seizures.

Benzodiazepine intoxication: dizziness, slurred speech, confusional state, blurred vision, anxiety, sometimes a paradoxical agitation, drowsiness.

Benzodiazepine withdrawal: anxiety, insomnia, circulatory disorders, gastrointestinal disorders, seizures, tremor, diaphoresis, delirium.

#### Treatment

Benzodiazepine or barbiturates intoxication requires vital function support. The benzodiazepine antidote is flumazenil, which is a competitive antagonist at the benzodiazepine receptor, but should be given with caution when the person has a history of seizures or long-term use of benzodiazepines.

In order to prevent withdrawal, gradual dose reduction is required. Under the conditions in which the withdrawal has started, the following should be administered: anticonvulsants (carbamazepine), beta blockers, antidepressants.

#### Inhalants

These are volatile substances that produce chemical vapors that can be inhaled to produce a psychoactive effect or to alter the state of consciousness. The term is used to describe a very broad category of substances that are administered almost exclusively by inhalation.

#### Clinical manifestations

Acute intoxication:

- Mental manifestations: inebriated apathy or agitation, diminished cognitive functions, increased impulsivity and aggression, alternating between disinhibition and euphoria to psychoses with hallucinations and body schema disorders.
- Somatic manifestations: gastric disturbances, reduced reflexes, diplopia, inhalant specific halitosis, perioronasal stains of dyes or colorants.
- Complex, severe organic consequences related to central and peripheral neurological lesions.
- Nitrites can cause sudden death, immunosuppression, alterations of erythrocytes.
- Butane, propane: sudden death by cardiac effect, risk of burns.

- Freon: sudden death, respiratory obstruction (by freezing of the airways), liver damage.
- Methyl chloride: tissue hypoxia, cardiac and hepatic toxicity
  
- Nitrous oxide: sudden death through cerebral hypoxia, perceptual disorders, motor incoordination, cardio-respiratory depression, severe hypotension.
- Toluene: brain injuries with severe cognitive dysfunction, visual and auditory disorders, sudden death (cardiac lesions), liver and kidney damage
- Trichloroethylene: sudden death, liver cirrhosis, reproductive complications, visual and auditory disorders.

#### Chronic intoxication:

- Neurotoxic effects: psychosis, deterioration.
- Various toxic effects: Hepatic, cardiac, pulmonary, and muscular lesions.
- Fetal toxic effects: skeletal, neurological abnormalities, low birth weight

#### Treatment

##### Acute intoxication:

- There is no antidote, and the breathing disorders, arrhythmias, psychotic and confusional states are treated as usual.

##### Chronic intoxication:

- Treatment of psychiatric organic disorders.

No withdrawal syndrome is described.

## Chapter XV – INTELLECTUAL DEFICIT (MENTAL RETARDATION)

### **General considerations:**

Mental retardation represents the shutdown of psycho-ontogenesis because of an organic or neurological cause in the first part of an individual's life (age 0-12). Mental retardation mostly affects the faculties that contribute to the global level of intelligence (cognitive, verbal and social skills). Subjects diagnosed with mental retardation do not represent a homogenous group, but a broad spectrum of clinical presentation types and behavioral patterns. Mental retardation does not have a unique cause, mechanism, prognosis or outcome. Maladaptive behaviors should not be automatically considered as part of mental retardation or as a sign of "organicity". As with all individuals, these behaviors could be linked or caused by negative life events or may be the symptom of a comorbid psychopathological disorder.

Mental retardation can be accompanied by any other somatic or mental disorder.

### **Epidemiology:**

Life-time prevalence of mental retardation in the general population is 1 %. Mild mental retardation has a prevalence of 0.4-0.6 % in the general population and moderate, severe and profound mental retardation have a combined prevalence of 0.4 %.

The prevalence of other mental disorders is 3 to 4 times higher in subjects with mental retardation than in healthy subjects.

### **Etiology and pathophysiology:**

The intellectual abilities of a subject mostly depend on the integrity of the central nervous system (CNS). Numerous biomedical causes may influence the integrity of the CNS and may initiate the process of which leads to mental retardation.

What has to be taken into account is the fact that the term "mental retardation" describes the general level of functioning, including intellectual and adaptive abilities. Besides the CNS integrity, these are influenced by other factors as well, like: general health state of the individual, environmental factors (parental care, learning / schooling opportunities, social support network) and psychological factors (self-perceived image, psychopathological characteristics, motivation).



**Etiological factors:**

- Prenatal causes: genetic disorders (Down syndrome, Prader-Willi syndrome, fragile X syndrome, neurofibromatosis, congenital hypothyroidism, Williams syndrome, phenylketonuria, Tay-Sachs disease), maternal infections (cytomegalovirus, toxoplasmosis, rubella, HIV), toxic causes (foetal alcohol syndrome), prematurity, radiation, physical trauma.
- Perinatal causes: infections (meningitis, herpes), hypoxia, physical trauma, hypoglycemia, hyperbilirubinemia.
- Postnatal causes: infections (meningitis, encephalitis), toxic causes (lead poisoning), strokes, tumors, physical trauma, severe malnutrition, iodine deficiency.
- Unknown causes (idiopathic).

**Classification of mental retardation** is made according to the IQ score (intelligence quotient) of the assessed subjects (by using standardized IQ tests / scales), and is as follows:

- Profound mental retardation (IQ score below 20)
- Severe mental retardation (IQ score 20-34)
- Moderate mental retardation (IQ score 35-49)
- Mild mental retardation (IQ score 50-69)
- Borderline intelligence (IQ score 70-84).

Additionally, several other “dimensions” of mental retardation have been described. These can help conceptualize the assessment:

- I- Intellectual abilities
- II- Adaptive behavior (practical, social and conceptual abilities)
- III- Social participation, interaction and roles
- IV- Physical and mental health, etiological factors
- V- Cultural context.

**Clinical picture:****a.) Borderline intelligence (IQ score=70-84)**

Affected individuals present memory and learning disabilities when put in stressful situations which overcome their level of intelligence and their ability to cope with stress. They have relatively good global functioning and do not need social protection.

**b.) Mild mental retardation (IQ score=50-69)**

Are able to learn spoken language, reading, writing and calculus at a basic level, but take longer to do so (when compared to un-afflicted children). That is why they need schooling in special schools.

They do not acquire abstract thinking, but are able to learn self-sustenance (sphincter control, eating, dressing and washing abilities). They also acquire self-administration skills and may thus work in domains which require practical (not intellectual) skills.

They are easy to manipulate and are thus likely to become “marionettes” or “executants”.

Subjects with mild mental retardation may present adequate social conduct or inadequate social behavior, like: notable emotional and social immaturity, lack of ability to handle child-raising responsibilities, the difficulty to adapt to social or cultural traditions, because they do not understand the consequences of their actions. They may rarely have the following comorbid disorders: epilepsy, autism, hyperkinesia, facial dysmorphism, spastic cerebral paralysis, visual or hearing disorders.

**c.) Moderate/severe mental retardation (IQ score=20-49)**

Subjects with these types of mental retardation are able to learn spoken language (rudimentary vocabulary), but cannot be taught to write, read or basic mathematical skills.

They acquire walking skills very late (when compared to other children) and have self-sustenance skills, but only under supervision. They do not acquire self-administration skills. They are able to perform stereotypical, easy tasks, such as knitting, but only under supervision.

They often need care in specialized institutions and often present: epilepsy, autism, hyperkinesia, facial dysmorphism, spastic cerebral paralysis, visual or hearing disorders.

**d.) Profound mental retardation (IQ score=0-20)**

The life of these subjects from a psychological point of view is rudimentary. Communication is non-verbal (moans, screams), they do not acquire walking skills, they have no self-sustenance abilities. They are unable to differentiate between what is edible and what is not. They require care in specialized institutions and frequently present epilepsy, autism, hyperkinesia, facial dysmorphism, spastic cerebral paralysis, visual or hearing disorders.

**Treatment:**

Mental retardation is a functional disability and thus treatment is aimed at reducing this disability.

There are 3 aspects in regards to treatment:

1. Treatment of the disorder which is causing mental retardation (ex: phenylketonuria)
2. Treatment of somatic and/or psychopathological disorders which contribute to the functional disability. Among the most frequently comorbid disorders / symptoms are: depression (antidepressants, mood stabilizers), psychomotor agitation / self-harm / hetero-aggression (typical neuroleptics <haloperidol> or atypical neuroleptics <olanzapine>, mood stabilizers <carbamazepine, sodium valproate>).
3. Interventions on the functional disability itself: depending on the patient's needs, supportive and/or educational interventions, parental and familial counselling, group activities (which improve socializing skills).

## Chapter XVI - NORMAL AGING

Aging consists of all physiological and psychological processes which modifies the structure and functions of an organ at adult stage.

Biological aging is the process by which the body loses along the time the ability to function in the surrounding environment (self-regulation, repair). The consequence of this process is to reduce the probability of old body survival.

We can talk about a concept of primary aging, based on survival gene scheduling and a concept of secondary aging effects due to the accumulation of pollutant from the environment or different diseases from which the body suffers.

We have in mind 3 forms of aging:

- a)** successful aging (with no associated pathologies in this stage and the limitations associated with functional capacity which occurs as a plain result of the passing of time);
- b)** normal aging (the limitation in capacity is present but not due to associated pathologies);
- c)** pathological aging (with the appearance of chronic progressive diseases and limitations of functional capabilities down to total dependency).

Aging causes are multifactorial, incompletely understood, taking into consideration both the intrinsic and extrinsic factors.

At the cellular level, aging occurs with various changes such as:

- the decrease of the anabolism and catabolism of cellular transmitters, also it lowers the number and sensitivity of receptors in these cell mediators;
- the reduction of oxidative phosphorylation inside the mitochondria with the reduction of the main intracellular power source;
- a decrease in the synthesis of a series of structural or enzymatic proteins, in cell repair capacity and nutrient uptake from the extracellular space;
- intracellular collagen enhancement.

### **Aging of the osteoarticular and muscular system**

With aging the loss of muscle mass is accompanied by the diminution of muscle strength. Also decrease muscle mass (sarcopenia) will lead to the reduction of the percentage of calories burned in the muscles, the excess being deposited in the adipose tissue that will have an android

distribution. This does not lead to abnormal motor activity but it leads to movement difficulties after prolonged bed rest.

At skeletal level we can find a decrease in the protein matrix, as well as bone demineralization giving rise to osteoporosis with the risk of femoral neck fractures.

At joint level, cartilage degenerates and arthritis will appear with the limitation of mobility.

Also the aging person will slightly lose height due to the spinal column decrease as well as kyphosis.

### **Aging of the cardiovascular system**

The heart fills with lipofuscin, the number of myocytes decreases which leads to the hypertrophy of the remaining ones, thus the myocardial fibrosis occurs. Ventricle wall will be more rigid and diastolic dysfunction occurs. As a consequence, systole contribution is increasing at ventricular filling. Aortic and mitral valves will calcify and lose their elasticity. As a result of the increase in vascular resistance, following their aging, left ventricular hypertrophy occurs.

Cardiac output at rest may be normal, but there is a risk of atrial systole loss with the installation of heart failure, especially in atrial fibrillation. During physical exercise, due to adrenergic receptor sensitivity decrease, it results a more diminished heart rate growth, aspect that leads to increased stroke volume (SV).

The vessels undergo the process of arteriosclerosis (reduction in elasticity of the vascular wall with the diminishing of the quantity and quality of elastic fibers and calcium deposit) and atherosclerosis (deposits of atheroma plaque in the vascular wall with the narrowing of the lumen). Arteriosclerosis will lead to systolic hypertension, which is a major risk factor for cerebrovascular accidents.

By lowering the sensitivity of the baroreceptors to changes in blood pressure, blood pressure homeostasis will be disrupted with the risk of orthostatic hypotension, which in turn is responsible (along with various medications, dehydration or venous problems) of syncope or confusional states that may occur in elders.

### **Respiratory system**

Alveolar sacs and alveoli become enlarged due to loss of lung elasticity. The decrease of chest amplitude motion occurs with mobilizable lung volume reduction. The vital capacity (VC) decreases, reducing the lung ventilation during physical exercise. The cough reflex and the activity of the ciliated bronchial epithelium decreased with high possibility to infection.

### **Renal-urinary system**

The decrease of renal blood flow and renin-angiotensin aldosterone system takes place. Reduction of the number of glomerulus, thickening of the basal membrane and associated tubules with changes in the arteriolar walls, results in decreased kidney function (filtration, reabsorption, secretion). The decrease in glomerular filtration requires that the dose of drugs, administered at elders, is to be reduced to half of the adult dose. The enlargement of the prostate increases the difficulty in micturition (dysuria). At women the bladder elasticity decreases with the incapability to pass urine correctly.

Due to clinical consequences, the frequency of chronic kidney disease in acute extrarenal pathologies increases with hemodynamic impact regarding the kidneys and iatrogenic renal complications. Most frequently, hypo- and hypernatremia are encountered.

### **Nervous system**

Anatomic: the brain volume decreases with age (both the gray substance and the white substance). Lobe brain damage is not symmetrical. Damage is most important in the frontal lobes (the prefrontal cortex - the headquarter of executive functions) and medio-temporal- hippocampus, while the occipital lobe less affected.

At neuron level: neurons decrease in some regions are compensated by synapse and dendritic cell increase. This phenomenon is possible due to brain neuroplasticity.

### **Biochemical:**

Although biochemical studies showed a functional decline of major neurotransmitter classes, it is considered that dopamine decrease, determine tardiness in the process of mental operation.

In old age there is a decrease in the number of:

- dopamine receptors,
- dopamine reuptake pumps,
- dopamine storage vesicles.

In terms of cognitive functions, the following changes appear:

### **Global damage**

- the speed of information processing decreases
- the speed of response decreases (mental operations are slower)

### Impaired perception:

With age, eyesight and hearing decrease and correction using glasses or hearing devices is only partial. These deficits will increase the effort and tardiness in processing the received information.

### Disturbance in attention:

- attention dispersion and commutation from one stimulus to another or task to another, decreases;
- decreases the inhibition function of irrelevant stimuli, as well as having overloading working memory, as a consequence.

### Memory impairment implies a decline in:

- working memory
- association of past events with their context (e.g. a person remembers information but not its source, or the person who supplied it)
- voluntary and active fixation (requiring mental effort) new information
- voluntary and active evocation, (requiring mental effort) information from mnemonic deposits

There will be little or no damage on:

- semantic memory (vocabulary)
- implicit memory
- passive evocation
- information recognition (recognition of drawings)

### Dementia

Dementias are a group of disorders characterized by an overall deterioration of the psyche (especially cognitive function, it can also social behavior affectivity) acquired, progressive and spontaneous (irreversible). Cognitive functions frequently affected in dementia are represented by: attention, memory, ability to learn, orientation, thinking, calculation and judgment.

Their prevalence and incidence increases with age, so 20% of people over 80 years are affected by this pathology. They have long been regarded as simple aspects of aging, being underdiagnosed.

Dementias have a varied etiology, and can occur at any age, representing a heterogeneous group of neurological or systemic diseases affecting the central nervous system, but they are among the most common neurodegenerative disorders.

Alzheimer's disease is the most common type of dementia, followed by vascular dementias and dementia with Lewy bodies.

Depending on the etiopathogenic mechanism, dementias can be divided into the following classes:

1. degenerative dementia: Alzheimer's disease, Pick's Disease, Parkinson's Disease, Huntington's Disease, Lewy body dementia,
2. dementia induced by the use of psychoactive substances: alcohol induced dementia, etc.
3. vascular dementia: Dementia infarct, lacunar cerebral infarcts strategic
4. dementia induced by general somatic diseases: AIDS, Syphilis, SSPE, Creutzfeld-Jakobs, hypothyroidism, hypercalcemia, hypoglycemia, liver disease, brain tumors, hematomas, etc.

### **Alzheimer's disease**

#### **Epidemiology**

Alzheimer's is the most common type of dementia (55% of total dementias). The prevalence increases with age with 5% at 65 years and 25% after 80 years. It is more common in women.

The disease onset is between 40 and 90 years. In the past Alzheimer was thought to be a pre-senile dementia (occurring before 65 years), characterized by specific histopathological changes (neurofibrillary tangles, amyloid plaques between nerve cells and granular vacuolar degeneration)

It was subsequently found that the same changes occur in what was in the past called senile dementia (onset after 65 years). Currently two nosological entities were reunited under the name of Alzheimer's disease, which may have an early onset (under 65 years) and a late one (after 65 years).

#### **Anatomopathology**

Disease-specific histopathological changes are highlighted in the cortex and hippocampus, which consists in the next triad:

- neurofibrillary tangles (cortex, hippocampus)
- beta amyloid senile plaques (cortex, hippocampus)
- granular vacuolar degeneration (hippocampus)



### **Neurofibrillary tangles**

Normally, tau protein stabilizes the microtubules through which neurotransmitters are transported intracellular from the nucleus to the terminal button and representing component of the cytoskeleton. Excessive phosphorylation of tau protein reduces its interaction with the microtubules, with consecutive aggregation of the protein in the form of intracellular neurofibrillary tangles and microtubules, with the death and degeneration of the microtubules.

### **Beta amyloid senile plaques**

Beta amyloid is obtained by abnormal splitting of the amyloid precursor protein which leads to the accumulation of the abnormal amyloid in plaques (extracellular senile plaques), which will prevent the synaptic transmission through direct or indirect neurotoxic effect, stimulating the microglia to produce free radicals and cytokines.

### **Granular vacuolar degeneration**

Is noticed in the pyramidal layer of the hippocampus, but sometimes can be found in the neo-cortex. The affected cells present one or more vacuoles with argyrophilic micro-granulations in the middle.

By their death, the number of the neurons will drop massively. Also, we can find an important reduction in the number of dendrites (as opposed to normal aging, where the reduction of neurons is associated with a compensatory increase in dendritic arborization)

It produces an astrocyte proliferation (astrogliosis)

Macroscopic changes (recorded at autopsy or by CT scans) shows:

- cortical atrophy initially interesting the hippocampus and temporal lobe, subsequently extending to the other lobes; primary sensory and motor areas are spared;

- widening gap between the skull and the brain

- enlargement of the grooves (sulci) between the cortical gyri

- enlargement of the ventricles (hydrocephalus ex vacuo)

There is a correlation between the number of cortical histological lesions (especially in the fibrillary ones located in the temporal associative areas) and the severity of clinical dementia.

### **Etiopathogeny**

Alzheimer's disease is a primary dementia because the cause is not known. There are many assumptions involving:

1. **Genetic factors:** For early-onset Alzheimer's disease were found mutations in three genes. Mutations in the APP (Amyloid Precursor Protein) gene on chromosome 21, mutations in PS-1 gene (Presenilin 1) on chromosome 14 and PS-2 gene (presenilin 2) from chromosome 1. The genetic component of late-onset Alzheimer's disease was demonstrated by epidemiological studies that have shown that a positive family history for dementia is a risk factor for Alzheimer's dementia. In this case, the apolipoprotein E gene (ApoE) is involved, namely the E4 allele on chromosome 19, gene that is involved in the faulty synthesis of apolipoproteins responsible for removing blood cholesterol and amyloid from CNS (central nervous system). Synthesis of an abnormal apolipoprotein E affects the removal of beta-amyloid. Amyloid plaques accumulates extracellularly, "suffocating" neurons and disturbing cholinergic synapse transmission. The result is the death of cholinergic neurons inside the nucleus basalis of Meynert with memory disorders (initially the fixing of new information) and attention disorders.

These mutations occur in 5-10% of all cases of Alzheimer's dementia, with autosomal dominant inheritance. In 1% of all cases of Alzheimer's dementia we have trisomy 21.

2. **Biochemical factors:** affecting neurotransmitter systems, particularly acetylcholine activity. Acetylcholine is the neurotransmitter of the ascending reticular activating system. The greatest amount of acetylcholine found in neurons is situated in the nucleus basalis of Meynert and septal nuclei, whose axons are distributed diffusely on the cortex maintaining the waking state, necessary for a better concentration of attention. Also, these neurons connect with the hippocampus, premises of the mnemonic fixation function. In Alzheimer's disease, the death of cholinergic neurons from the nucleus basalis of Meynert and septal nuclei, causes a significant decrease in cholinergic function (impairment of attention and memory). This assumption was the basis for therapeutic strategies for Alzheimer's disease.

3. **Toxic factors:** excess aluminum. It's about a disorder of aluminum elimination, which may have toxic effects on the brain. High concentrations of aluminum were found in senile plaques (neuritic plaques).

4. **Infectious factors:** a slow virus infection

5. **Autoimmune factors**

Among the risk factors we validate family history, older age and the presence of Down Syndrome.

## Clinical presentation

### Early stage:

Onset is insidious, memory disorders consist of episodic memory impairment, short-term reduced capacity to acquire new information (damage of the hippocampus). Entourage often underestimates the memory disorders, putting the blame out on old age.

Subjects forget names, addresses, tasks, words, figures, where they put things. If the patient is still active, can become neglectful and mistakes can be made. At first, the mnemonic deficit can be acknowledged and compensated by automatism, lists, question and repetitions, or hidden (the subject offering various excuses to explain forgetting or time disorientation: they use calendars, often misplace their glasses, not interested in TV or press). Awareness of the mnemonic deficit onset, can induce anxiety or depression.

Brutal onset occurs in special situations (when leaving home - visits to relatives, hospitalization for intercurrent diseases), decompensating the patient by losing recognizable spatial landmarks. At this stage of dementia, the patient is capable of self-care and can fulfill simple tasks.

### Medium stage:

As much as the lesions and atrophy extend to the temporal lobes, parietal, occipital and frontal ones, it can appear:

-by affecting the temporal lobes: speech disorder, such as circumlocution (the subject finds it difficult to recall and name objects or actions, and uses phrases that replace the term or describe the action), paraphasia (the production of unintended syllables, words, or phrases during the effort to speak), sensory aphasia (TSA);

-by affecting the parietal lobes: ideomotor apraxia (IMA), dressing dyspraxia, constructional apraxia, semantic amnesia, acalculia, agraphia;

-occipital lobe damage: spatial disorientation (the subject can wander in town or in hospital if admitted), incorrect assessment of distances, prosopagnosia, alexia;

-frontal lobe atrophy: working memory impairment (the difficulty to perform two mental operations simultaneously), impairments of long-term memory with recently acquired memory loss, impairment of executive functions with the incapacity of anticipating the consequences of their acts (loss of discernment), organization, planning and self-monitoring. The role of executive functions is essential in solving existential problems, their damage will increase the subjects dependency to the entourage. Also, the ability of abstraction is affected (thinking is concrete and stereotypical),

anosognosia (total absence of insight), affective indifference, preoccupation restriction accompanied by the ritualization of everyday life, with loss of motor functions.

Some personality traits intensifies, such as: egocentrism, cognitive rigidity, stingy and suspicious.

Sometimes memory impairment induces delusions involving that family members, neighbours or caretakers are trying to trick them and steal their possessions (but in fact the subject forgot about the place of the items). Also, hallucinations may appear, mostly visual.

Regarding the affect: irritability, depression, mood swings or emotional blunting may occur.

The subject must be assisted in simple and self-care activities. Also, he must be constantly overseen to avoid accidents (falls or fire).

#### Severe stage:

In this stage, the lesions and atrophy have spread throughout the cortex and begin to inquire the subcortical structures.

Front primitive reflexes are released (sucking reflexes, palmar grasp reflex, orientation and palmomental reflex), sphincter incontinence appear and walking disorders. Affection is superficial, labile, or the subject becomes apathetic, indifferent.

Speech becomes unintelligible, verbigeration or mutism appear.

Long-term memory is severely impaired, the subject is no longer able to provide information about his own biography, only very little.

Epileptic seizures may occur, abnormal swallowing due to extrapyramidal hypertonia.

The subject becomes cachectic and entirely dependent on the entourage: to be fed, washed and supervised. Often, the family is overwhelmed and the subject is institutionalized (hospitals for the chronically mentally ill or in nursing homes).

#### Diagnosis of Alzheimer's dementia

Certainty diagnosis of Alzheimer's dementia is only histopathological (presence of specific lesions: neurofibrillary tangles, beta amyloid senile plaques and neurofibrillary degenerations).

Diagnosis is generally considered when mnesic accusations appear.

The diagnosis of presumptive Alzheimer's disease is supported by:

- deficits in two or more cognitive areas, with their progressive deterioration and namely language (aphasia), the execution of sequential motor function (apraxia), perceptions and interpretation (agnosia), executive function, memory;
- unaltered consciousness;
- significant impairment of social behavior or regression towards previous autonomy;
- gradual onset and chronic course;
- not due to other neurological conditions, somatic disorders, toxic substances or drugs;
- onset between 40 and 90 years, usually after the age of 65;
- family history of dementia, especially neuropathological confirmed;
- laboratory tests: normal cerebrospinal fluid (CSF), normal electroencephalogram (EEG) or non-specific changes; CT, MRI - progressive cerebral atrophy, enlargement of sulci, ventricular dilatation, enlarged pericerebral space;
- global cognitive assessment with MMS (mini-mental state), clock test, 5 word memory test, verbal fluency test;

Differential diagnosis is made with:

1. **Delirium** (acute onset, evolution is short, fluctuating, reversible, lasting: days - weeks (maximum 6 months); vagility and orientation damage).
2. **Depression in old age** (the mnemonic deficit is often accused, not hidden; memory deficits are selective – very good memory towards the sad events in life and memory shortage for happy events; the affective disorder is significant and precedes the cognitive deficiency; malaise morning)
3. **Other types of dementia** (vascular dementias, Pick's disease, Parkinson's disease, Huntington's chorea, myxedema, etc.). In case of vascular dementia, we find focal neurological signs, with a relatively sudden onset the onset and progressive evolution (in steps). In dementias due to other general medical conditions (Pick's disease, HIV, etc.) historical data, physical examinations, laboratory tests are important.
4. **Amnesic syndrome** (severe memory impairment without other significant cognitive deterioration).
5. **Normal aging** (cognitive decline is not so significant as to support a diagnosis of dementia)

### **Evolution, prognosis, complications**

The disease progression is often slowly but irreversible. Death occurs in 4 to 10 years from diagnosis and it's due to swallowing disorders. Forms of Alzheimer's dementia with a family history, has an early onset and death occurs faster.

#### **Complications are represented by:**

- injury by dropping
- delirium with psychomotor agitation
- depression
- anxiety

### **Treatment**

The general management of the disease, in addition to the medical treatment, implies a series of other socio-legally interventions, such as:

- organization and adaptation of care depending on the degree of dependency;
- if necessary, putting the patient under guardianship and protection (keeping in mind that there is the danger that the patient will officially entitle their goods or properties to other people or parties that would take advantage of the patient's lack of judgment);
- teaching the patients caregivers about the evolution of the disease and what they have to do (write down the food recipes, learn how to use the electronic appliances used by the person who manifests Alzheimer's symptoms or to prevent the access to potentially toxic substances. It is sometimes the case that members of the family of the patient suffering from Alzheimer are invited to psychotherapy sessions);
- correction of other deficits (hearing loss and visual impairment);
- home care in the initial stages (it is recommended for the patient not to be taken out from the environment to which he is used and which provides the reference cues) or placement in a specialised medical unit (in advanced stages)

#### **Management of medication**

Specific treatment of the Alzheimer disease should be initiated as soon as the diagnostic is known. In this case a curative treatment will not be taken into account, but only a symptomatic treatment, which has the role of slowing down the gradually deteriorative evolution of the disease. Furthermore, this

type of treatment has the potential in the first place to attempt to prevent the occurrence of behavioural eating disorders and slow the process of independence loss, which might lead to the institutionalization of the patient.

The choice of medication will be made in accordance with the progress of the disease.

In the case of light symptoms (MMSE>20), the option will be made for cholinesterase inhibitors: Donepezil 5-10 mg/day; Rivastigmine 6-12 mg/day; Galantamine 12 - 24 mg/day.

For moderate form (MMSE between 10 and 19) an acetylcholinesterase inhibitor is recommended, associated or not with the memantine (antiglutamatergic drug), which is also recommended for MMSE scores of less than 15.

At this stage, memantine can also be recommended as alternative to the combined medication (10-20 mg/day).

In the context of severe form (MMSE <10), memantine is the first choice of treatment. In the event of unsatisfactory clinical response, memantine will be associated with cholinesterase inhibitors.

Continued treatment is performed in severe stages only if the doctor believes that there are benefits for the patient, otherwise medication can be discontinued.

Discontinuation of medication is avoided if somatic symptoms occur or during hospitalisation. If interrupting medication is needed, it will be considered to resume it in the shortest possible time.

Cholinesterase inhibitors (Donepezil, Rivastigmine, Galantamine) destroys acetylcholine by blocking acetylcholinesterase and get to improve the level of acetylcholine in the synaptic cleft of nucleus basalis Meynert. They are generally well tolerated by adults, but among side effects we can mention cholinergic side effects (respiratory depression, bradycardia, hypotension, nausea, vomiting, abdominal cramps, sialoreea, sweating, seizures).

Galantamine, except the effect of acetylcholinesterase inhibition, also plays a role in the modulatory effect of the nicotinic receptor involved in memory and attention.

Rivastigmine reversibly inhibits acetylcholinesterase and butyrylcholinesterase, also involved in the modulation of the level of acetylcholine. The activity of the latter increases in the late stages of Alzheimer's dementia, increasing the indication of rivastigmine for late stages dementia.

Memantine is a NMDA antagonist. Its use is based on the hypothesis of glutamatergic excitotoxicity. According to this, it is considered that amyloid plaques cause the glutamate to be released in an excitotoxic manner.

Notable side effects of memantine are restlessness, urinary incontinence and insomnia.

Other medications used in the treatment of dementia are:

a) Nootropics (piracetam, Pramistar, Cerebrolysin) are used in light or moderate forms of the disease as monotherapy or adjunctive medication if acetylcholinesterase inhibitors are not tolerated.

b) Antioxidants (Selegiline, a standardized extract of Ginkgo biloba, vitamin E) are used in light and moderate forms of the disease and as adjunctive treatment

c) Vasodilators (Piritinol cinnarizine, pentoxifylline) as well as adjunctive Treatment.

It will also consider the treatment of vascular risk factors in patients with Alzheimer's disease or those with mixed Alzheimer's and cerebrovascular disease (statins, antiplatelet, hypotensor, etc.).

The emergence of comorbidities or psychiatric symptoms requires antidepressant medication (Tianeptine, Venlafazină, Trazodone) antipsychotic medication (haloperidol, risperidone, quetiapine) or anxiolytic (lorazepam, oxazepam)

### **Vascular dementias**

They are the most common dementia after Alzheimer's disease. They are based on a brain damage whose cause is ischemic or hemorrhagic stroke.

Vascular dementia can be divided into three subtypes:

a) cortical vascular dementia or multi-infarct dementia, where we have cortical and subcortical infarcts in territories of cerebral arteries, in which typical symptoms, unilateral sensory-motor changes and abrupt onset of cognitive decline and aphasia

and

b) subcortical vascular dementia, or dementia including lacunar cerebral microvasculature and Binswanger's disease, is manifested clinically by pure motor hemiparesis, bulbar signs, dysarthria, emotional lability or specific deficits in executive function.



c) Mixed cortical and subcortical vascular dementia, with mixed type the component (cortical and subcortical). Frequently raised are dementias by strategic infarcts ("strategically" placed in key areas of the brain)

### **Aetiology**

The main causes of vascular dementia are cerebrovascular diseases and their risk factors. Thus in the most common situations we have arterial system deterioration, cardiac embolic events, impaired intracerebral vessels or hemodynamic mechanisms.

In almost all patients with vascular dementia, aetiology is multifactorial.

Risk factors for vascular dementia can be divided into:

- vascular diseases (hypertension, atrial fibrillation, myocardial infarction, diabetes, generalized atherosclerosis, dyslipidemia, smoking)
- demographic (age, education)
- genetics (family history, individual genetic characteristics)
- factors related to cerebrovascular accident (stroke's location and size)
- the presence of hypoxic ischemic events (cardiac arrhythmias, heart failure, seizures, pneumonia)

### **General characteristics of vascular dementia:**

- acute onset with gradually deterioration (after each stroke);
- fluctuating intensity of symptoms (in terms of performance on cognitive tests) due to state of delirium (confusional states);
- cognitive deficits affect certain sectors leaving them intact on the other, depending on the location of infarcts (look "speckled")
- cognitive deficit is often realized with the advent of "catastrophic reaction" (tears)
- the history of the patient can reveal the vascular risk factors (strokes, cardiovascular disease, in particular ischemic heart disease, hypertension, etc.)

### **Diagnosis**

The diagnosis of vascular dementia is supported by the appearance of cognitive decline compared to the previous level of functioning evidenced by clinical examination and neuropsychological testing. Cognitive deficit should not interfere with normal daily activities beyond the determinism of a stroke.

Cerebrovascular disease will be documented by the presence of focal neurological signs and imaging (brain CT or MRI)

Also, there must be a cause-effect type relationship between dementia and cerebral-vascular disease supported by one of the next two types: cognitive impairment is preceded by a stroke spent in the last three months or abrupt or fluctuating deterioration of cognitive functions with staging progression.

The diagnosis of vascular dementia is supported by the following features: early appearance of gait (parkinsonian type, small steps or apraxia -ataxia); difficulty in maintaining posture with a history of frequent falls; urological disease with unexplained urinary symptoms (pollakiuria, urinary urgency, etc.); pseudobulbar syndrome; changes in personality or emotion, abulia, emotional incontinence, and psychomotor retardation and dysexecutive syndrome.

### **Paraclinical**

In the diagnosis of vascular dementia as imaging methods, cerebral tomography and cerebral nuclear magnetic resonance are used. In terms of visual imaging lesions in vascular dementia, the following conclusions can be drawn:

1. There is not one type of pathological lesion, but a combination of infarcts, ischemic lesions in the white matter, and various degrees of atrophy;
2. Infarcts associated with vascular dementia tend to be bilateral, multiple and localized in the dominant hemisphere and limbic structures;
3. White matter lesions, visible on CT or cerebral MRI, in vascular dementia are enlarged, located periventricularly and in the depth of the white matter
4. It is questionable to diagnose vascular dementia if we have a single and small cerebral lesion at the imaging level
5. The absence of cerebral lesions on CT or cerebral MRI contravenes the diagnosis of vascular dementia

To differentiate vascular dementia from other types of dementia, the Hachinski ischemic score is used.

In vascular dementia, death occurs through a new vascular accident or may be due to the disease responsible for strokes (acute myocardial infarction). The average duration of development of vascular dementia is 5 years.

### **Treatment**

It is intended to prevent the emergence of new strokes of all kinds in order to avoid further cognitive impairment of these patients (antiaggregants/antiplatelet, statins, hypotensives, etc.).

Lately, clinical trials conducted with cholinesterase inhibitors have shown superior efficacy to placebo in vascular dementia, so they may be associated with secondary prevention treatment.

Patients with Alzheimer's disease and associated cerebrovascular disease had a good response to galantamine.

### **Frontotemporal dementia (FTD) or Pick's disease**

It is a degenerative disease, characterized by circumferential symmetrical atrophy of frontal and temporal lobes. A family history of the same affection is commonly found in the first degree relatives of the patient.

Histopathologically speaking, we find that Pick cells are neurons with argentophilic cytoplasmic inclusions (Pick corpuscles). We also have a neuronal rarefaction with astrocytic gliosis.

The onset of dementia is slow and occurs before the age of 65. At the forefront of the clinical picture, we find frontal type behavioral disorders with change in patient personality. In evolution we find the early loss of normal social behavior with disinhibition (inadequate jokes, antisocial acts, inappropriate social impulses, etc.), inflexibility with excessive cognitive rigidity, hyperorality (excessive consumption of food, alcohol, excessive smoking, changes in diet, etc.), stereotypical and persevering behavior (excessive walking, dancing, singing, palm beatings, excessive preoccupation with ritualization of dressing, impulsiveness, disturbances of attention, affecting executive functions (organization, planning, discernment, judgment, discernment). There are also symptoms of an affective nature such as depression, anxiety, unjustified elation, emotional lability, affective indifference, apathy, lack of empathy, amimic, or language disorders such as spontaneous spelling and vocabulary reduction, verbal stereotyping, echolalia or mutism.

Spatial orientation and praxias are preserved. At neurological examination, primitive reflexes or incontinence, or late tremor, akinesia, stiffness can be detected early.

Paraclinical examinations reveal normal EEG and at imaging level, frontal-temporal lobe changes. SPECT (single-photon emission computed tomography) detects frontotemporal hypoperfusion; PET (positron emission tomography) detects frontal-temporal glucose hypometabolism, and MRI, CT - predominant frontotemporal atrophy.

### **Lewy body dementia**

It is considered to be the second form of degenerative dementia, as frequency, after Alzheimer's dementia.

Lewy bodies are intracytoplasmic neuronal spherical inclusions composed of intermediary neurofilament proteins, which are abnormally cleaved and phosphorylated.

Within this condition, 3 main psychopathological syndromes have been described:

1. Parkinsonian syndrome associated with degeneration of subcortical neurons, especially in the black substance;
2. Dementia syndrome associated with degeneration of cortical neurons, especially in the frontal, insular, temporal, and anterior cingulus;
3. Autonomous falls with orthostatic hypotension and syncope, associated with degeneration of sympathetic neurons in the spinal cord.

The clinical picture is characterized by a progressive cognitive decline sufficiently high to interfere with social activity or usual occupation, fluctuating cognitive deficits with pronounced variations in attention and consciousness, the presence of well-formed recurrent visual hallucinations, systemic delirium, presence of clinical signs of parkinsonism, repeated falls, syncope, or transient loss of consciousness.

Also highlighted is the high sensitivity to neuroleptics that accentuates parkinsonian syndrome or may even cause sudden death. Evolution is rapidly progressive.

### **Delirium (Mental confusion)**

It is produced by decompensating a somatic disease, or induced by sedative drugs with long half-life. It is more common in elderly than in adults.

It is a medical emergency that, when not identified, leads to death.

Predisposing factors for this pathology are represented by many chronic diseases, polymedication, malnutrition, immobilization, contention, the use of permanent urinary catheter, chronic underlying disorders, delirium history.

The most common precipitating factors are represented by stroke, subdural hematoma, seizures (neurological causes), drugs, withdrawal from benzodiazepines, cerebral ischemia (hypotension, heart failure, pulmonary embolism, myocardial ischemia), metabolic abnormalities (hypoxia, hypercapnia, dehydration, hypoglycemia, hypercalcemia, etc.), fever, infections, toxins and so on.

It is characterized by:

- Denivelation of the current field of consciousness with loss of clarity and coherence of thought (change of vigilance)
- temporal and spatial disorientation, for situation and allopsychic (often false recognition, disturbance of consciousness about the environment and less about himself)
- decrease of concentration and persistence of attention
- immediate and short term memory impairment
- thinking slow, restrictive, repetitive, inconsistent
- perception disorders like illusions, visual hallucinations, often denied (for fear of psychiatric labelling)
- anxiety accompanied by psycho-motor disturbance or psycho-motor inhibition with obnubilation
- reversing the sleep-wake rhythm
- somatic symptoms of the cause that caused delirium

The intensity of the psychic symptoms is fluctuating, with vesperal aggravation.

Often the diagnosis is put wrongly:

1. Only based on behavioral disorders (disorganized, incomprehensible) generated by cognitive disorders that may occur in the absence of delirium:

- If the patient does not find the words to understand what he wants to do (for example, when he wants to go to the toilet) or dysphasia;
- If the patient has space orientation trouble due to lesions of the parietal nondominant occipital cortex;

2. When the elderly's deafness can make him / her not understand the questions or inquiries of the examiner too well;

3. When the elderly cannot focus on the examiner's request due to fatigue or foreign and noisy environment

In the elderly, the differential diagnosis should be made between delirium and dementia (often, however, delusion overlaps with dementia).

The following table lists some clues that could help differentiate between delirium and dementia.

Delirium	Dementia
Acute onset	Insidious onset
Acute, fluctuating, reversible evolution	Chronic, progressive, irreversible evolution
Duration: days, weeks	Duration: years
Impact of temporo-spatial vigilance and orientation with immediate and short-term memory impairment	Short and long lasting memory damage

#### Treatment

Treatment of trigger factor is essential in symptom remission. Symptomatic treatment involves providing a quiet environment, the correction of vitamin deficiencies and electrolyte imbalances, analgesic treatment, and in case of anxiety and psychomotor restlessness it may be administered short half-life anxiolytic (lorazepam, oxazepam, alprazolam), neuroleptics in case of hallucinations and psychomotor restlessness (low-dose haloperidol, risperidone).

#### **Depression at the third age**

It is often underdiagnosed, being masked by somatic symptoms and attributed to age. It affects 30% of people over 75 years. Third Age, through its peculiarities, is one of the crossroads of existence requiring an adaptation of the individual to:

- Progressive deterioration of health, sometimes by cumulative somatic pathology. Hence the growing interest for the body and hypochondriac concerns of the elderly. In addition, degenerative joint disease or other functional limitations imposed by somatic pathology can generate feelings of incapacity and disability.

- The loss of social status, the relationships that result from the social position with the decrease of income through retirement. Adaptation to a smaller budget often correlated with additional medication costs makes the elderly to save and care for money. In this context, anxiety may arise (caring for tomorrow, ideas of prejudice).

- Social and financial losses include losses in the family sphere (death of the life partner) or in the sphere of social relations (loss of friends and acquaintances) leading to loneliness and social isolation.

- When retiring from active life, through retirement, is suddenly done, not prepared in advance, it can lead to a person who is accustomed to activity, to loss of existential meaning (especially if the elderly is alone or left alone through the death of a spouse). The risk of suicide should not be excluded.

Among the risk factors we can mention a history of psychiatric pathology, sensory deficits, mourning, chronic diseases (especially debilitating), the period following a stroke, hypothyroidism and some drugs.

Its classic form is manifested in psycho-motor retardation with profound feeling of pain, anhedonia, auto depreciation, self inhibition, decreased appetite and sleep disorders. It can often be masked by somatic and hypochondrial ideas.

Cotard syndrome may also be encountered (delusion of negation of the world or the presence or function of organs, delusion of immortality and enormity). There is also a delusional form of depression, with ideas of persecution, poisoning or material ruin, sometimes auditory hallucinations. As associated symptoms we also find deep anxiety, psycho-motor a restlessness, pseudo confusion syndrome, melancholic stupor.

In the case of memory disorders at third age, the differential diagnosis between dementia and depression at third age ("pseudodementia") is required.

Depression	Dementia
Acute, accurate onset	Insidious, hard to tell onset
The duration of the cognitive deficit depends on the duration of the depressive episode (weeks, months)	Progressive, spontaneously irreversible evolution
Mnesical deficiency is accused by the patient	Mnesical deficiency is hidden by the patient
Affecting both short-term and long-term memory to the same extent. Selective amnesia for happy life events.	Particularly affecting short-term memory. In time, long-term memory will be affected as well.
The affective disorder is important and precedes the cognitive deficit	The affective setting is lax, superficial
Morning depression worsening	Vesperal aggravation of symptoms

Short-term prognosis is considered favorable, but in long-term, episodes may become more frequent and without complete recovery, resulting in dementia.

### **Treatment**

The most commonly used antidepressants are selective serotonin reuptake inhibitors. In the event of anxiety association, opt for sedatives such as mianserin or mirtazapine administered in the evening.

Also, temporary anxiolytic association may be associated in the initial phase in the event of generalized anxiety.

Choosing antidepressants should take into account somatic comorbidities (cardiovascular disease, prostate adenoma), hepatic and renal function, interactions with other disease associated drugs.



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