

Anxiety Disorders

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All humans experience **FEAR** and **ANXIETY**:

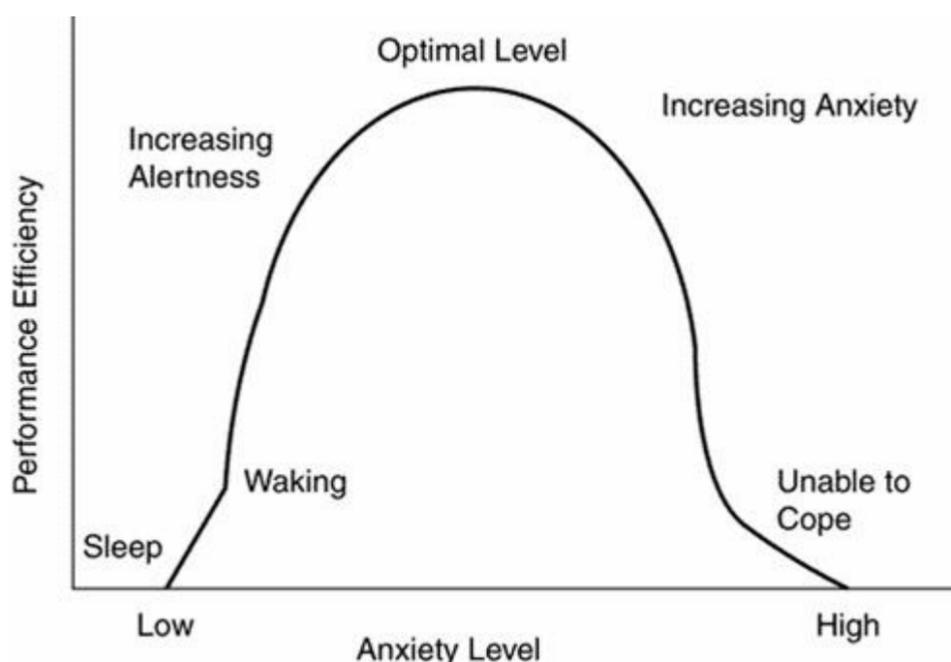
FEAR - emotional, physical, behavioral response to *immediately recognizable external threat*

- **cause** of fear is obvious and understandable.

ANXIETY - abnormal *fear out of proportion* to any external stimulus.

- anxiety is distressing, unpleasant emotional state (emotional arousal) of nervousness and uneasiness.
- anxiety **causes** are less clear (fear that seems to arise from unknown source).
- *anxiety is less tied to exact timing of threat* - it can be anticipatory before threat, persist after threat has passed, or occur without identifiable threat.
- anxiety is accompanied by physical changes and behaviors similar to those caused by fear!
- **some degree of anxiety is adaptive** (can help to prepare, practice, and rehearse so that functioning is improved and can help to be appropriately cautious in potentially dangerous situations); beyond certain level, anxiety causes performance efficiency to decrease → **dysfunction and undue distress** → further increase in anxiety – anxiety becomes maladaptive and considered disorder.
- **PANIC** is most extreme form of anxiety.

Yerkes-Dodson curve showing relationship between emotion arousal (anxiety) and performance:



EPIDEMIOLOGY

- ANXIETY DISORDERS - most common psychiatric disorders (lifetime prevalence 15%; female-to-male ratio = 3:2.).
 - 25% healthy individuals are anxious at some point in their lives (7.5% of these people have diagnosable anxiety disorder in any given month).
- high rates of **comorbidity** with *major depression* and *alcohol / drug abuse*.

ETIOPATHOPHYSIOLOGY

- interaction of **biopsychosocial factors** (incl. genetic vulnerability*) with **situations / stress / trauma**.

*anxiety disorders (except acute and posttraumatic stress disorders) **run in families** (heritability is polygenetic); but some patients appear to acquire same disorders as their relatives through learned behavior (even normal child has difficulty remaining calm and composed in presence of anxious parent)

Major mediators:

- **CNS** - norepinephrine and serotonin; corticotropin-releasing factor may be involved.
e.g. overactivity of noradrenergic systems projecting from locus caeruleus into forebrain regions
- **PNS** - sympathetic nervous system.

CLINICAL FEATURES

1. Psychological symptoms

- 1) apprehension, worry, fear, anticipation of misfortune, sense of doom or panic
- 2) irritability, hypervigilance, insomnia
- 3) fatigue
- 4) difficulty concentrating
- 5) derealization (world seems strange or unreal) and depersonalization (patient feels unreal or changed)
- 6) predisposition to accidents

2. Somatic complaints (many patients visit their primary care physicians for physical symptoms)

- 1) **CNS** - headache, dizziness.
 - 2) **C/V** - hypertension, tachycardia / arrhythmias, palpitations, chest pain.
panic disorder frequently presents to ED with fear of MI; patients with pre-existing cardiac abnormalities may have cardiac arrhythmias under stressful conditions (H: β -blockers)
 - 3) **GI** - dry mouth, upset stomach, diarrhea.
 - 4) **GU** - frequent urination.
 - 5) **RESPIRATORY** - lump in throat, tachypnea-hyperventilation (\rightarrow shortness of breath, paresthesias, weakness, carpopedal spasm due to respiratory alkalosis, lightheadedness, altered consciousness).
anxiety can exacerbate obstructive respiratory conditions
 - 6) **SKIN** - diaphoresis, cool & clammy skin, sweaty palms.
 - 7) **MUSCLE** - tremor, trembling, motor tension, hyperreflexia, easy startling, fidgeting.
- most anxiety disorders begin in **childhood \div early adulthood**.
 - new-onset anxiety in older adults should prompt search for unrecognized general medical condition, substance abuse disorder, or major depression.
 - ability to tolerate given level of anxiety varies from person to person.
 - one person's passion may be another's anxiety (e.g. some find speaking before group exhilarating, whereas others dread it).
 - anxiety can be so distressing and disruptive that depression may result.
 - severe anxiety disorders may be complicated by **suicide!**
 - chronic anxiety \rightarrow increased risk for **cardiovascular** morbidity and mortality.

DSM-IV-TR classification of anxiety disorders

(all categories include significant distress or interference with normal functioning or routines caused by symptoms): lifetime prevalence

1. **Panic disorder** (lifetime prevalence 1.5-5.0%)
2. **Generalized anxiety disorder** (lifetime prevalence 4.1-6.6%)
3. **Obsessive-compulsive disorder (OCD)** (lifetime prevalence 1.7-4.0%)
4. **Specific phobias**
5. **Social phobia** (lifetime prevalence 2.6-13.3%)
6. **Posttraumatic stress disorder (PTSD)** (lifetime prevalence 1-9.3%)
7. **Acute stress disorder (ASD)**
8. **Adjustment disorder with anxious features**
9. **Anxiety due to general medical condition** (old name - **organic anxiety disorder**) - anxiety caused by medical and surgical disorders (anxiety may be presenting complaint!); examples: pheochromocytoma, hypoglycemia, arrhythmias, asthma, hyperthyroidism, temporal lobe epilepsy.
10. **Substance-induced anxiety disorder** (formerly was included with organic anxiety disorder): abstinence of CNS depressants, intoxication with CNS stimulants or sympathomimetics (incl. caffeine beverages), chinese restaurant syndrome (monosodium glutamate ingestion).

Some primary psychiatric disorders may be associated with anxiety (which may be presenting complaint):

1. 70% **depressed** patients feel anxious (20-30% of apparent cases of anxiety are caused by underlying depression); 20-50% depressed patients have panic attacks (40%-90% patients with panic disorder become depressed).
2. Patients who experience **psychotic** disorganization often display considerable anxiety (may obscure underlying severe disturbance).
3. Anxiety is most common emotion experienced in **delirium** (frightened by sudden disruption of cognitive abilities)
4. Anxiety is common in **dementia** when mental syndromes are made worse by intercurrent illness or by sudden change in environment (e.g. change in roommate of hospitalized demented patient).
5. **Adjustment disorder**.

DIAGNOSIS

N.B. anxiety disorders have *one of longest differential diagnosis lists* of all psychiatric disorders!

When probability of causative general medical disorder is low:

- 1) CBC
- 2) chemistry profile
- 3) thyroid function tests
- 4) urinalysis
- 5) urine drug screen

PET - increased metabolism in *medial temporal lobe* and *insular cortex* during panic attacks.

TREATMENT

Anxiety merits treatment if following apply:

- 1) other causes are not identified
- 2) anxiety is very distressing and interferes with functioning
- 3) anxiety does not stop spontaneously within few days

LIFESTYLE

- discontinue **caffeine-containing products**.
- review **OTC preparations** and **herbal remedies** (*ephedrine* and other herbal compounds may precipitate / exacerbate anxiety).
- at least mild-to-moderate daily **exercise** program.

COGNITIVE BEHAVIORAL THERAPY

Effective for phobias (treatment of choice!), panic anxiety, generalized anxiety, situational anxiety, OCD.

- in mild cases, behavioral therapy alone is sufficient; drug therapy may be needed in more severe cases (SSRIs are first choice).

Systematic desensitization - patients are taught **deep muscle relaxation**; then taught to **visualize scene** involving thoughts that are opposite of anxious thinking such as feeling safe, relaxed, and in control; next, patients imagine anxiety-provoking situations.

- as soon as anxiety begins to emerge, scene that induces relaxation is revoked until anxiety ceases; anxiety-provoking and comforting scenes are repeatedly paired until thought of former no longer causes anxiety.
- beginning with situation that provokes least anxiety, patients gradually move up hierarchy of situations to ones that are most feared.
- when patients can visualize most anxiety-provoking scene while still feeling relaxed, less anxiety is experienced in corresponding real-life situation.
- to consolidate this gain, "**in vitro**" **desensitization** in physician's office must be followed by "**in vivo**" **desensitization** in actual situations by using combination of relaxation and exposure while again progressing from least to most anxiety-provoking situation.

Adjunctive behavioral techniques - useful for any type of anxiety.

Hypnosis helps patients concentrate on calming thoughts that are incompatible with anxiety.

Relaxation techniques: because individual cannot feel tense and relaxed at same time, any method that decreases tension tends to relieve anxiety.

Biofeedback is useful for patients who prefer to learn to relax with machine or without anyone else present; level of muscular tension (usually in forearm or frontalis muscles) is "fed back" through visual or auditory stimulus to help patients learn to decrease motor tension and, with it, anxiety.

For hyperventilation - **rebreath into paper bag** held over nose and mouth (CO₂ accumulates and reverses respiratory alkalosis).

OTHER PSYCHOTHERAPEUTIC APPROACHES

(interpersonal therapy, psychodynamic therapy, marital therapy, family therapy, group therapy)

Effective for **situational anxiety**, **generalized anxiety**, and **anxiety related to identifiable intrapsychic conflict**.

Not effective for **panic attacks** and **phobias**.

- psychotherapy may be facilitated by medication and behavioral techniques.
- encourage to talk about what stress means to patient (greater sense of mastery, which is incompatible with helplessness of anxiety, is facilitated by having patient put situation into words).

ANTI-ANXIETY AGENTS (MINOR TRANQUILIZERS)

- indicated for panic anxiety, generalized anxiety disorder, acute situational anxiety, agoraphobia, OCD, PTSD, and other anxiety disorders when they are not responses to specific trauma or conflict.

- also indicated if 3-month trial of psychotherapy and behavior therapy for treatment of exogenous anxiety is unsuccessful.
- drugs facilitate *psychotherapy* and *behavior therapy*.

1. Benzodiazepines – most effective anti-anxiety drugs!

- drugs of choice for short courses (< 6-8 weeks) - acute situational anxiety, adjustment disorder, anticipatory anxiety associated with panic attacks, generalized anxiety disorder, panic disorder.
- if long-term use of benzodiazepines seems necessary - obtain confirmatory opinion from second physician - chronic benzodiazepine is associated with **tolerance**, **withdrawal**, and **treatment-emergent anxiety!!!**
 - benzodiazepines are likely to interfere with cognitive-behavioral therapy!
 - avoid in patients with prior history of alcohol or other drug abuse.
 - closely monitor for unauthorized dose escalation or obtaining benzodiazepine prescriptions from multiple sources.

2. Antidepressants (esp. SSRI) – drugs of first choice for chronic use!

- effective for panic disorder, generalized anxiety, OCD, PTSD.
- do not interfere with cognitive-behavioral therapy.

3. BUSPIRONE used in long-term therapy of GENERALIZED ANXIETY disorders (efficacy comparable to benzodiazepines!); may require 1-2 weeks to reach therapeutic effect. see p. Rx3 >>**4. Barbiturates** - prescribed **only in very rare case** of patient who has been taking them for years and **cannot be withdrawn**.**5. Antihistamines** (e.g. **HYDROXYZINE**, **DIPHENHYDRAMINE**) - frequently used for **elderly** patients; not as effective as other anti-anxiety drugs.**6. Antipsychotics** - indicated only for anxiety **associated with psychoses**.**7. Anticonvulsants** (e.g. **DIVALPROEX**, **GABAPENTIN**) - have role in treatment (esp. in patients with high potential for abusing benzodiazepines).**8. β -blockers** (e.g. **PROPRANOLOL**) - for anxiety accompanied by **signs of adrenergic stimulation** (e.g. sweating, tremor) and for **performance anxiety** ("one dose for stage fright"); safe for long-term use; **ATENOLOL** may reduce social phobia.**9. Other: MEPROBAMATE** (largely replaced by benzodiazepines).**PSYCHOSURGERY**

- for rare cases of severe treatment-refractory OCD.

ELECTROCONVULSIVE THERAPY

- not effective.

- recurrent panic attacks (i.e. not all people who experience panic attack will develop panic disorder).

PANIC ATTACK – sudden unexpected **unprovoked (spontaneous)** episode of intense anxiety; anxiety does not have particular content associated with it (i.e. panic anxiety does not involve fear of any specific circumstance).

if panic attacks recur predictably in temporal relationship to trigger; these panic attacks usually implicate specific phobia-type diagnosis (e.g. social phobia)!

- reach peak within 10 minutes and subside in < 1 hour.
- may wake patients from sleep.
- **sense of dread** is most prominent psychological symptom - may be masked by or seem to be reaction to **PHYSICAL SYMPTOMS (autonomic arousal)** that frequently accompany panic attacks (to make DSM diagnosis, 4 of 13 must be present):
 - 1) palpitations, pounding heart, accelerated heart rate
 - 2) sweating
 - 3) trembling or shaking
 - 4) sense of shortness of breath or smothering
 - 5) feeling of choking
 - 6) chest pain or discomfort
 - 7) nausea or abdominal distress
 - 8) feeling dizzy, unsteady, lightheaded, or faint
 - 9) derealization (feelings of unreality) or depersonalization (feeling detached from oneself)
 - 10) fear of losing control or going crazy
 - 11) fear of dying
 - 12) numbness or tingling sensations
 - 13) chills or hot flashes

Although uncomfortable - at times extremely so - panic attacks are not medically dangerous!

- insight and judgment are intact!
- **physical examination** (to exclude physical disorder!!!) – nonspecific signs of *sympathetic hyperactivity*.

DSM-IV-TR criteria for panic disorder: at least one panic attack followed by ≥ 1 month worries about:

- a) having more panic attacks
- b) consequences of panic attack (e.g. that patient is losing control or having heart attack)
- c) change in behavior caused by panic attacks (e.g. not leaving house).

Clinical course may evolve gradually in **stages**:

1. **Subclinical** anxiety attacks
2. **Full-blown** panic attacks
3. **Hypochondriacal fears** of occult disease
4. Development of **anticipatory anxiety** about panic attacks
5. **Agoraphobia** (phobic anxiety toward places or situations in which escape may be difficult or embarrassing if panic did occur)

Note: AGORAPHOBIA is not stand-alone disorder; it is descriptive term [e.g. panic disorder with agoraphobia]
6. **Abuse** of drugs / alcohol to control anxiety
7. **Depression** (lifetime prevalence of major depression 50-60%)
8. **Social limitations**

- **women** : men = 2-3 : 1
- bimodal distribution of highest incidence: late adolescence and mid 30s.
- frequency of panic attacks varies from several attacks day to only few attacks year.
- **suicidal ideation / completed suicide** have been associated with panic disorder.
- etiopathophysiologic theories:
 - a) **serotonergic model** - exaggerated postsynaptic receptor response to synaptic serotonin, subsensitivity of 5HT_{1A} receptors.
 - b) **catecholamine model** - increased sensitivity to adrenergic CNS discharges, with hypersensitivity of presynaptic α_2 receptors.
 - c) **locus ceruleus model** - panic symptoms are due to increased local discharge resulting in adrenergic neuron stimulation, similar to more general catecholamine theory; locus ceruleus activity affects hypothalamic-pituitary-adrenal axis, which can respond abnormally to clonidine in patients with panic disorder.
 - d) **lactate model** - symptom production by postulated aberrant metabolic activity induced by lactate.
 - e) **false suffocation carbon dioxide hypothesis** - hypersensitive brainstem receptors.
 - f) **GABA model** - decreased inhibitory receptor sensitivity.
 - g) **neuroanatomic model** - panic attacks are mediated by "fear network" in brain that involves amygdala, hypothalamus, and brainstem centers.
 - h) **genetic hypothesis** has attempted to refer panic disorder to definable genetic loci, without success to date (heritability rates range 0.3-0.6%).

TREATMENT

Reassurance and calming environment + **antidepressant** (SSRIs are used as first-line agents for long-term management).

- all antidepressants (except bupropion) have been found effective for panic disorder; FDA approved: **VENLAFAXINE**, **IMIPRAMINE** (10 mg \times 3/d), **PAROXETINE**, **SERTRALINE**, **FLUOXETINE** (best if depression is present; may initially increase anxiety).
- control is gradually achieved over 2-4 weeks (*SSRIs can cause initial exacerbation of panic symptoms!* - begin with lowest dose with increase at follow-up visit).
- improvement should appear within 1 month; if improvement has not begun within 4-6 weeks \rightarrow **benzodiazepine**:
 - benzodiazepines act fast (preferable in ED) but carry liability of dependence (benzodiazepines can be reasonably used as initial adjunct, while SSRIs are titrated to effective dose).
 - may be used as *standing-dose* or *prn* schedules.
 - most widely used are:
 - ALPRAZOLAM** (0.5 mg \times 2/d; dosing may need to be increased up to 10 mg/d)
 - CLONAZEPAM** (1-5 mg/d).

Alprazolam has been widely used, but it is currently discouraged because of its higher dependence potential. Clonazepam has become favored replacement - longer half-life and fewer withdrawal reactions.
- **refractory panic disorder** – try β -blockers, CLONIDINE, calcium channel blockers, antipsychotics, BUSPIRONE, anticonvulsants (DIVALPROEX, GABAPENTIN).

Panic control therapy (modification of **cognitive behavioral therapy**) - redefining *symptoms of panic attack* (such as dizziness or shortness of breath) as *harmless physiologic responses* to anxiety rather than signs of catastrophic illness.

N.B. psychodynamic psychotherapy is not effective!

- facilitated by actual induction of panic symptoms (e.g. by spinning patient around in chair to produce dizziness).
- behavioral therapy is especially useful for agoraphobia (it rarely responds to drugs, because patients often continue to fear they might have panic attack, even long after their panic has been well controlled by drug therapy) - patients are told:
 - 1) not to avoid situations
 - 2) to understand that their worries are unfounded
 - 3) to respond instead with slow, controlled breathing (or other methods that promote relaxation).

Combination approach (psychotherapy + pharmacotherapy) yields superior results to either single modality!

GENERALIZED ANXIETY DISORDER (GAD)

GENERALIZED ANXIETY – persistent excessive (unrealistic) worry about **many* actual life circumstances / events / conflicts** (i.e. fear of specific but multiple circumstances).

*multiple (≥ 2) worries, which often shift over time (i.e. focus of worry is broader than in other anxiety disorders)

- worrying is difficult to control!
- often begins in childhood ÷ adolescence (but may begin at any age).
- course is fluctuating and chronic, with worsening during stress.
- most patients have other **comorbid psychiatric disorders** (major depression, specific phobia, social phobia, panic disorder).
- suicidal ideation / completed **suicide** have been associated with GAD.

DSM-IV criteria: at least 6 months of almost daily generalized anxiety accompanied by at least three of six additional symptoms of anxiety:

- a) restlessness or feeling keyed up [angl. *sujaudinimas*]
- b) easy fatigability
- c) difficulty concentrating or mind going blank
- d) irritability
- e) muscle tension
- f) insomnia.

- PANIC ANXIETY and GENERALIZED ANXIETY often accompany each other:
 - subpanic anxiety may mimic generalized anxiety;
 - anticipatory anxiety is type of generalized anxiety.

TREATMENT

1. **SSRI**; FDA approved: **VENLAFAXINE, ESCITALOPRAM, PAROXETINE, DULOXETINE**.
 2. **Benzodiazepines** - rapidly effective (start with SSRI; once antidepressant becomes effective, benzodiazepine is tapered).
 3. **BUSPIRONE** (alternative to SSRI) – FDA approved.
 4. **β -blockers**.
- 30% patients do not recover with appropriate pharmacotherapy - diagnosis may be incorrect (e.g. patient may have anxiety secondary to personality disorder, depression, or psychosis), or anxiety may be caused by medical or substance-related disorder.

Relaxation training (!), hypnosis, biofeedback, psychotherapy (supportive and cognitive-behavioral) is challenging because of diffuse focus of symptoms.

OBSESSIVE-COMPULSIVE DISORDER (OCD)

DEFINITIONS

OBSESSIONS - unwanted and bothersome recurrent (persistent) ideas, images, and impulses that intrude upon patient and cannot be pushed out of consciousness.

- obsessions are experienced as senseless or repugnant and **patient tries to ignore or resist** them.
- if **poor insight** is present, patients do not view obsession as absurd; if poor insight reaches **delusional** proportions, patients are convinced that obsessions are realistic or justified.

COMPULSION - irresistible need to perform activity (obsessions and compulsions usually go together).

RITUALS - stereotyped repetitive behaviors (physical or mental actions) that must be performed with subjective sense of necessity (to *ward off unwanted future happenings* or to *satisfy obsession*) and often have symbolic meaning.

- may be physical (e.g. handwashing) or mental (e.g. repeating series of numbers to oneself).
- these activities may consume patient's whole day, rendering him unable to complete any necessary task.
- connection between obsessions and compulsions may have element of logic (e.g. hand washing to avoid disease), in other cases, relationship may be illogical and idiosyncratic (e.g. counting to 50 over and over to prevent grandpa from having heart attack).
- anxiety may be associated with obsession, and ritual performance may temporarily relieve this anxiety.

To differentiate OCD from psychosis, patient must realize that thoughts or behaviors are irrational.

DSM-IV criteria: individual expresses either obsessions or compulsions.

OBSESSIONS are defined by following 4 criteria.

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

COMPULSIONS are defined by following 2 criteria:

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

- at some point during course of disorder, **person recognizes** that obsessions or compulsions are **excessive or unreasonable**; this does not apply to children.
- obsessions or compulsions cause **marked distress**; are **time consuming** (take > 1 h/d); or **significantly interfere** with person's normal routine, occupational or academic functioning, or usual social activities or relationships.
- if *another Axis I disorder is present*, content of obsessions or compulsions is **not restricted to it** (such as preoccupation with food and weight in presence of eating disorder, hair pulling in presence of trichotillomania, concern with appearance in body dysmorphic disorder, preoccupation with drugs in substance use disorder, preoccupation with having serious illness in hypochondriasis, preoccupation with sexual urges in paraphilia, or guilty ruminations in presence of major depressive disorder).
- disorder is not due to direct physiologic effects of *substance* or *general medical condition*.
- additional specification of "**with poor insight**" is made if, for most of current episode, person does not recognize that symptoms are excessive or unreasonable.

EPIDEMIOLOGY, ETIOLOGY

- 2% of the global population (one of the highest global burdens of psychiatric disability).
- males ≈ females.
- usual onset - 10-24 years.
- **concordance** for monozygotic twins 80-87% (vs. 47-50% for dizygotic twins).
- few pediatric cases are thought to be associated with group A β-hemolytic streptococcal infections - **pediatric autoimmune neuropsychiatric disorder associated with streptococcus (PANDAS)**; H: early antibiotics.

CLINICAL FEATURES

- **comorbid psychiatric disorders** are common (esp. depression, Gilles de la Tourette's syndrome).
- OCD is chronic disorder; without treatment, symptoms may wax and wane but rarely remit spontaneously.
- OCD may be quite disabling.
- obsessions and related compulsions often fall into common categories:

Obsessions	Associated Compulsions
Fear of contamination – often first obsession!!!	Washing, cleaning
Need for symmetry, precise arranging	Ordering, arranging, balancing, straightening until "just right"
Unwanted sexual or aggressive thoughts or images	Checking, praying, “undoing” actions, asking for reassurance
Doubts (e.g. gas jets off, doors locked)	Repeated checking behaviors
Concerns about throwing away something valuable	Hoarding

- individuals often have obsessions and compulsions in several categories.
- **severity is scored** with **Yale and Brown OCD Scale (YBOCS)** - 40-item scale in which patients answer 20 questions related to obsessions and 20 related to compulsions - high scores are associated with more severe OCD symptoms.

TREATMENT

Antidepressants in high doses (reduce symptoms but do not cure them; clinical response may take 6-10 weeks to become apparent!):

- a) **SSRI**; FDA approved: **FLUOXETINE, SERTRALINE, PAROXETINE, FLUVOXAMINE.**
- b) serotonergic **tricyclic** – **CLOMIPRAMINE** (FDA approved for OCD).
- c) serotonin-norepinephrine reuptake inhibitors: **VENLAFAXINE, DULOXETINE.**

N.B. serotonin abnormalities are involved in OCD!

- only ½ patients experience symptom reductions of 30-50%; others fail to achieve even this degree of relief.

Cognitive behavioral psychotherapy – first line therapy for OCD (more effective than drugs!!!)

Exposure and response prevention (ERP) - patients are exposed to stimulus that evokes rituals (e.g. touching toilet seat) and are then helped to refrain from engaging in compulsive behavior (e.g. handwashing) for increasing lengths of time while using adjunctive techniques to control resulting anxiety.

"Stop thinking" - **mental variant** of response prevention in which patients repeat obsessive thought until it seems overwhelming and then terminate thought while saying "stop" out loud.

- benefit of behavior therapy persists for ≥ 6 years after completion (vs. symptoms usually return rapidly after medication discontinuation).

Psychosurgery - for severe, treatment-refractory OCD (40-60% patients):

To disrupt pathological activity between **thalamus and orbitofrontal cortex**, and between **caudate and lenticular nucleus** - play a significant role in mediating OCD symptoms (functional neuroimaging consistently reports hyperactive cortico-striato-thalamo-cortical circuits in patients with OCD; this aberrant activity appears to be significantly reduced in successfully treated patients)

- a) **anterior cingulotomy** to interrupt *orbitofrontal-subcortical circuit* (that mediates strong emotions and autonomic responses to those emotions) - stereotactic placement of bilateral lesions in anterior cingulate cortex; may be done with SRS – risk of **akinetie mutism** (anterior cingulate syndrome).
- b) **anterior capsulotomy** – established and most effective procedure; first reported by Talairach in France in 1949; may be done with SRS.
- c) **deep brain stimulation** – targets must be **bilateral!**:
 - 1) **anterior limb of internal capsule (ALIC)** is approved by FDA (2009) for OCD, i.e. Medtronic Reclaim® DBS Therapy.
FDA approval: bilateral stimulation of ALIC as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant OCD in adults who have failed at least three SSRIs.
 - 2) bilateral **subthalamic nucleus** (Level I evidence); target 2 mm anterior and 1 mm medial to target commonly used in Parkinson disease.
 - 3) bilateral **nucleus accumbens s. VC/VS (ventral capsule/ventral striatum)** (Level II evidence)

DBS of VC/VS (NAcc area) vs. anterior capsulotomy

Pepper JJ, Hariz M, Zrinzo L. “Deep brain stimulation versus anterior capsulotomy for obsessive-compulsive disorder: a review of the literature”, *J Neurosurg.* 2015 May;122(5):1028-37

- 20 studies reporting on 170 patients.
- DBS of VC/VS and NAcc area → 40% decrease in YBOCS score.
- Anterior capsulotomy (AC) → 51% decrease in YBOCS score (p = 0.004).
- AC patients were 9% more likely to go into remission than DBS patients (p = 0.02).
N.B. DBS patients had significantly worse preoperative YBOCS scores (33 vs. 30) and longer duration of OCD.
- complication rates: AC patients were 25% more likely to have clinically significant **weight gain** (p = 0.0002); **wound infection** was 5% more common after DBS than after AC (p = 0.02).

PHOBIC DISORDERS

PHOBIA - **persistent, unreasonable (irrational), intense fear** in response to *presence* or *anticipation* of situations, circumstances, or objects.

- although phobia is recognized (by patient) as inappropriate, phobic stimulus is **consciously avoided** or **endured only with intense distress** (if not having companion nearby, anxiety may intensify to level of panic attack).
- females : males = 2-3 : 1 (more men seek for social phobia treatment - due to career issues).

CLASSIFICATION

I. AGORAPHOBIA

("fear of market place") - fear about being in *situations* from which *escape might be difficult or embarrassing* or for which *help may not be available* in event of panic or other forms of discomfort or distress.

Note: 75% patients have panic disorder [*PANIC DISORDER WITH AGORAPHOBIA*]

- **common agoraphobic situations:** being away from home, sitting in middle of row of seats in theater, being on bridge or in elevator, traveling in car or airplane.

II. SOCIAL PHOBIA

- fear of *interpersonal situations* (i.e. fear of humiliating oneself in social or performance situations that involve social scrutiny).

- often patient concerns that his anxiety will be apparent through sweating, blushing, vomiting, or trembling (sometimes as quavering voice) or that ability to keep train of thought or find words to express themselves will be lost.
- panic attacks may occur in social situations.
- school refusal is often presentation in children.
- patients have substantial *associated morbidity* (suicidal ideation, social isolation, substance abuse).

Agoraphobia and social phobia are also classified as **GENERAL PHOBIAS** (vs. **SPECIFIC PHOBIAS**)

Less impairment is observed in specific phobias than in general phobias.

III. SPECIFIC PHOBIAS

- phobia of *specific object / situation* (often that many normal people may find uncomfortable).

1. **Animal type** - fear of animals or insects; usually begins in childhood.
2. **Natural environmental type** - fear of storms, height, etc.; usually begins in childhood.
3. **Blood-injection-injury type** - fear of seeing blood or injury or receiving injection; often **familial** and associated with **vasovagal syncope** (unlike other phobias).
4. **Situational type** - fear of specific situations (such as elevators, bridges, enclosed places) but without panic disorder or other agoraphobic symptoms; similar to panic disorder with agoraphobia in age of onset, familial aggregation, and sex ratios.
5. **Other type** - fears of other stimuli:
space phobia - fear of falling if not near wall or other means of physical support

Phobia	Object
Acrophobia	heights
Amatophobia	dust
Astraphobia	thunder and lightning
Aviophobia	flying
Belonephobia	needles, pins, or other sharp objects
Brontophobia	thunder
Claustrophobia	confined spaces
Eurotophobia	female genitals
Gephyrophobia	crossing bridges
Hemophobia	blood
Hydrophobia	water
Odontiatophobia	dentists
Ophidiophobia	snakes
Phartophobia	passing gas in public place
Phasmophobia	ghosts
Phobophobia	having fears or developing phobia
Spargarophobia	asparagus
Triskaidekaphobia	all things associated with number thirteen
Trypanophobia	injections
Zoophobia	animals (usually spiders, snakes, or mice)

TREATMENT

Cognitive behavior therapy is treatment of choice - de-linking specific response from stimulus:

Graduated "in vivo" exposure places phobic patients (who are usually accompanied by family member, friend, or physician for reassurance) in situations that evoke anxiety → anxiety is gradually relieved through process called habituation;

- if patient becomes overwhelmingly anxious in phobic situation → start with **systematic desensitization**. *see above*
- relaxation techniques and hypnosis are used to change association between phobic situations and anxiety to association of those situations with relaxation and control.

SOCIAL PHOBIA – **cognitive behavior therapy** ± **antidepressants** (SSRIs*, MAO inhibitors) for at least 6-12 months (→ taper), group therapy, occasionally **β-blockers** (for short term on prn basis, e.g. before public performance; **PROPRANOLOL** 10-40 mg PO is generally preferred).

*FDA approved: **PAROXETINE**, **SERTRALINE**, **VENLAFAXINE**

SPECIFIC PHOBIAS – **cognitive behavioral therapy**.

AGORAPHOBIA → see *PANIC DISORDER* >>

PROGNOSIS

- if untreated:

AGORAPHOBIA waxes and wanes; may disappear, because some affected people conduct their own form of exposure therapy.

SOCIAL PHOBIA - almost always chronic.

SPECIFIC PHOBIAS - prognosis is variable (it may be easy to avoid situation or object that causes fear).

SCHOOL REFUSAL (s. SCHOOL PHOBIA)

- **most common manifestation of pediatric anxiety disorders!!!**

SCHOOL REFUSAL largely supplanted term **"SCHOOL PHOBIA"**.

- children who refuse to go to school have:
 - a) **separation anxiety** ("I am worried that I will never see you again"); separation anxiety suffered by parent also may manifest as school refusal.
 - b) **social phobia** ("I am worried kids will laugh at me").
 - c) **panic disorder** (e.g. homosexual panic in older child).
 - d) schizophrenia.
 - e) malingering (e.g. child has not completed homework assignment).
 - f) legitimate cause (e.g. gangs, cruel teacher).
- most children state their discomfort in terms of **somatic complaints**: "I cannot go to school because I have stomachache"; such complaint can lead to some confusion because child is often telling truth - upset stomach, nausea, and headaches often develop in children with anxiety!
 School phobia is "great imitator"!
- after physical disease is excluded, **child should be sent back to school immediately** so that school avoidance is not reinforced by staying home.

- **psychotherapy** for parents and child (\pm short term **anxiolytics**) are helpful.

POSTTRAUMATIC STRESS DISORDER (PTSD)

- **pathological anxiety that develops after exposure** to events / circumstances that involved actual death / injury / threat to physical integrity of oneself / others and **that evoked** intense fear / helplessness / horror.

- for **children**, *developmentally inappropriate sexual experience* may be considered traumatic event (even if not involved violence or physical injury).
- may appear immediately or may be delayed for ≥ 6 months (**PTSD with delayed onset**).
- **symptoms** (**last > 1 month**; if last > 3 months = **chronic PTSD**):
 - 1) **reexperiencing initial trauma**:
 - a) **intrusive memories** of event.
 - b) **nightmares** about trauma.
 - c) spontaneous or triggered **flashbacks** (dissociative states in which events are relived as if happening).
e.g. loud noises of fireworks might trigger flashback of being in combat, which in turn might cause patients to seek shelter or prostrate themselves on ground for protection
 - d) intense **psychologic distress** with internal or external cues to trauma.
 - e) **physiological reactivity on exposure** to trauma cues.
 - f) children reexperience event through repetitive play.
 - 2) **avoidance** of stimuli associated with trauma; **emotional numbing**;
 - a) avoidance of thoughts or conversation related to trauma
 - b) avoidance of activities, places, or people related to trauma
 - c) amnesia for important trauma-related events
 - d) decreased participation in significant activities
 - e) feeling detached or estranged from others
 - f) restricted affect
 - g) foreshortened sense of future.
“**Emotional numbing**” - general lack of interest, social withdrawal, subjective sense of feeling “numb”, foreshortened expectation of future (e.g. “I will not live to see 20”).
 - 3) **hyperarousal**:
 - a) difficulty staying or falling asleep
 - b) irritability or anger outbursts
 - c) difficulty concentrating
 - d) hypervigilance
 - e) exaggerated startle response.

- often associated with **war veterans** ($\approx 30\%$ people who have spent time in war zone experience PTSD), but also seen in individuals who have **witnessed murder**, and victims of **sexual assault**.
- over time, untreated and undertreated individuals are susceptible to *deterioration of personal and work relationships* and to development of *substance abuse or dependence*.
- patients are at risk of committing *suicide*.
- **AMYGDALA** activation is key feature implicated in PTSD; **orbitofrontal cortex** normally exerts inhibiting effect on this activation.

TREATMENT

- many treated individuals recover completely (or nearly completely).

Exposure psychotherapy (group therapy may be helpful)

- *discussion of trauma* as means of achieving retroactive mastery.
- *confrontations with perpetrators* can be helpful.
- *desensitization to situations* that evoke reexperiencing or avoidance is often necessary (e.g. flooding, technique involving prolonged exposure to adverse stimuli, has been used with some success on veterans).
- legal trial processes may add more pain.

Adjunctive techniques – **biofeedback**, **medications**:

- a) **SSRIs** (effective for reexperiencing and emotional numbing, not effective for hyperarousal; FDA approved: **SERTRALINE**, **PAROXETINE**)
- b) **CARBAMAZEPINE**
- c) **β -blockers** (control hyperarousal symptoms).
- d) **PRAZOSIN** – effective for insomnia in PTSD patients.

Surgical treatment

- case report of **right amygdala laser ablation** (for concurrent epilepsy) successfully palliating PTSD.

ACUTE STRESS DISORDER (ASD)

- diagnosis new to DSM-IV.
- traumatic event is defined exactly as in PTSD.
- **symptoms**:
 - 1) **reexperiencing** *see PTSD >>*
 - 2) **avoidance** *see PTSD >>*
 - 3) **arousal** *see PTSD >>*
 - 4) acute or delayed **dissociative symptoms** – at least 3 of following [must include a)]:
 - a) emotional numbing (detachment or absence of emotional responsiveness)
 - b) decreased awareness of surroundings (e.g. feeling in daze)
 - c) derealization
 - d) depersonalization
 - e) dissociative amnesia (unable to remember significant parts of event).
- ASD **begins within 1 month of event** and **lasts** 2 days \div 4 weeks; if lasts ≥ 1 month \rightarrow diagnosis is changed to PTSD (ASD may be just variant or, at most, precursor of PTSD).

TREATMENT

- to prevent / minimize ASD, some experts recommend **systematic debriefing*** to assist people who were involved in or witnessed traumatic event as they process what has happened and reflect on its effect; other experts concern that CISD may be quite distressful for some patients, and may even impede natural recovery.
*called **critical incident stress debriefing (CISD)**.
- only recommended **drugs** – for sleep improvement.

OTHER

- anxiety symptoms do not meet criteria for specific DSM-IV diagnosis but still cause significant distress or disability.

- psychotherapy is effective!

ADJUSTMENT DISORDER

- after exposure to obvious stress*, patients experience anxiety / depression/ impairment in excess of that which would normally be expected.

*that most people would consider upsetting but not life-threatening (unlike stress disorders); divorce and geographic relocation are examples

- symptoms appear soon (within 3 months) after event (i.e. extreme acute response to environmental stress).
- symptoms resolve within 6 months after stress is over.

SITUATIONAL ANXIETY

- even relatively minor situation is overwhelming because it recalls other situations in which individual was unable to cope or that aroused unresolved conflict.

- relatively well-adjusted patient may experience only transient symptoms, whereas underlying psychosis may be precipitated in more marginally compensated patient.

ANXIETY ABOUT DEATH

- even nonfatal illnesses may remind individuals of their mortality.

- reassure that patient will not be left alone and in pain.

ANXIETY ABOUT MUTILATION, LOSS OF PROWESS, LOSS OF ATTRACTIVENESS

- common in patients who feel that love, approval, and self-esteem are dependent on their strength or beauty.

- patients become anxious if illness threatens their appearance or prowess.
- patients may attempt self-reassurance by demonstrating attractiveness (e.g. by behaving seductively) or strength (e.g. by exercising conspicuously) in inappropriate or even dangerous ways.

ANXIETY ABOUT LOSS OF SELF-ESTEEM

- common in patients whose self-esteem is fragile.

- patients experience illness as imperfection, weakness, or failure → attempts to bolster sense of self-worth by boasting about importance and superiority (e.g. insisting on being treated only by most senior or well-known physician and treating others as worthless inferiors).
- patient should be approached with appropriate deference (e.g. telephone for patient in intensive care unit during acute illness should be granted).

SEPARATION ANXIETY

- persistent, intense, and developmentally inappropriate fear of separation from major attachment figure (e.g. mother in pediatric patients).

- patient groups:
 - a) children > 24 months (N.B. separation anxiety is normal emotion in children 8-24 months – because of incomplete memory and no sense of time, children fear that departure of their parents is permanent)
 - b) regressed adults (function psychologically more as children than as adults) become frightened when they are separated from important caregivers.
 - commonly encountered in physically ill people, as well as in overly dependent individuals and some patients with psychotic and personality disorders.
- when separation is forced, patients are distressfully preoccupied with reunification.
- separation distress may be expressed *directly* (as anxiety) or *indirectly* (complaints of pain, when left alone - calls for assistance with trivial matters; in children – school refusal).
- separation scenes are typically painful for both mother and child.
 - child often wails and pleads with such desperation that mother is unable to leave, child often develops somatic complaints.
 - child's demeanor is normal when mother is present (this can give false impression that problem is of minor consequence).

MANAGEMENT

- behavioral therapy ± SSRIs.
 - regular separations are systematically enforced.
 - goodbye scenes should be kept as brief as possible (parent should leave without responding at length to child's crying).
 - separation anxiety is worse when child is hungry or tired (feeding child and letting him nap before leaving may help).
 - encourage person with whom parents are leaving child to create distractions.
 - successfully treated children are prone to relapses after holidays.
- for acutely hospitalized patients:
 - family and close friends should be encouraged to be with patient as much as possible, and unrestricted visiting should be allowed.
 - nursing staff should be encouraged to visit patient frequently for brief periods before patient asks for help to avoid teaching patient that only way not to be left alone is to complain (patient's room should be close to nurse's station to facilitate frequent, brief visits).
 - roommate should be provided.

STRANGER ANXIETY

- patients who suffer from separation anxiety also may react adversely to unfamiliar people (e.g. hospitalized patient feels distress at hospital staff shift changes).

- normal in children 8-24 months - manifested by crying when unfamiliar person approaches (even grandparents may suddenly be viewed as strangers).

MANAGEMENT

- if stranger (e.g. grandparent) is coming to watch child for few days while parents go away, he should arrive day or two early and spend some time with family.
- for acutely hospitalized patients:
 - as much continuity in personnel as possible (e.g. same nurse to patient each day).
 - unfamiliar visitors should be limited, changes in roommates minimized.

ANXIETY ABOUT LOSS OF CONTROL

- illness / hospitalization may be threatening to people who have strong need to feel in complete control of their life and environment.
- patient may attempt to gain sense of control by refusing to comply with physician's advice, by becoming excessively demanding, by making physician feel helpless, or by otherwise asserting control over those who are in caregiving role or who are healthy.
- management: patient should be allowed as much control as possible over his treatment (e.g. patient should be consulted about which treatment schedules seem most reasonable to him).

ANXIETY ABOUT DEPENDENCY

- patients who fear loss of control also commonly have anxiety about being dependent on others.
- fear of dependency is common in people whose normal dependency needs were not met in childhood (e.g. because of parental illness or unavailability).
- patients may become hostile toward potential caregivers, may ignore signs of increasing illness.
- management: reassure that illness and dependency required by it are temporary.

ANXIETY ABOUT INTIMACY

- patients with concerns about dependency may also be afraid of becoming too close emotionally to caregivers or loved ones.
- to protect themselves, they maintain greater-than-normal emotional distance or even hostility.
- management: intimacy should not be forced; patient's sense of formality (e.g. by always using patient's last name) should be respected.

ANXIETY ABOUT BEING PUNISHED

- patients with underlying sense of guilt about real or imagined transgressions may have conscious or unconscious expectation of punishment.
- patients attempt to relieve guilt (or avoid worry about when they will be punished) by self-inflicted punishment (e.g. through unhappy marriage, repeated accidents, not recovering from illness, and other self-destructive behaviors).
- management: attempt to uncover source of their guilt (expressive psychotherapy).

SIGNAL ANXIETY

- when awareness of previously unconscious, unresolved psychological conflict is stimulated by some external occurrence (e.g. patient had mixed feelings about parent and patient's age is same as that of parent at time of death), anxiety may signal emergence of conflict.
- this anxiety calls forth unconscious **psychological defenses (ego defenses)** - help to avoid anxiety by keeping conflict out of patient's awareness:
 - repression (forgetting)** - automatic process by which memories, thoughts, feelings are excluded from awareness.
 - rationalization** - explaining away psychologically meaningful data (e.g. "I'm anxious only because of low blood sugar").
 - reaction formation** - feeling opposite of one's true emotion in order not to be aware of it (e.g. experiencing excessive affection toward someone who actually elicits hostility).
 - isolation of affect** - experiencing content of thought without its associated emotions.
 - denial** - remaining unaware of some aspect of reality (e.g. feeling that one does not have to be afraid of consequences of illness because one is not really sick).
 - projection** - attributing one's own motives to someone else.
 - projective identification** - incompletely projecting intense emotional state (usually anger) onto another individual while inducing emotion in object of projection through provoking behavior → patient then experiences original emotion, but he feels that only reason he has emotion or thought is that he is attempting to protect himself from other individual's affect.
- management: attempt to *resolve underlying conflict*.
 - when patients cannot tolerate awareness of their motives, they should be helped to *develop less disabling defenses* against them (e.g. isolation of affect rather than denial of it, or denial of anxiety rather than denial of situation that causes it).
 - behavioral and adjunctive measures (e.g. relaxation training) may help lessen signal anxiety.

BIBLIOGRAPHY for ch. "Psychiatry" → follow this [LINK >>](#)