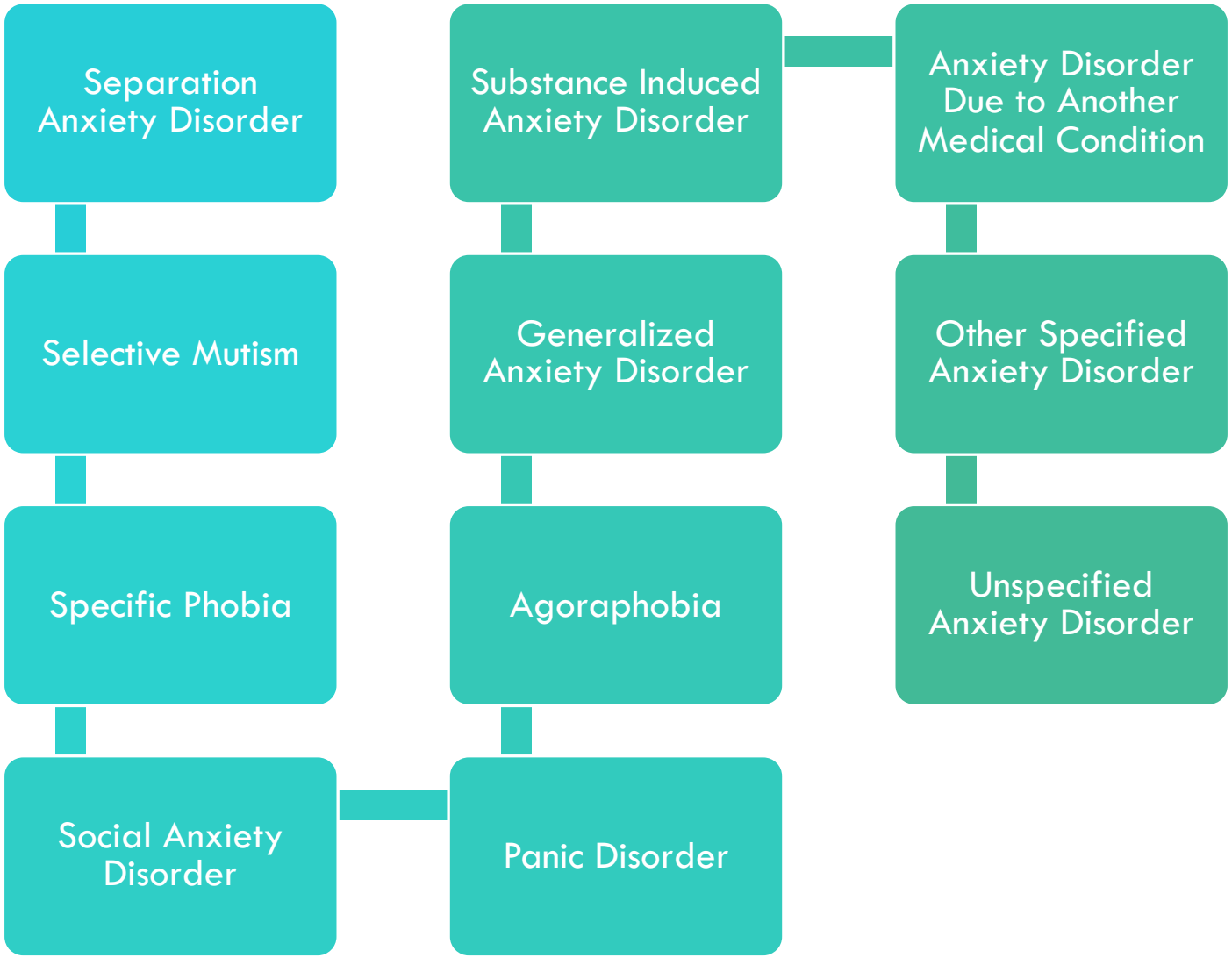
ANXIETY DISORDERS

RC Rounds – Dr. A. Jewett

OVERVIEW OF ANXIETY DISORDERS



Focus on **attachment figure**
3 of distress over separation, losing them, something bad happening, refusal to leave home, no sleepovers, **nightmares**, somatic complaints
At least **4 weeks in kids, 6 mo in adults**

SEPARATION ANXIETY DISORDER

Developmentally inappropriate and excessive fear of anxiety concerning separation from those to whom the individual is attached, as evidence by at least three of the following:

- Recurrent excessive distress when anticipating or experiencing separation from home or from major attachment figures
- Persistent and excessive worry about losing major attachment figures or about possible harm to them such as illness, injury, disasters, and death
- Persistent and excessive worry about experiencing an untoward event (ie. Getting lost, being kidnapped, having an accident, becoming ill) that causes separation from major attachment figures
- Persistent reluctance or refusal to go out, away from home, to school, to work or elsewhere because of fear of separation
- Persistent and excessive fear of or reluctance about being alone or without major attachment figures at home or in other settings
- Persistent reluctance or refusal to sleep away from home or to go to sleep without being near a major attachment figure
- Repeated nightmares involving the theme of separation
- Repeated complaints of physical symptoms (ie. Headaches, stomachaches, nausea, vomiting) when separation from major attachment figures occurs or is anticipated

The fear, anxiety, or avoidance is persistent, lasting at least 4 weeks in children and adolescents and typically 6 mo or more in adults

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

The disturbance is not better explained by another mental disorder, such as refusing to leave home because of excessive resistance to change in autism spectrum disorder, delusions or hallucinations concerning separation in psychotic disorders; refusal to go outside without a trusted companion in agoraphobia, worries about ill health as in GAD etc.

4% of kids, 1.6% adolescents, 1% adults
Most common anxiety disorder in kids under 12
Majority do not go on to have anxiety disorders

SEPARATION ANXIETY DISORDER

At least 4 weeks in children and adolescents under age 18, 6 mo in adults	When alone, especially in the evening or the dark, young children may report unusual perceptual experiences like seeing people peering into their room, frightening creatures reaching for them	May be children who are described as demanding, intrusive, in need of constant attention	As adults – dependent or overprotective
In children 4%, in adolescents 1.6%, in adults 0.9-1.9%	Most prevalent anxiety disorder in children under 12	Clinical samples – M=F, community more F	Onset may be as early as preschool age, can occur anytime in childhood
In some, may persist through adulthood; however, the MAJORITY of children are free of impairing anxiety disorders over their lifetime	Younger children may be more reluctant to go to school, less likely to describe fears	As they get older, worries emerge, specific dangers	Adults with this disorder are typically overconcerned about their offspring and spouses, marked discomfort when separated

Separation anxiety may be heritable (73%)
Reluctance to attend school, nightmares, somatic complaints
Highly comorbid with GAD and specific phobia in kids

SEPARATION ANXIETY DISORDER

Risk factors:

- **Life stress, especially a loss, divorce, move, disaster**
- In young adults – leaving parental home, entering romantic relationship, becoming a parent
- **Parental overprotection and intrusiveness** may be associated with separation anxiety disorder
- May be heritable – 73% in one study, **higher rates in girls**
- Children with separation anxiety disorder display particularly enhanced sensitivity to respiratory stimulation using CO_2 enriched air

Wide variation in cultures, must differentiate separation anxiety from high value some cultures place on interdependence in families

Girls have more reluctance to attend or avoid school than boys

Indirect expression of fear more in males – ie. Limited independent activity, reluctance to be away from home, distress when contact with spouse or offspring is not possible

May be associated with **increased risk for suicide** – not unique to separation anxiety

Different from GAD → worries specific to attachment figures

Not SAD → school avoidance is from **fear of being judged negatively** by others rather than to worries about being separated

Highly comorbid with GAD and specific phobia in children

In adults → specific phobia, PTSD, panic disorder, generalized anxiety disorder, social anxiety disorder, agoraphobia, OCD, and PDs; also depression and bipolar

SELECTIVE MUTISM

Consistent failure to speak in specific social situations in which there is an expectation for speaking (ie. At school) despite speaking in other situations

The disturbance interferes with educational or occupational achievement or with social communication

The duration of the disturbance is at least 1 mo (not limited to the first month of school)

The failure to speak is not attributable to lack of knowledge of or comfort with the spoken language required in the situation

The disturbance is not better explained by a communication disorder (ie. Childhood onset fluency disorder) and does not occur exclusively during the course of autism spectrum disorder, schizophrenia, or another psychotic disorder

Relatively rare, 0.03-1%
Onset by age 5
Very comorbid with SAD
Overprotective parent

SELECTIVE MUTISM

- Will speak at home in presence of immediate family members, but often not even close friends or other relatives
- High social anxiety
- Often will use nonverbal means to communicate
- Excessive shyness, fear of embarrassment, social isolation, withdrawal, clinging, compulsive traits, negativism, temper tantrums, oppositional behavior
- Generally have normal language skills but can have a communication disorder too – anxiety piece is key
- In clinical settings, almost always given an additional dx of another anxiety disorder (most common social anxiety disorder)
- Relatively rare, point prevalence 0.03-1%
- Does not vary by sex or ethnicity, more in young children than adolescents/adults
- Onset usually before age 5 but typically not recognized until school entry
- Many individuals outgrow clinically, longitudinal course is unknown → most continue to have social anxiety
- Some children who are speaking a second language may refuse to speak because of lack of knowledge of language → not purely selective mutism
- Can cause severe impairment in school and social life
- **Most common comorbid condition = social anxiety disorder**
- Different from other communication disorders in that it is situation specific
- Risk factors:
  - Negative affectivity or behavioral inhibition
  - Parental history of shyness, social isolation, social anxiety
  - Subtle receptive language difficulties
  - Social inhibition on part of parents
  - Overcontrolling or overprotective parents – even more than other anxiety disorders
  - Shared genetics with social anxiety disorders

Scary thing
Provokes fear, avoids, excessive
6 months or more
Animal, disaster, blood, situations, choking or vomiting

SPECIFIC PHOBIA

Marked fear or anxiety about a specific object or situation (ie. Flying, heights, animals, receiving an injection, seeing blood) – in kids may be crying, tantrums, freezing

The phobic object or situation almost always provokes immediate fear or anxiety

The phobic object or situation is actively avoided or endured with intense fear or anxiety

The fear or anxiety is out of proportion to the actual danger posed by the object or situation and cultural context

The fear, anxiety, or avoidance is persistent, typically lasting for 6 mo or more

The fear, anxiety, or avoidance causes clinically significant distress or impairment

Not better explained by sx of another mental disorder

Code based on phobic stimulus:

- Animal (spiders, insects, dogs)
- Natural environment (heights, storms, water)
- Blood-injection-injury (needles, invasive medical procedures, blood, injury)
- Situational (airplanes, elevators, enclosed places)
- Other (choking or vomiting, loud sounds, costumed characters)

75% have more than 1, most have 3
Prevalence 7-9%, highest in adolescence, but still one of most common in elderly
Females more than males
Onset age 10

SPECIFIC PHOBIA

Common to have multiple phobias; the average person with specific phobia has THREE

75% have more than one phobia

People with situational, natural environment, and animal phobias → sympathetic nervous system arousal

Blood-injection-injury → vasovagal fainting or near-fainting response

Emphasis on amygdala

Prevalence is 7-9%

5% in children, 16% in 13-17 year olds, lower rates in older individuals (3-5%) → likely diminished severity to subclinical levels

Females more than males (2:1), rates vary across stimuli (animal, natural environment, situational specific phobias more in females, **BII phobia equal in both genders**)

Sometimes occurs after traumatic event but often they cannot remember the reason for onset of phobias

Develops in early childhood, **majority before age 10**; median age of onset 7-11

Situational specific phobias later age of onset

Phobias that persist into adulthood are unlikely to remit for the majority of individuals

In children, fear may be expressed as crying, freezing, or clinging; they also are unable to understand concept of avoidance

Fears very common in children, but usually transient, do not meet time criteria

Though prevalence in lower in older populations, it is **one of the more commonly experienced disorders in late life**

- May be more likely to endorse natural environment specific phobias or phobia of falling
- Tends to co-occur with medical concerns including CAD, COPD
- More likely to attribute anxiety symptoms to medical conditions
- More likely to manifest anxiety in an atypical manner (anxiety and depression)
- Associated with decreased quality of life and may be a risk factor for a major NCD

High risk of suicide, likely due to comorbidities
Phobia specific genetics
More phobias more impairment
Why not agoraphobia
Lots of comorbidities, for elderly - depression

SPECIFIC PHOBIA

Risk factors:

- Negative affectivity or behavioral inhibition
- Parental overprotectiveness, parental loss and separation, physical and sexual abuse
- **In some cases, negative encounter with stimulus – but not necessary**
- May be a genetic susceptibility, phobia specific

Latin, Asian and African countries have lower rates

60% more likely to make a suicide attempt – likely 2nd to comorbid personality disorders and other anxiety disorders

Similar rates of impairment in function as other anxiety disorders

Distress increases with number of phobias

If only one feared situation, then specific phobia not **agoraphobia (needs two);** also more focus on fear of not being able to escape

Rarely seen in absence of other psychopathology, depression in older adults; anxiety disorders, depressive and bipolar disorders, somatic symptom disorders, personality disorders (particularly dependent)

SPECIFIC PHOBIA GUIDELINES

Lifetime prevalence of **10-13%, 12 mo 7-9%**

Rates among **adolescents particularly high, lifetime 36.5%**

More in **women**

Age of onset **5-12**

Animal and BII phobias in childhood, situational phobias later onset (late adolescence, early adulthood)

Less than 10% only have one fear, **mean number is three**

Comorbid with **SUDs, mood, other anxiety disorders (panic, SAD, GAD), personality disorders**

Exposure based treatments are treatment of choice, high degree of success in providing remission

In vivo and virtual reality can be effective; **in vivo superior**

Most effective if **sessions grouped closely together, exposure is prolonged, real (not imagined)** and **provided in multiple different settings,** and **some degree of therapist involvement**

Even one session can have efficacy, but a greater number of sessions predicts more favorable outcomes

No evidence that flooding or gradual exposure is more effective, but **progressive exposures are more tolerable**

If BII phobia → **exposure therapy combined with muscle tension exercises to prevent fainting**

D-cycloserine – partial agonist at the NMDA receptor may improve extinction of fear in people with phobias undergoing behavioral exposure therapy

Yohimbine – noradrenaline agonist – can facilitate fear extinction – enhanced emotional memory

Minimal role for pharmacotherapy due to the success of ERP

Can give benzos if necessary for a one time symptom relief (ie. Dental procedure, MRI, flight)

Table 18 Psychological treatments with demonstrated efficacy in specific phobias

Psychological treatment	Phobia
Exposure-based treatments	All specific phobias [57,311,312]
Virtual reality exposure	Heights [327-329], flying [319,321-324], spiders [331,332], claustrophobia [330]
Computer-based self-help programs	Spiders [334,335], flying [323], small animals [336,337]
Applied muscle tension (exposure combined with muscle tension exercises)	Blood-injection-injury type [311,315,316]
Cognitive therapy and exposure	Dental [318], flying [319,320]

Fear of judgment in peers
Provoke anxiety, avoidance, excessive, distress
6 mo or more
Can be just performance

SOCIAL ANXIETY DISORDER

Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others (ie. Having a conversation, meeting unfamiliar people, being observed, eating or drinking, giving a speech, performing)

In children, anxiety must occur in peer settings and not just during interactions with adults

The individual fears that he or she will act in a way or show anxiety symptoms that will be negatively evaluated (ie. Will be humiliating or embarrassing, will lead to rejection or offend others

The social situations almost always provoke fear or anxiety (in kids can be crying, tantrums, freezing, shrinking)

The social situations are avoided or endured with intense fear or anxiety

The fear or anxiety is out of proportion to the actual threat posed by the social situation and to the sociocultural context

The fear, anxiety, or avoidance is persistent, typically lasting 6 mo or more

The fear causes clinically significant distress or impairment

The fear is not attributable to effects of substance or medication condition

The fear is not better explained by another mental disorder

If another medical condition is present, the fear is clearly unrelated or excessive (ie. Parkinson's, obesity, disfigurement from burns)

Specify if performance only (restricting to speaking or performing in public)

7% prevalence, decreases with age
Highest in adolescence
More F than M
Onset age 13

SOCIAL ANXIETY DISORDER

Some individuals fear offending others – ie. With eye contact, especially in specific cultures

Fears vary – hand shaking, avoid pointing, fear sweating, avoid handshakes, fear blushing, avoid intimate topics, fear urinating in public washrooms

Avoidance can be extensive or subtle (ie. Refusing school vs. overpreparing speech, limiting eye contact)

Clinical impairment important – ie. If lose out on job promotions because of fear

Self medication w alcohol is common (ie. Drink before party)

Blushing is hallmark physical response

7% prevalence, higher in US than Europe other some other countries

Prevalence rates decrease with age → 2-5% in older adults

More in F than M, gender difference most pronounced in adolescents and young adults

Heightened help seeking behavior in male patients, gender roles

Median **age of onset is 13 years; 75% onset between 8-15**

If onset in adulthood, likely after stressful or humiliating event or significant life change requiring new social roles

May diminish in marriage and re-emerge after divorce

Adolescents have a broader pattern of fear and avoidance, including dating compared with younger children

Older adults have social anxiety at lower levels but across a broader range of situations (younger adults have higher levels of anxiety for specific situations)

In older adults, anxiety may concern disability due to declining sensory functioning (hearing, vision) or embarrassment about appearance (ie. Parkinson's tremor) or functioning due to conditions, incontinence, cognitive impairment

30% have remission within 1 year, 50% within a few years

60% without treatment have a course of several years or longer

SOCIAL ANXIETY DISORDER

Risk Factors:

- Behavioral inhibition, fear of negative evaluation
- Childhood maltreatment and adversity are risk factors, not causal
- Behavioral inhibition strongly genetically influenced (children with high behavioral inhibition are more susceptible to environmental influences such as socially anxious modelling by parents
- **SAD is heritable (performance less so) – 2-6 x greater chance**

Cultural component

- **Taijin kyofusho** (Japan and Korea) – fear that they are making other people uncomfortable – almost w delusional intensity
- **Immigrant status has lower rates of anxiety disorders**
- Societies with strong collectivistic orientations may report high levels of social anxiety but low prevalence of social anxiety disorder

Females have a greater number of social fears and comorbid depressive, bipolar, and anxiety disorders; males more likely to fear dating, have ODD or conduct, and use substances to relieve symptoms

Paruresis (shy bladder) more in males

Elevated rates of school drop out, **decreased employment, being single, unmarried or divorced, not having children**

Not being employed is a strong predictor for the persistence of SAD

Only 12% of "shy" individuals in the US have sx that meet criteria for SAD

Often comorbid with other anxiety disorders, MDD, SUDs

Onset of SAD usually precedes other disorders except for specific phobia and separation anxiety disorder

Social anxiety disorder also comorbid with avoidant personality disorder

In children, comorbid with high functioning autism and selective mutism

SOCIAL ANXIETY DISORDER GUIDELINES

One of the most common, lifetime **8-12%**, more in F than M

More in developed vs developing countries

Early age of onset, age 12, chronic and unremitting course

Higher risk if low educational achievement, low SES, being single or separated, having comorbid MDD

Highest rates of comorbidity with **MDD and other anxiety disorders**

Avoidant PD, BDD, SUD, ADHD, schizophrenia also commonly occur with SAD

Psychological treatment (CBT) is gold standard non-pharm agent in SAD

Restructuring and challenging maladaptive thoughts , exposure

Similar efficacy between CBT and pharm, but CBT may last longer

Group and individual good

No evidence for B blockers, levetiracetam, quetiapine, buspirone

Pregabalin reduced relapse

St. John's wort failed

CBT may be more effective in maintaining benefits than exposure therapy alone

CBT and pharmacotherapy appear to have similar efficacy for the acute treatment of SAD, but after tx discontinuation, gains achieved with CBT appear to persist longer than those achieved with pharm

In most studies, adding pharm does not increase benefits of CBT

First line = antidepressant = escitalopram, fluvoxamine, fluvox XR, paroxetine, sertraline, or venlafaxine XR, or pregabalin

Second line = benzos, citalopram, gabapentin, phenelzine

Pregabalin maintains benefits and prevents relapse

1st = ESP, fluvox, pregab, venlafaxine XR
2nd = alprazolam, clonazepam, citalopram, gabapentin, phenelzine
Adjunct = aripiprazole, buspirone, paroxetine, risperidone
NOT = atenolol, buspirone mono, imipramine, levetiracetam, propranolol, quetiapine
Note – bupropion, atomoxetine, clomipramine, fluoxetine*, mirtazapine, olanzapine 3rd line

Table 21 Recommendations for pharmacotherapy for SAD

First-line	Escitalopram, fluvoxamine, fluvoxamine CR, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR
Second-line	Alprazolam, bromazepam, citalopram, clonazepam, gabapentin, phenelzine
Third-line	Atomoxetine, bupropion SR, clomipramine, divalproex, duloxetine, fluoxetine, mirtazapine, moclobemide, olanzapine, selegiline, tiagabine, topiramate
Adjunctive therapy	**Third-line:** aripiprazole, buspirone, paroxetine, risperidone **Not recommended:** clonazepam, pindolol
Not recommended	Atenolol*, buspirone, imipramine, levetiracetam, propranolol*, quetiapine

CR = controlled release; SR = sustained release; XR = extended release.

*Beta-blockers have been successfully used in clinical practice for performance situations such as public speaking.

Note: although there is limited evidence for citalopram in SAD, it is likely as effective as the other SSRIs, in contrast there are negative trials of fluoxetine in SAD suggesting it may be less effective than other SSRIs [382,449].

PANIC DISORDER

Recurrent unexpected panic attacks (panic attack = abrupt surge of intense fear or discomfort that reaches a peak in minutes and during which time **four or more** of the following symptoms occur):

- Palpitations, pounding heart, accelerated HR
- Sweating
- Trembling or shaking
- Sensations of SOB or smothering
- Feelings of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded or faint
- Chills or heat sensations
- Paresthesias (numbness or tingling sensations)
- Derealization (feelings of unreality) or depersonalization (being detached from oneself)
- Fear of losing control or going crazy
- Fear of dying

- Culture specific syndromes may be seen but do not count toward the four (ie. Headache, tinnitus, screaming or crying)
- At least one of the attacks has been followed by **1 month or more** of one or both of the following:
  - **Persistent concern or worry about additional panic attacks** and their consequences (ie. Losing control, having a heart attack, going crazy)
  - **A significant maladaptive change in behavior related to the attacks** (ie. Behaviors designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations
- Not from effects of substance or medical condition
- The disturbance is not better explained by another mental disorder (ie. Not SAD, OCD, PTSD, etc)

PANIC DISORDER

Nocturnal panic attacks – waking from sleep in panic → at least once in ¼-1/3 of people with panic disorder

Often also report constant or intermittent feelings of anxiety that are more broadly related to health and mental health concerns (ie. Catastrophic outcome from a mild physical symptom or medication side effect)

Relatively intolerant of medication side effects

2-3% prevalence

Females more than males (2:1)

Low rates before age 14 (<0.4%), gradual increase during adolescence, and **peak in adulthood**

Declines in older individuals – likely diminished severity to subclinical levels

Median age of onset **20-24 years**

Usually chronic, but waxing and waning

Only a minority have full remission without subsequent relapse within a few years

Lower prevalence in older adults may be related to age-related dampening of the autonomic nervous system response, also tend to relate their panic attacks to stressful situations (under-endorsement)

PANIC DISORDER – RISK FACTORS

Risk factors:

- Negative affectivity
- Anxiety sensitivity (symptoms are harmful)
- History of fearful spells in childhood
- Sometimes separation anxiety, not consistent
- Reports of childhood experiences of sexual and physical abuse are more common in panic disorder than in certain other anxiety disorders
- Smoking is a risk factor
- Identifiable stressors reported before first panic attack (interpersonal, bad drug experience, death)
- Amygdala dysfunction
- Increased risk for panic disorder in offspring of parents with anxiety, depressive, and bipolar disorders
- Asthma also associated (past history, comorbid, fam hx)

PANIC DISORDER

Vietnamese – hit by the wind, Latin Americans – attack of the nerves, khyal/soul loss in Cambodians

Associated with COMT gene in females only

Agents with disparate MOA like sodium lactate, caffeine, yohimbine, CO_2, cholecystokinin – can provoke panic attacks in panic disorder much more than in healthy controls

Related to hypersensitive medullary CO_2 detectors

Higher rate of suicide attempts and SI even when other risk factors taken into account

Full symptom attacks more morbidity than limited symptom attacks

Other specified if full-spectrum attacks – unexpected – have never been experienced

Rule out hyperthyroidism, hyperparathyroidism, pheochromocytoma, vestibular dysfunction, seizure disorders, CV conditions, COPD, arrythmias, substance use

If onset after 45 or atypical sx (vertigo, LOC, loss of bladder or bowel control, slurred speech, amnesia) → rule out medical or substance

Comorbid with other anxiety disorders, especially agoraphobia, MDD, Bipolar, mild ETOH use disorder; can be seen as a severity makrer of comorbid illness if onset occurs after comorbid disorder

10-65% with panic also have MDD, in 1/3 depression precedes panic, 2/3 depression occurs with or following panic

PANIC DISORDER - GUIDELINES

Lifetime and 12 mo prevalence = 5% and 2.5%

Prevalence of panic attacks is considerably greater at 28.3% lifetime

40-70% of people with panic disorder will have nocturnal panic attacks

Rates of agoraphobia are lower 1%

Panic is higher in women, patients who are middle aged, widowed/divorced, and low income

Comorbidities with anxiety, mood, impulse control or SUD

MDD very common comorbidity with an estimated 35-40% of patients with panic disorder

More in medical conditions – thyroid disease, cancer, chronic pain, cardiac disease, irritable bowel syndrome, migraine, allergic and respiratory diseases

CBT has level one evidence, significantly favored over medications

Exposure, cognitive restructuring and other CBT techniques had the most consistent evidence of efficacy for tx; most effective is exposure for panic, for agoraphobia, combined more than single

CBT with interoceptive exposure is superior to relaxation therapy for panic

Both individual and group settings

Can use virtual reality

Bibliotherapy, telephone, v/cd, or internet based CBT is more effective than wait list or controls, as effective as face to face CBT, and may be cost-effective especially for agoraphobic patients who cannot attend clinic

All seems to be effective – whether therapist support needed, materials given all at once vs paced, briefer number of sessions, etc.

PANIC DISORDER - GUIDELINES

Predictors of decreased response = severity of panic, strength of blood/injury fears, earlier age of initial onset of panic symptoms, comorbid social anxieties and degree of agoraphobic avoidance

Combo therapy is superior to CBT or pharmacotherapy alone during acute treatment phase

After termination, combined = psychotherapy > pharmacotherapy

Benzos plus CBT may be inferior to CBT alone

In people tx with antidepressants, CBT decreased relapse rate

Benefits of CBT were maintained for up to three years

For people who became panic free with exposure therapy → 93% remained in remission after two years and 62% after 10 years

CBT alone may be insufficient if comorbid moderate to severe MDD, severe, frequent panic attacks or rapid worsening of agoraphobia or SI

First line agents = SSRIs, venlafaxine

Second line = TCAs (clomipramine), reboxetine, mirtazapine, benzos (may be useful for short term management, initiation of SSRI)

Third line = moclobemide (significant efficacy in severely ill patients, may be useful in tx resistant patients), phenelzine, tranylcypromine, atypical antipsychotics, duloxetine

Adjunctive clonazepam

Pindolol plus fluoxetine in tx resistant panic disorder resulted in significant improvement

Also adjunct with atypicals, divalproex

NOT RECOMMENDED: Buspirone, propranolol, tiagabine, trazodone, carbamazepine

Table 15 Recommendations for pharmacotherapy for panic disorder

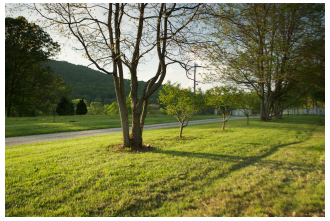
First-line	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, paroxetine CR, sertraline, venlafaxine XR
Second-line	Alprazolam, clomipramine, clonazepam, diazepam, imipramine, lorazepam, mirtazapine, reboxetine
Third-line	Bupropion SR, divalproex, duloxetine, gabapentin, levetiracetam, milnacipran, moclobemide, olanzapine, phenelzine, quetiapine, risperidone, tranylcypromine
Adjunctive therapy	**Second-line**: alprazolam ODT, clonazepam **Third-line**: aripiprazole, divalproex, olanzapine, pindolol, risperidone
Not recommended	Buspirone, propranolol, tiagabine, trazodone

CR = controlled release; ODT = orally disintegrating tablets; SR = sustained release; XR = extended release.

PANIC ATTACK SPECIFIER

- 11.2% prevalence in general population
- Females more than males, but more prominent in panic disorder
- Prevalence rates increase after puberty
- Onset 22-23
- Uncommon in preadolescent children
- **Smoking is a risk factor**
- Increased likelihood of later developing anxiety disorders, depressive disorders, bipolar disorders
- Also associated with impulse control disorders and substance use disorders
- Usually peak within minutes and subside within minutes
- For a proportion, attack preceded by cardiorespiratory instabilities

AGORAPHOBIA






Marked fear or anxiety about two or more of the following five situations:

- Using public transportation (ie. Automobiles, buses, trains, ships, planes)
- Being in open spaces (ie. Parking lots, marketplaces, bridges)
- Being in enclosed places (ie. Shops, theaters, cinemas)
- Standing in line or being in a crowd
- Being outside of the home alone

The individual fears or avoids these situations because of **thoughts that escape might be difficult or help might not be available** in the event of **developing panic-like symptoms or other incapacitating or embarrassing symptoms** (ie. Fear of falling in elderly, fear of incontinence)

The agoraphobic situations almost always provoke fear or anxiety

The agoraphobic situations are **actively avoided, require the presence of a companion, or are endured with intense fear or anxiety**

The fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context

The fear, anxiety, or avoidance is persistent, typically lasting for **6 mo or more**

Causes clinically significant distress and impaired functioning

If another medical condition (ie. Inflammatory bowel disease, Parkinson's disease) is present, fear, anxiety, or avoidance is clearly excessive

The fear, anxiety, or avoidance is not better explained by the sx of another mental disorder

Agoraphobia is diagnosed irrespective of the presence of panic disorder; can diagnose both

AGORAPHOBIA

Other incapacitating symptoms can include vomiting, diarrhea, sense of disorientation, getting lost, fear of falling

Frequently believe that escape might be difficult or help might be unavailable

Avoidance can include choosing a job close by so you do not need to use public transportation, arranging for food delivery to avoid supermarkets, or using distraction to get through the situation

In most severe forms, can cause individuals to become homebound → depressive symptoms and alcohol or sedative abuse are common

1.7% of adolescents and adults per year

Females 2 x more than males

Peaks in late adolescence and early adulthood

Older adults 0.4%

30-50% have panic attacks/panic disorder preceding agoraphobia

The majority of individuals with panic disorder show signs of anxiety and agoraphobia before the onset of panic disorder

In 2/3, initial onset before 35 y o

Incidence risk in late adolescence and early adulthood, second increased risk after age 40

Overall mean age of onset is 17 years, but if no preceding panic attacks, 25-29 years

Course is typically persistent and chronic, **complete remission is rare (10%) unless disorder is treated**

In children – most common situation is being outside home alone, more fear around getting lost

Older adults – being in shops, standing in line, and open spaces, more fear around falling, panicking

AGORAPHOBIA

Risks:

- Behavioral inhibition and neurotic disposition
- Anxiety sensitivity – anxiety symptoms are harmful
- Negative events in childhood or other stressful events
- Family climate of reduced warmth and increased overprotection
- **Heritability is 61% - of all phobias, agoraphobia has the strongest and most specific association with genetic factors**

Males have higher rates of comorbid substance use

More than **1/3 unable to work** and are completely housebound, severe impairment

Caution in medical disorders – must use clinical judgment to determine whether fear or avoidance is clearly in excess (ie. Fainting in TIAs, diarrhea in Crohn's)

Majority also have other mental disorders, most frequently other anxiety disorders (phobias, panic, social anxiety disorder), depressive disorders, PTSD, ETOH use disorder

Depressive disorders and SUDs typically occur secondary to agoraphobia, **anxiety disorders before**

GENERALIZED ANXIETY DISORDER

Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 mo, about a number of events or activities (such as work or school performance)

The individual finds it difficult to control the worry

The anxiety and worry are associated with three or more of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 mo); **note – only one item is required in children**

- Restlessness or feeling keyed up or on edge
- Being easily fatigued
- Difficulty concentrating or mind going blank
- Irritability
- Muscle tension
- Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)

The anxiety, worry, or physical symptoms cause distress or impaired fxn

Not from substance or medical condition

Not better explained by another mental disorder

GENERALIZED ANXIETY DISORDER

How do you distinguish between normal worry and GAD?

- **Excessive and interfere with functioning; normal worries are manageable and can be put to the side**
- Worries in GAD more pervasive, pronounced, distressing, longer duration, occur without precipitants
- **Everyday worries much less likely to be accompanied by physical symptoms – ie. Restlessness or feeling keyed up or on edge**

Often experience somatic symptoms – sweating, nausea, diarrhea, exaggerated startle

Autonomic hyperarousal (elevated HR, SOB, dizziness) less prominent

Other stress syndromes commonly accompany – headaches, IBS

0.9% in adolescents, 2.9% in adults (range 0.4-3.6%)

Lifetime risk 9.0%

Females 2 x more likely

Peaks in middle age and declines across later years of life

More in European descent and developed countries

Many individuals say they have felt nervous all their lives, but **median age onset is 30 (LATER than other anxiety disorders)**

Rare before adolescence

Chronic and wax and wane throughout the lifespan, rates of full remission are very low

Worry about school and sport performance in kids, adults more well-being of family and health; age appropriate

Younger adults have greater severity of sx

Children tend to be overly conforming, perfectionist, unsure of themselves, redo tasks, overzealous in reassurance and approval seeking

Risks:

- Behavioral inhibition, negative affectivity, harm avoidance
- Some association with childhood adversity or parental overprotection, not specific
- **1/3 genetic, overlap with MDD**

More in females than males, different comorbidities (**females – anxiety disorders and unipolar depression), males (SUD)**

GUIDELINES

Lifetime prevalence 6%, 12 mo 1-4%

More in Caucasians, females

Bimodal onset – late teens to early 20s, then 30—40s

High comorbidity with anxiety and MDD, medical conditions, pain syndromes, HTN, CV and gastric conditions

CBT significantly reduces symptoms, comparable to pharm

Individual and group equally effective, but individual may be earlier

Combo tx more effective than CBT alone at post treatment but not at six mo follow up – no evidence to support routine recommendation

Vortioxetine – serotonin modulator – conflicting results, second line

Pregabalin first line, as effective as benzos

Good evidence for quetiapine XR – second line due to SE

Not recommended – beta blockers

Agomelatine also first line

Bupropion XR second line

Table 24 Recommendations for pharmacotherapy for GAD

First-line	Agomelatine, duloxetine, escitalopram, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR
Second-line	Alprazolam*, bromazepam*, bupropion XL*, buspirone, diazepam*, hydroxyzine, imipramine, lorazepam*, quetiapine XR*, vortioxetine
Third-line	Citalopram, divalproex chrono, fluoxetine, mirtazapine, trazodone
Adjunctive therapy	**Second-line:** pregabalin **Third-line:** aripiprazole, olanzapine, quetiapine, quetiapine XR, risperidone **Not recommended:** ziprasidone
Not recommended	Beta blockers (propranolol), pexacerfont, tiagabine

CR = controlled release; XL = extended release; XR=extended release.

*Note: These have distinct mechanisms, efficacy and safety profiles. Within these second-line agents, benzodiazepines would be considered first in most cases, except where there is a risk of substance abuse, while bupropion XL would likely be reserved for later. Quetiapine XR remains a good choice in terms of efficacy, but given the metabolic concerns associated with atypical antipsychotic, it should be reserved for patients who cannot be provided antidepressants or benzodiazepines. Please refer to text for further rationale for the recommendations.

ESP, agomelatine, duloxetine, pregabalin, venlafaxine XR
Second – pams, bupropion, buspirone, quetiapine, vortioxetine
Third – citalopram, fluoxetine, mirtazapine, trazodone
Adjunctive = pregabalin
Not recommended – propranolol

GENERALIZED ANXIETY DISORDER

SUBSTANCE INDUCED ANXIETY DISORDER

Panic attacks or anxiety is predominant in the clinical picture

There is evidence from the history, physical examination, or lab findings of both 1 and 2

- Symptoms developed soon after substance intoxication, withdrawal, or exposure to med
- Involved substance is capable of producing sx above

Not better explained by an anxiety disorder that is not substance induced

Not exclusively during a delirium

Clinically significant distress or impairment

Tidbits:

- Intoxication with alcohol, caffeine, cannabis, phencyclidine, other hallucinogens, inhalants, stimulants (cocaine) and other substances
- Withdrawal from alcohol, opiates, sedatives, hypnotics, anxiolytics, stimulants
- Medications = anesthetics, analgesics, sympathomimetics, bronchodilators, anticholinergics, insulin, thyroid meds, OCPs, antihistamines, antiparkinsonian meds, steroids, antihypertensives, anticonvulsants, Li, antidepressants, antipsychotics
- Heavy metals and toxins – gasoline and paint, CO, CO2
- Rare 0.002% in population, likely higher in clinical settings

ANXIETY DISORDER DUE TO ANOTHER MEDICAL CONDITION

Panic attacks of anxiety is predominant in the clinical picture

Evidence from hx, px, labs that the disturbance is the direct consequence of another medical condition

Not better explained by another mental disorder

Not exclusively in a delirium

Causes clinically significant distress or impairment

Tidbits:

- **Hyperthyroidism, pheochromocytoma, hypoglycemia, hyperadrenocortisolism, CHF, PE, a fib, COPD, asthma, pneumonia, vitamin B12 def, porphyria, neoplasms, vestibular dysfunction, encephalitis, seizure disorders**

OTHER SPECIFIED ANXIETY DISORDER

Limited symptom attacks

Generalized anxiety not occurring more days than not

Khyal cap (wind attacks)

Ataque de nervios (attack of the nerves

ANXIETY GUIDELINES

Lifetime prevalence of anxiety disorders is as high as 31%

Women more than men

Increased risk of having a comorbid major depressive disorder

Up to 40% of people with anxiety are untreated

Anxiety disorders are associated with a significant **1.7-2.5 x increased risk of suicide attempts (panic disorder, PTSD, GAD)** even in the absence of a mood disorder

Risk factors: family or personal history of mood or anxiety disorders, personal history of childhood stressful events, especially child abuse, loneliness, low education, adverse parenting, chronic somatic illnesses, being female, behavioral inhibition

Family history is associated with a more recurrent course, greater impairment, and greater service use

Early onset for phobias and separation anxiety disorder, later for GAD, panic and PTSD (24+)

More than **50% have multiple anxiety disorders and almost 30% will have three or more**

Also comorbid with **substance use and mood disorders (52% with bipolar, 60% MDD, and 47% with ADHD)**

Comorbid disorders are associated with poorer treatment outcomes, greater severity, and chronicity, more impaired functioning, increased health service use, and higher tx costs

Higher rates of HTN, CV disease, GI disease, arthritis, thyroid disease, respiratory disease, migraines, and allergic conditions

ANXIETY GUIDELINES

Baseline assessment – ROS, medications, OTC, substance use, anxiety symptoms, functioning, baseline labs (CBC, fasting lipids, electrolytes, glucose, TSH, liver enzymes, utox), monitor every 1-2 weeks, and then every 4 weeks; closer monitoring if children younger than 10, older or medically ill patients, patients on meds associated with metabolic changes and those on multiple meds

In most disorders **psychotherapy = pharm, combo has limited evidence** → not routine, but if no response to CBT or limited response, trial of pharmacotherapy advisable and vice versa

ANXIETY GUIDELINES

Components of CBT

- Exposure
  - Encourage patients to face fears
  - Patients learn corrective info through experience
  - Extinction of fear occurs through repeated exposure
  - Successful coping enhances self-efficacy
- Safety Response Inhibition
  - Patients restrict their usual anxiety-reducing behaviors (ie . Escape, need for reassurance)
  - Decreases negative reinforcement
  - Coping with anxiety without using anxiety reducing behavior enhances self-efficacy
- Cognitive Strategies
  - Cognitive restructuring, behavioral experiments and related strategies target patients' exaggerated perception of danger
  - Provides corrective information regarding the level of threat
  - Can also target self-efficacy beliefs
- Arousal Management
  - Relaxation and breathing control skills can help patient control increased anxiety levels
- Surrender of Safety Signals
  - Patient relinquishes safety signals (ie. Presence of a companion, knowledge of the location of the nearest toilet)
  - Patients learn adaptive self-efficacy beliefs

ANXIETY GUIDELINES

Most common side effects with SSRIs and SNRIs are headache, irritability, GI complaints, insomnia, sexual dysfunction, weight gain, increased anxiety, drowsiness and tremor

Most side effects occur transiently and early, first two weeks of treatment, but others such as sexual dysfunction and weight gain may persist for the duration of tx

SSRIs/SNRIs linked with GI bleeds especially when used with NSAIDs

Also SSRIs inked to low bone mineral density and increased risk of fractures and hyponatremia

Warning for children – increased risk of SI and behavior

Benzos – sedation, fatigue, ataxia, slurred speech, memory impairment and weakness; withdrawal, rebound, dependence, substance use disorder, increased risks of falls and fractures, cognitive impairment

Tx 2-8 weeks for effect, full response up to 12 weeks or more

Therapy should be continued for at least 12-24 mo for most patients

Meds should be initiated at low doses and titrated to the recommended dosage range at one to two week intervals over four to six weeks

Psychotherapy usually 12-20 weeks

Response is usually 25-50% reduction in symptoms, remission is loss of diagnostic status, usually a score

Can use clinical global impression scale (CGI) or **Hamilton Anxiety Rating Scale (HARS)** to assess anxiety symptoms and follow

ANXIETY GUIDELINES

Women in pregnancy and postpartum period

- SSRIs – increased risk of cardiac defects, with paroxetine specifically

- increased risk of neonatal adaptation syndrome (PNAS)

- **sertraline best for breastfeeding and pregnancy**

Children and adolescents

- **most common in adolescents and children = anxiety disorders**

- specific phobias common, lifetime prevalence 10-35%

- **BII and animal fears are most common in pediatric populations**

- **earliest age of onset compared to other psychiatric disorders**

- separation anxiety disorder and the phobias have a much earlier age of onset than OCD, GAD, panic, or PTSD

- **elevates risk of MDD, other anxiety disorders, and SUD in adulthood**

- prevention programs have demonstrated benefits

- psychological treatments preferred

- **good evidence for SSRIs in OCD, SAD – fluoxetine**

- **fluoxetine and fluvoxamine in separation anxiety disorder and GAD**

- **in pediatric PTSD – drugs not more effective than CBT alone, not recommended**

- **combo of sertraline and CBT superior to both monotherapies in separation anxiety disorder, GAD, or SAD**

ELDERLY

Subthreshold anxiety increases the prevalence to be more than general population

Depression is most common comorbid disorder with anxiety – poorer outcomes of both

Present differently – avoidance, don't identify anxiety as anxiety but physical sx, assessing function change is harder

CBT is good and equals pharm, may benefit from learning and memory aids

Pregabalin is good in GAD, citalopram, sertraline

COMORBID CONDITIONS

MDD in 20-36% of patients; 60% of MDD has a comorbid anxiety or related disorder

Increases suicidality, functional impairment, lowers remission rates

If anxiety and MDD, do SSRI or SNRI, quetiapine

In anxiety patients, 14% also meet criteria for bipolar disorder

One of most common comorbidities for bipolar is anxiety (52%)

Olanzapine or LTG added to Li helpful for anxiety

ADHD – 47% have anxiety disorder – most common SAD (22.7%), specific phobia, PTSD, panic, and GAD – figure out which has most severe sx and treat first, atomoxetine can help

Medical comorbidities higher in GAD, panic, PTSD

Duloxetine for chronic pain

Table 32 DSM-5 diagnostic criteria for anxiety and related disorders specific to children

Anxiety or related disorder	DSM-5 diagnoses specific to children
Separation anxiety disorder	• Developmentally inappropriate and excessive fear or anxiety concerning separation from those to whom the individual is attached, as evidenced by ≥3 of the following: ○ Distress when separation occurs, worry about loss or separation, reluctance to leave home, be alone, or go to sleep because of fear of separation, nightmares involving separation, or complaints of physical symptoms (e.g., headaches, upset stomach) when separation occurs • Duration of at least 4 weeks • Onset before 18 years of age • The disturbance causes clinically significant distress or impairment in social, academic (occupational), or other important areas of functioning
Selective mutism	• Consistent failure to speak in specific social situations in which there is an expectation for speaking (e.g., at school) despite speaking in other situations
Anxiety or related disorder	**Changes to adult DSM-5 diagnostic criteria specific to children**
Specific phobia	• The fear or anxiety may be expressed by crying, tantrums, freezing, or clinging • Other specifiers: loud sounds or costumed characters
SAD (social phobia)	• The anxiety must occur in peer settings, not just during interactions with adults • The fear or anxiety may be expressed by crying, tantrums, freezing, clinging, shrinking, or failure to speak in social situations
OCD, panic disorder	• No pediatric specific criteria
PTSD	• Qualifiers in children ○ Intrusion symptoms: repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed; there may be frightening dreams without recognizable content; trauma-specific re-enactment may occur in play • Specific subtype for children ≤6 years of age
GAD	• Less stringent criteria for symptoms than in adults

Adapted from DSM-5 [26].

Table 33 Strength of evidence of treatments for anxiety and related disorders in children and adolescents

Disorder	Antidepressants	Benzodiazepines and other treatments
OCD	Fluoxetine (Level 1) [1264-1269]	**Antipsychotics**
	Clomipramine (Level 1) [1274-1276]	Adjunctive aripiprazole (Level 3) [1293]
	Citalopram (Level 2) [1264,1270]	**Other**
	Fluvoxamine (Level 2) [1271]	Riluzole (Level 4) [1294]
	Paroxetine (Level 2) [1272]	
	Sertraline (Level 2) [1273]	
Panic disorder		**Anxiolytics**
		Clonazepam (Level 4) [1287,1288]
		Alprazolam (Level 4) [1289]
SAD	Fluoxetine (Level 1) [1227,1277]	**Anxiolytics**
	Fluvoxamine (Level 2) [1278]	Alprazolam (Level 2, -ve) [1290]
	Paroxetine (Level 2) [1279]	
	Venlafaxine XR (Level 2) [1282]	
	Escitalopram (Level 3) [1280]	
	Sertraline (Level 3) [1281]	
	Mirtazapine (Level 3) [1283]	
Separation anxiety disorder	Fluoxetine (Level 2) [1277]	**Anxiolytics**
	Fluvoxamine (Level 2) [1278]	Clonazepam (Level 2, -ve) [1292]
GAD	Fluoxetine (Level 2) [1277]	**Anxiolytics**
	Fluvoxamine (Level 2) [1278]	Alprazolam (Level 2, -ve) [1290]
	Sertraline (Level 2) [1284]	
School-refusal	Citalopram (Level 4) [1285]	**Anxiolytics**
	Adjunctive imipramine (Level 2) [1259]	Alprazolam (Level 2, -ve) [1291]
PTSD	Sertraline (Level 2, -ve) [1286]	
	Adjunctive sertraline (Level 2, -ve) [946]	

XR = extended release; (-ve) = negative.

PEARLS FROM LONDON REVIEW COURSE – DR. MARK WATLING

Illness anxiety disorder is not an anxiety disorder

GPSMAPS = generalized, panic, social anxiety, selective Mutism, agoraphobia, phobias, separation anxiety

Panic = two or more unexpected attacks

4/13 panic symptoms

Panic disorder must have persistent concern/worry about more attacks or their consequences, a significant maladaptive change in behavior related to attacks; otherwise is just a panic attack

Agoraphobia = thoughts that escape might be difficult or might not be available in the event of panic symptoms or other incapacitating embarrassing symptoms

In social anxiety – avoidance can be in initiating and maintaining conversations, dating, being assertive, inconveniencing others, talking to authority figures, attending social gatherings

Performance examples = public speaking, playing music, performing, pumping gas, eating in front of others, crossing at a crosswalk, waiting to turn left at a light, making mistakes in public, working out at the gym, having a picture taken, mowing the lawn, shoveling the walk

PEARLS FROM LONDON REVIEW COURSE – DR. MARK WATLING

Generalized anxiety = excessive uncontrollable worry, 3/6 physical sx

Make sure that you tag physical sx to worry – restlessness, easily fatigued, difficulty concentrating, irritability, muscle tension, sleep disturbance

Separation anxiety disorder is the most prevalent under age 12

In children – highly comorbid with GAD and specific phobias; in adults, SAD high comorbidity with all anxiety disorders, OCD, PTSD, MDD, Bipolar

Most evidence in SAD for CBT/exposure, family involvement, early intervention

Selective mutism – most get better, more F, usually after age 8, get better, little evidence for theory that it arises out of trauma

As adults, people with a history of selective mutism do less well in school, work, communication, and higher rates of psych disorders

PEARLS FROM LONDON REVIEW COURSE – DR. MARK WATLING

Why are some people more anxious than others?

Psychological influences

Learning and experiences – direct experience, vicarious acquisition, info and instruction

Thoughts, beliefs, assumptions – common anxious patterns of thinking in various anxiety disorders – ie. World is dangerous

Behavior – how a person responds to anxiety - avoidance, safety behaviors

Social – occupation, religion, gender, cultural expectations, media

Biological – genetics in NT/receptors, serotonin, norepi, GAB

Excitation of the cortico-striatal-thalamic-cortical loop gives rise to worry and obsessions

Top risk factors for developing an anxiety disorder: family history of anxiety, personal history of anxiety or mood disorder), childhood stressful life events/trauma, being female, chronic medical illnesses (asthma, diabetes, obesity, CV disease), behavioral inhibition

Panic disorder - 20 x risk of suicide to general population, 30-50% also have agoraphobia

PEARLS FROM LONDON REVIEW COURSE – DR. MARK WATLING

Social anxiety disorder – very difficult to finish school, lower SES, unmarried

In GAD, 68% have another psychiatric illness

Phobias in 13%, median age of onset 7

Anxiety disorders – more common in females

How to inhibit neuronal excitability:

- Increase serotonergic input to these circuits – SSRIs, TCAs, SNRIs, MAOIs, azapirones
- Increase GABA – benzos
- Block glutamate – alpha 2 delta ligands – pregabalin and gabapentin
- Increasing serotonin input to the amygdala results in a blunting of the outputs from the amygdala to the rest of the key areas in the fear response
- When a benzo binds to GABAA – it allows for enhanced inhibitory action by GABA, which results in reduced neuronal activity in the amygdala and the cortical-striatal-thalma-cortical loops – worry; some anticonvulsants also seem to have an enhancing effect on GABA transmission through other means
- Alpha 2 delta ligands bind to voltage sensitive calcium channels which in turns blocks the release of excitatory neurotransmitters like glutamate – when this occurs in the amygdala or in the CSTC, than an anxiolytic effect may result; therefore pregabalin or gabapentin which have their anxiolytic effect through a different mechanism than benzos or SSRIs/SNRIs and may be helpful in non responders or partial responders with augmentation

ESP = escitalopram, sertraline, paroxetine

Benzos only first line for phobias

Second line for PDA, SAD, GAD

Pregabalin first line for SAD, GAD

PEARLS FROM LONDON REVIEW COURSE – DR. MARK WATLING

Gabapentin 2nd line for SAD, 3rd for PDA

Venlafaxine also first line

For phobias – meds often not used because CBT so effective, short term benzos only when acute relief necessary

D-cycloserine added to CBT may enhance CBT

Treating anxiety disorders – significant improvements should be in 6-8 weeks, may take up t o 10-12 weeks

Should continue meds until avoidance behavior is overcome (not just until anxiety symptoms have subsided); meds for at least 12 mo if not indefinitely

Benzos a viable treatment option for adults with GAD – especially in the initial treatment phase with careful tapering after 4-8 weeks

PEARLS FROM LONDON REVIEW COURSE – DR. MARK WATLING

Vortioxetine – mixed data; not in GAD, helpful in panic, mixed in social

Vilazodone – not first line, some improvement in SAD

Buspar 2nd line for GAD

No great evidence for beta blockers; some in panic as augment, performance anxiety (not general social anxiety)

Some evidence for balneotherapy, exercise – best in high intensity, lavender oil, kava (but risk of hepatotoxicity)

Scales = **GAD (less than 7 on HAM-A**, Hamilton rating scale for anxiety; social anxiety <30 – Liebowitz social anxiety scale, panic disorder severity scale – less than 7

50% response to first line treatment with GAD, 70% with SAD, 60% with panic

PEARLS FROM LONDON REVIEW COURSE – DR. MARK WATLING

Non response:

- Treatment related factors = premature discontinuation by physician, premature discontinuation by patient, inadequate dosing, wrong treatment
- Patient related factors = poor medication adherence, co-morbidities, illness severity, stress, slow vs. fast metabolizer, genetic differences (short arm vs long arm of 5HT transporter gene), patient family factors, substance use, caffeine
- Logistic factors = cost of medication, frequency of follow up, availability of CBT

When a first line medication fails to work – what next?

- Wait long enough, ensure compliance, maximize the dose, diagnose and treat comorbid conditions, reconsider the diagnosis, consider CBT, augment if the response is partial (meds/CBT), switch to another medication

CBT is as effective as medication (70%)

Panic = interoceptive exposures, breathing retraining, relaxation

SAD = situational exposures, social skills, assertiveness

GAD = worry scripts, imaginary exposures, problem solving

Phobias = applied muscle tension, direct, graduated exposure, VR

Pros and cons of CBT and meds:

- Meds: easy, effective, accessible, side effect risk, cost, relapse on discontinuation
- CBT: long lasting effects, no side effects, time commitment, often inaccessible, costly if private

PEARLS FROM OTTAWA REVIEW COURSE – DR DIANE MCINTOSH

OCD = distinct via cortico-striatal-thalamic circuit

Threat → thalamus → amygdala (inputs from cortex, locus ceruleus, hippocampus, cortex) → fear

Thalamus is a relay centre between subcortical areas and the cortex – all sensory impulses except smell go through the thalamus; ie. Retina → thalamus (lateral geniculate nucleus) → primary visual cortex

Hippocampus = home movies of your life

Thalamus to prefrontal cortex → slower but lots of information, careful evaluation of sensory input, more options for response, consults amygdala but not overly influenced by the amygdala's predictable fear response

Adversity has been altered amygdala volume, reduced PFC thickness and volume, increased amygdala reactivity during emotion processing, altered communication between amygdala and PFC

Early life stress alters fronto-amygdala circuitry, promoting a risk for mental illness

HPA – major biological system coordinating the body's acute and chronic responses to stress

Cortisol is potent anti inflammatory hormone that prevents widespread tissue and nerve damage associated with stress and inflammation; chronic anxiety and depression leads to chronically high levels of cortisol which can provoke inflammation

PEARLS FROM OTTAWA REVIEW COURSE – DR DIANE MCINTOSH

Chronically high cortisol results in glial cell dysfunction = increases risk of dementia

Reduction in glial cell density and number is the most prominent feature of cell pathology in depression

Chronic high stress → chronic high cortisol → astrocytes and microglia stop doing their job → inflammation causes neuron damage and death

Reduced volume of brain due to reduced neurogenesis, synaptogenesis, neuroplasticity

BDNF grows brain cells

PEARLS FROM OTTAWA REVIEW COURSE – DR DIANE MCINTOSH

People with anxiety disorders exhibit abnormalities in the acquisition and extinction of conditioned fear responses

Consolidation = transient memory shifts to long term memory

Long term memories remain in a labile state

Can have memory reconsolidation

Treatment for traumatic memories – giving extinction training to humans during the reconsolidation window effectively redefines fearful memories as safe

80% of MDD have anxious distress specifier – longer duration of illness and greater likelihood of treatment non-response

Higher risk of suicide

Anxiety disorders are the most common psychiatric disorders of childhood and adolescence – 15-30%, many more than one

More in females, median onset latest in GAD

High recurrence rates – 60% for panic, 40% for SAD, 45% GAD

24% of all remitted patients relapse in 2 years and **33% rate of conversion to another anxiety disorder**

Risks = **panic and GAD more closely related to each other than specific phobias**

High anxiety sensitivity – misinterpretation of bodily symptoms, early behavioral inhibition, latent inhibition (good experiences reduce likelihood of developing fear with one bad experience), vicarious conditioning – developing anxiety through observation; sense of mastery and control over environment – helps adaptation to anxiety provoking situations

Course of anxiety disorder predicted by:

- **Age of onset (early is bad)**
- Having a partner – better to have one
- History of childhood trauma
- Residual symptoms
- Parental substance abuse
- Antidepressant discontinuation
- Mood disorder comorbidity
- **Agoraphobia and SAD most likely to have a severe chronic course**

PEARLS FROM OTTAWA REVIEW COURSE – DR DIANE MCINTOSH

SSRI/SNRI blocks reuptake of 5HT → reuptake blocked → 5HT increases quickly in synaptic cleft → post synaptic 5HT2/3 receptors overstimulated causing side effects → side effects decrease over 1-3 weeks as 5HT2/3 receptors desensitized

5HT1A receptor = anxiolytic/antidepressant

5HT2 = jitteriness, insomnia, sexual dysfunction

5HT3 = nausea and headache

Serotonin = sir raphe – raphe nuclei

Norepinephrine dampens noise, increases inhibition, inhibits distraction, can engage and disengage from stimuli, change focus to new stimuli, executive operations (judgment, planning/organization, problem solving, critical thinking, forward thinking, working memory)

In depressed and anxious state, at rest, no threat = extracellular NE low in PFC – fatigue, somnolence, cognitive impairment

In depressed anxious state, phasic reactivity in response to stress = neuronal firing rate very high, EC NE very high = anxiety, dysphoria, cognitive impairment

After three or more weeks of the NRI, or SNRI – reuptake blocked – EC NE increases, terminal alpha 2 receptors desensitize, brakes taken off exocytotic release of NE, tonic activity NE is increased – improved energy, attention, cognition

Attenuated phasic reactivity (decreased neuronal firing) and downregulated excitatory post-synaptic B receptors → both potentially anxiolytic

PEARLS FROM OTTAWA REVIEW COURSE – DR DIANE MCINTOSH

Asymptomatic resolution was the strongest predictor of remaining relapse/recurrence-free

Top 10 list:

- SSRIs – escitalopram, sertraline, fluoxetine for children
- SNRIs – desvenlafaxine, duloxetine, levomilnacipran (remember venlafaxine only SNRI at 225 mg)
- Multimodals – vortioxetine, vilazodone
- Mirtazapine
- Bupropion XL

First choice depression augmentation treatments

- AAPs – abilify, brexpiprazole, quetiapine
- Antidepressant combos – SSRI/SNRI/multimodal and bupropion, mirtazapine
- LI, T3, psychostimulants 2nd or 3rd line

Anxiety disorders may require higher doses and longer time to response/remission

Anxiety patients tend to be highly sensitive to side effects and a tendency to be sensitive to physical side effects particularly

Psychoeducation imperative – a brain illness, chronic condition, first 3-4 weeks are greatest challenge

Levomilnacipran – Fetzima – NSRI (norepi out of the gate, serotonin right away) – very good for pain though no indications

PEARLS FROM OTTAWA REVIEW COURSE – DR DIANE MCINTOSH

GAD has >90% comorbidity, only half seek treatment, late age of onset (30)

Measure GAD with **GAD 7 scale (5 mild, 10 moderate, 15 severe)**

Using threshold of 10, GAD7 has sensitivity of 89% and a specificity of 82% for GAD

GAD 7 moderately good at screening for panic, SAD, PTSD

PsychedUps GAD suggestions = escitalopram, sertraline, desvenlafaxine, duloxetine, levomilnacipran, vortioxetine, vilazodone (bupropion XL 2nd and mirtazapine 3rd line)

Next most common to phobia anxiety disorder is SAD – 13% lifetime, high comorbidity, onset in childhood/adolescence, low probability of remission without intervention, earlier onset more chronic debilitating course

Liebowitz Social Anxiety Scale – situations with fear and avoidance, 24 items

Psyched Ups suggestions for SAD = escitalopram, sertraline, desvenlafaxine, duloxetine, levomilnacipran, vortioxetine, vilazodone (bupropion, mirtaz 3rd line)

½-1/3 of individuals with panic have agoraphobia, 50-60% have MDD

Psyched up for panic = escitalopram, sertraline, fluoxetine, desvenlafaxine, duloxetine, levomilnacipran, vortioxetine, vilazodone (buprop 3rd and mirtaz 2nd line)

PEARLS FROM TORONTO REVIEW COURSE

Situational phobia most common in adulthood, animal and BII in childhood

Applied muscle tension (exposure and muscle tension) for BII

Virtual reality for heights, flying, spiders, claustrophobia

Cognitive therapy and exposure for dental and flying phobias

Computer based for spiders, flying, small animals

In GAD – magnitude of benefit from meds and CBT are comparable, combo as routine not recommended

GAD CBT focused on addressing intolerance of uncertainty, positive beliefs about worry, negative problem orientation, cognitive avoidance

PREVALENCE CHART

Disorder	Lifetime	12 mo
GAD	6%	1-4%
Panic	5%	2.5%
SAD	8-12%	7%
Separation Anxiety	4% kids, 1% adults	
Specific Phobia	10-13%	7-9%

PEARLS FROM K AND S

Panic

- 91% have other psych dx like MDD
- Prefrontal cortex = phobic avoidance, limbic system = anticipatory anxiety
- CO2, sodium lactate, bicarb – respiratory panic inducing
- Also cholecystokinin, caffeine, flumenazil, isoproterenol
- Hypersensitive suffocation alarm system
- No increased prevalence of mitral valve prolapse
- Decreased blood flow to R temporal lobe
- More loss and stressful life events in months before onset
- **60% have hx childhood sexual abuse (31% in other anxiety disorders)**
- **Hyperventilation causes alkalosis**
- Search for medical if ataxia, altered LOC, bladder dyscontrol, late life onset
- Alprazolam most studied – second line

Phobia

- **Most common mental disorder in females, second in men (first is SUDS)**
- F more than M except BII phobia
- Nature and BII phobia start age 5-9, situational mid 20s like agoraphobia
- BII phobia is very familial – unique with bradycardia and hypotension following initial tachy
- Space phobia – falling – rule out R hemisphere function
- Fear of society = amaxophobia
- Bimodal age of onset, childhood peak for animals, nature, BII, early adult for situational
- Rarely present for tx
- CBT best

PEARLS FROM K AND S

Social Anxiety Disorder

- 3-13%
- Females more than males, peak onset in teens
- Propranolol for performance only
- Decreased homovanillic acid concentrations, decreased striatal dopamine
- Differentiation between SAD and avoidant PD very hard
- Schizoid PD not interested in socializing

GAD

- Late adolescence to early adulthood
- Common in older adults too
- **Lots of comorbidity – 50-90%**
- 25% have panic disorder
- Occipital lobe has most benzo receptors
- Basal ganglia, limbic, frontal cortex also implicated
- **Buspar is agonist at 5HT1A**
- Possible subsensitivity at alpha 2 adrenergic receptors
- PET shows decreased metabolism in basal ganglia and white matter
- **Familial risks with panic disorder, GAD, OCD (PANIC MOST)**
- Often seek other doctors – like for chronic diarrhea
- Can be with medical conditions – cardiomyopathy, Parkinson's, COPD, chronic pain, primary biliary cirrhosis
- Epilepsy – right parahippocampal gyrus
- GAD – Sjogrens, graves, social phobia in Parkinson's, fear of falls

RESOURCES

Canadian Anxiety Guidelines 2014

K and S

Review Courses – Ottawa, London, Toronto

DSM V

OBSESSIVE-COMPULSIVE AND RELATED DISORDERS

RC Rounds – Dr. A. Jewett

Obsessive-Compulsive Disorder

- A. Presence of obsessions, compulsions, or both:
- Obsessions are defined by (1) and (2):
- 1. Recurrent and persistent thoughts, urges, or impulses that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.
- 2.The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).
- Compulsions are defined by (1) and (2):
- 1. Repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.
- 2.The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive.
- ***Note:*** Young children may not be able to articulate the aims of these behaviors or mental acts.
- B. The obsessions or compulsions are time-consuming (e.g., take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.
- D. The disturbance is not better explained by the symptoms of another mental disorder (e.g., excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation [skin-picking] disorder; stereotypies, as in stereotypic movement disorder; ritualized eating behavior, as in eating disorders; preoccupation with substances or gambling, as in substance-related and addictive disorders; preoccupation with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders; guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).
- Specify if:
- **With good or fair insight**: The individual recognizes that obsessive-compulsive disorder beliefs are definitely or probably not true or that they may or may not be true.
- **With poor insight:** The individual thinks obsessive-compulsive disorder beliefs are probably true.
- **With absent insight/delusional beliefs**: The individual is completely convinced that obsessive-compulsive disorder beliefs are true.
- Specify if:
- **Tic-related:** The individual has a current or past history of a tic disorder.

Obsessions or compulsions (intrusive, unwanted, attempts to ignore or resist) or both, time consuming (>1 hr) or significant distress, not substance and not other mental disorder
Specify insight and hx of tics

OCD – DSM V

- Inflated sense of responsibility, intolerance of uncertainty, over-importance of thoughts, need to control thoughts
- Poorer insight = worse long term outcome
- 30% have a lifetime tic disorder, most common in males with childhood onset – different course, themes, comorbidity
- Must be more than one hour per day
- Themes of obsessions and compulsions tend to be consistent over time in adults with the disorder and may be associated with different neural substrates
- Avoidance
- Prevalence approx. 1.2%, females more than males in adulthood, males more in childhood
- Onset 19.5 years, 25% of cases by age 14, onset after 35 unusual
- Males earlier onset than females; 25% of males before age 10
- Onset is typically gradual but in some cases acute
- If OCD is untreated, course is usually chronic with waxing and waning symptoms; some are episodic, some deteriorating
- Without treatment, remission rates in adults are low (20%) but for children, 40% experience remission by early adulthood
- Compulsions more easily diagnosed in children as observable, harder for them to explain obsessions

Poor insight = bad
30% lifetime tix d/o, more males, childhood
Themes tend to be consistent over time
M>F in kids, F>M adults
25% cases before age 14, average onset 19.5
1.2% prevalence
Earlier onset in M
Course chronic with waxing and waning sx, remission w/o tx 20%, kids 40%

OCD – DSM V

Higher rates of harm obsessions in kids, higher rates of sexual and religious obsessions in adolescents

Females more cleaning obsessions, males more forbidden thoughts and symmetry

Aggressive obsessions in perinatal period

Suicidal ideation in 50%, attempts in 25%, comorbid depression increases risk

Family dysfunction

76% have lifetime anxiety disorder (panic, SAD, GAD, phobia), 63% mood disorder, 41% depressive disorder, 23-32% OCPD, 30% tic disorder

Triad of OCD, tics and ADHD also seen in children

Also more BDD, trichotillomania, excoriation disorder, ODD

In patients with scz or sca, 12% have OCD – rates of OCD also elevated in Bipolar disorder, ED, Tourette's

Risk factors:

- *Temperament: greater internalizing symptoms, higher negative emotionality, behavioral inhibition in childhood*
- *Environmental: physical and sexual abuse in childhood, stressful or traumatic life events in childhood, sudden onset associated with infectious, immune cases*
- *Genetic: OCD 2x more common in first degree relatives in adults, among childhood onset, risk increased 10 fold!*
- *Dysfunction in orbitofrontal cortex, anterior cingulate cortex and striatum*

- SI in 50%, attempts 25%, increased by comorbid depression
- 76% have lifetime anxiety disorder, 63% mood disorder, 41% depressive disorder, 30% OCPD, 30% tics (note: OCPD not most common – anxiety disorder is)
- 12% of SCZ/SCA have OCD
- Childhood onset 10 fold increased risk for 1st degree relatives

Body Dysmorphic Disorder - Criteria

- Preoccupation with one or more perceived defects or flaws in physical appearance that are not observable or appear slight to others
- At some point during the course of the disorder, the individual has performed repetitive behaviors (ie. Mirror checking, excessive grooming, skin picking, reassurance seeking) or mental acts (comparing appearance with others) in response to the appearance concerns.
- The preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
- The appearance preoccupation is not better explained by concerns with body fat or weight in an individual whose symptoms meet diagnostic criteria for an eating disorder
- Specify if: with muscle dysmorphia: the individual is preoccupied with the idea that his or her body build is too small or insufficiently muscular
- With good or fair insight (probably not true), with poor insight (probably true), absent insight/delusional beliefs (completely convinced)

BDD = preoccupation with imagined flaw, repetitive behaviors, significant distress, not concern over weight/ED
Specify insight and muscle dysmorphia

BDD - DSM

3-8 hrs per day
Behaviors not pleasurable and can increase anxiety
Muscle dysmorphia in males
Insight is poor with 1/3 delusional, IOR
2.4%, slightly more F>M
Most common onset 12-13 (2/3 before 18)

- Used to be dysmorphophobia
- Most commonly skin, hair, or nose, but could be any body part, asymmetry
- Preoccupations are intrusive, unwanted, time consuming (3-8 hrs per day), difficult to resist or control
- Behaviors are not pleasurable and may increase anxiety and dysphoria, time consuming, difficult to resist or control
- Skin picking can cause damage, infections
- Muscle dysmorphia almost exclusively in males
- Body dysmorphic disorder by proxy – obsessed with defects in another's appearance
- On average insight is poor with a 1/3 having delusional beliefs
- Many have ideas or delusions of reference, believing that other people take special notice of them or mock them because of how they look
- Associated with executive dysfunction and visual processing abnormalities with a bias for analyzing and encoding details rather than holistic or configural aspects of visual stimuli
- Also have a bias for negative and threatening interpretations of facial expressions and ambiguous scenarios
- 2.4% prevalence, slightly more F than M
- Up to 9-15% in derm patients, 3-16% of cosmetic surgery patients
- Mean age of onset 16-17 years, most common age 12-13 (2/3 before 18)
- Typically subclinical concerns gradually becoming full BDD

BDD - DSM

Onset before 18 more likely to SA, comorbidities, gradual onset
Adult onset more acute
Males – muscles and genitals
High suicide risk, very impairing, 20% of kids drop out of school
MDD most common comorbid - after BDD onset
SAD, OCD, SUDs common

- Chronic, but can improve w evidence based tx
- Individuals w disorder onset before age 18 are more likely to attempt suicide, have more comorbidity, and have gradual onset than those with adult onset (more acute)
- Associated with high rates of childhood neglect and abuse, elevated risk in first degree relatives with OCD
- Taijin kyofusho in Japan is similar
- Males more likely to have genital preoccupations and females more likely to have a comorbid eating disorder, males muscle dysmorphia
- Risk for suicide high especially in adolescents
- Impairment can be as severe as housebound, 20% of kids drop out of school
- Different than an eating disorder – primary concern about being fat, though BDD can have weight concerns; can be comorbid
- Poorer insight than OCD
- Different than excoriation disorder → skin picking intended to improve skin defects
- If belief one emits a foul odor = olfactory reference syndrome, not BDD
- Body identity integrity disorder – desire to have a limb amputated – also not BDD
- Koro – fear that the penis is shrinking or retracting and will disappear and death will result (not BDD – fear of death)
- MDD most common comorbid disorder, onset after BDD
- Social anxiety disorder, OCD, SUDs also common

Hoarding Disorder – DSM V

- Difficulty parting with items, need to save, causes accumulation, significant distress or impairment
- Specify if excessive acquisition, insight

- Persistent difficulty discarding or parting with possessions, regardless of their actual value
- Difficulty is due to a perceived need to save the items and to distress associated with discarding them
- Difficulty discarding possessions results in the accumulation of possessions that congest and clutter active living areas and substantially compromises their intended use. If living areas are uncluttered, it is only because of the interventions of third parties (ie. Family members, cleaners, authorities)
- The hoarding causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (including maintaining a safe environment for self and others)
- The hoarding is not attributable to another medical condition (ie. Brain injury, cerebrovascular disease, Prader Willi)
- The hoarding is not better explained by another mental disorder (ie. Cognitive deficits in MNCD, restricted interests in ASD)
- Specify if: with excessive acquisition (if difficulty discarding possessions is accompanied by excessive acquisition of items that are not needed or for which there is no available space), with good, poor, or absent insight

Hoarding Disorder

- Majority have excessive acquisition – buying, then free items
- 2-6% prevalence, more in M
- 3 x more older adults> younger, increases in severity with time
- 75% comorbid mood or anxiety
- 20% OCD

- 80-90% of people with hoarding disorder display excessive acquisition
- The most frequent form is buying followed by free items (leaflets), stealing less common
- Most commonly saved items are newspapers, magazines, old clothing, bags, books, mail and paperwork
- Sometimes valuable items
- Intentional saving, not passive accumulation seen in other disorders
- Other common features of hoarding disorder include indecisiveness, perfectionism, avoidance, procrastination, difficulty planning, and organizing tasks and distractibility
- Animal hoarding - even more unsanitary conditions and poorer insight
- 2-6% prevalence, significantly greater in M
- Three times more in older adults (55-94) compared to younger
- Appears to begin early in life and spans into late stages (ie. Age 11-15), significant impairment by mid-30s
- Increases in severity with each decade of life, chronic course
- Risk factors: indecisive temperament, stressful or traumatic life events, familial – 50% have a relative that also hoards
- Universal phenomenon across cultures
- Females have more acquisition behaviors
- Damage to the anterior ventromedial prefrontal and cingulate cortices has been associated with an excessive accumulation of objects – clear they did not have this before
- 75% have a comorbid mood disorder or anxiety disorder (MDD in 50%, then SAD, GAD, 20% OCD)

Trichotillomania – DSM V

Pull hair, lose hair, try not to, causes distress
Routines around pulling
1-2% prevalence, F>M 10:1
In kids, M=F
Comorbidities = MDD, excoriation

- Recurrent pulling out of one's hair, resulting in hair loss
- Repeated attempts to decrease or stop hair pulling
- The hair pulling causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
- The hair pulling or hair loss is not attributable to another medical condition (ie. Derm)
- Hair pulling is not better explained by the symptoms of another mental disorder (ie. Attempts to improve a perceived defect or flaw in appearance)
  - *Can be scalp, eyebrows, eyelids*
  - *May occur in brief episodes throughout day or more sustained periods that continue for hours*
  - *May have routines around pulling, ie. Certain hair, may bite or swallow hair after pulled*
  - *Varying states of awareness*
  - ***Tonsure trichotillomania – nearly complete baldness except a narrow perimeter around the margins of scalp and nape of neck***
  - *Some individuals have urge to pull other's hair or hairs from other fibrous materials*
  - *1-2% prevalence, females more than males 10:1*
  - *Among children, M = F*
  - *Dermoscopy shows* ***decreased hair density, short vellus hair, broken hairs with different shaft lengths***
  - *Can get random sequelae: digit purpura, carpal tunnel, blepharitis, dental damage, trichobezoars*
  - *Most commonly accompanied by MDD and excoriation disorder*

Excoriation (Skin-Picking) Disorder - Criteria

- Skin picking, lesions, try to stop, distress, not scabies, not cocaine
- 1.4%, more F
- Often begins w skin condition like acne

- Recurrent skin picking resulting in skin lesions
- Repeated attempts to decrease or stop skin picking
- The skin picking causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
- Not attributable to a substance (cocaine) or med condition (scabies)
- Not better explained by another mental disorder
- Tidbits:
  - *May pick at healthy skin, minor skin irregularities, pimples or calluses or scabs*
  - *Face arms and hands but can be any*
  - *Use fingernails, tweezers, pins*
  - *Sometimes up to several hours per day*
  - *Requires that skin lesions occur but often will conceal with makeup or clothes*
  - *May be accompanied by rituals – ie. Searching for particular scab to pull, may examine, play with, or swallow the skin after it has been pulled*
  - *May be preceded by tension, and then relief*
  - *Pain not often reported*
  - *Some people do it automatically without full awareness*
  - *Often not done in front of others*
  - *Lifetime prevalence 1.4%, most female, onset adolescence*
  - *Frequently begins with derm condition like acne, course chronic, waxing and waning*

Substance/Medication Induced OC and related disorder

- *Criteria:*
  - *Obsessions, compulsions, skin picking, hair pulling, other body-focused repetitive behaviors, or other symptoms characteristic of obsessive-compulsive and related disorder predominate the clinical picture*
  - *Evidence from hx, px, or labs that the sx developed during or after substance intoxication or withdrawal or exposure to a med AND the involved substance is capable of producing the sx*
  - *The disturbance is not better explained by an OCD and related disorder that is not substance induced*
  - *The disturbance does not occur exclusively during the course of a delirium*
  - *The disturbance causes clinically significant distress or impairment in social, occupational, or other areas of functioning*
  - *Specify if: with onset during intoxication, during withdrawal or after medication use*
- *Tidbits:*
  - *Very rare*
  - *Can occur in stimulants, heavy metals and toxins*

OC and related disorder due to another medical condition

Criteria:

- *Obsessions, compulsions, preoccupations with appearance, hoarding, skin picking, hair pulling, other body-focused repetitive behaviors, or other symptoms characteristic of obsessive-compulsive and related disorder predominate the clinical picture*
- *Evidence from hx, px, or labs that the disturbance is the direct pathophysiologic consequence of another medical condition*
- *The disturbance is not better explained by another mental disorder*
- *The disturbance does not occur exclusively during the course of a delirium*
- *The disturbance causes clinically significant distress or impairment in social, occupational, or other areas of functioning*
- *Specify if: with OCD like symptoms, with appearance preoccupations, with hoarding symptoms, with hair pulling symptoms, with skin pulling symptoms*

Sydenham's chorea → group A strep rheumatic fever – neuro manifestation – obsessions, compulsions, attention deficit, emotional lability (in addition to carditis, arthritis)

PANDAS – post-infectious autoimmune disorder characterized by the sudden onset of obsessions, compulsions, and/or tics accompanied by a variety of acute neuropsychiatric symptoms in the absence of chorea, carditis, or arthritis after Group A strep infection

Remains controversial → now PANS (pediatric acute onset neuropsychiatric symptoms) or CANS (idiopathic childhood acute neuropsychiatric symptoms)

Cerebral infarction resulting in striatal damage can cause OCD like sx

Other specified OC and related disorder

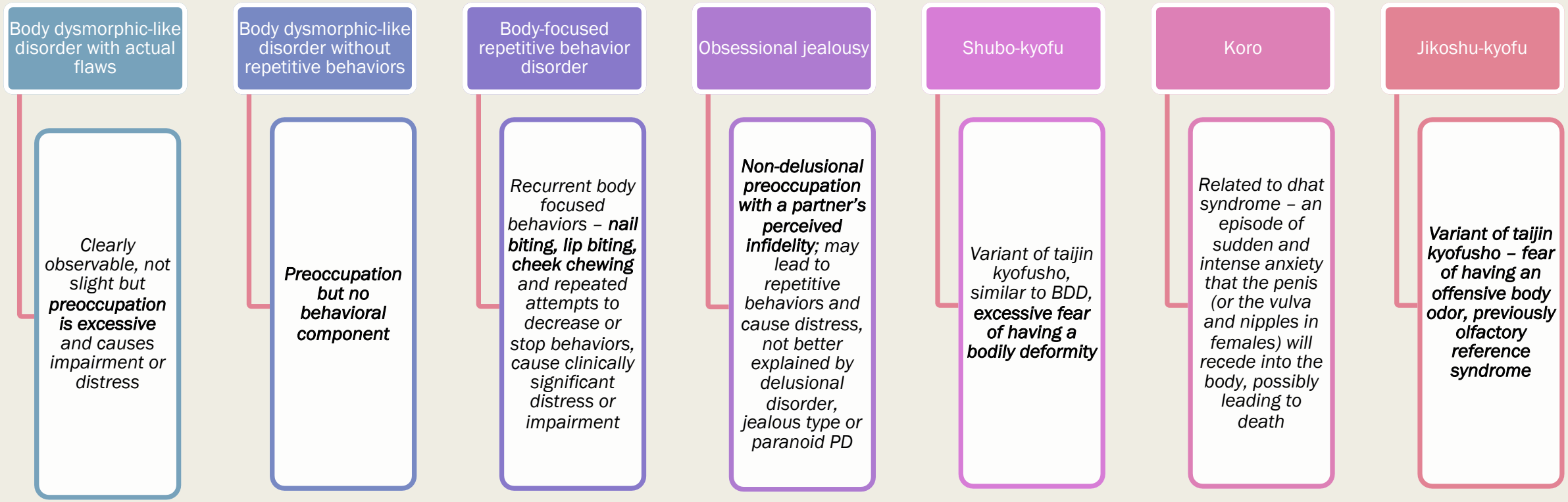


Table 27 Recommendations for pharmacotherapy for OCD

First-line	Escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
Second-line	Citalopram, clomipramine, mirtazapine, venlafaxine XR
Third-line	IV citalopram, IV clomipramine, duloxetine, phenelzine, tramadol, tranylcypromine
Adjunctive therapy	**First-line:** aripiprazole, risperidone **Second-line:** memantine, quetiapine, topiramate **Third-line:** amisulpride, celecoxib, citalopram, granisetron, haloperidol, IV ketamine, mirtazapine, N-acetylcysteine, olanzapine, ondansetron, pindolol, pregabalin, riluzole, ziprasidone **Not recommended:** buspirone, clonazepam, lithium, morphine
Not recommended	Clonazepam, clonidine, desipramine

IV = intravenous; XR = extended release.

GUIDELINES

1st = ESP, fluoxetine, fluvoxamine
2nd = citalopram, clomipramine, mirtazapine, venlafaxine
Adjuncts – abilify, risperidone 1st, memantine, quetiapine, Topamax 2nd
NO to buspirone, clonazepam, Li, morphine adjunct
NO to clonazepam, clonidine, desipramine for tx

Guidelines

- 1-2% prevalence, mean onset 20
- CBT, ERP first line – equal or superior to pharm
- Combo better than pharm, = CBT alone
- No to naltrexone
- Symmetry and hoarding may have worse response

- Relatively uncommon, yet severe – lifetime 1-2.3%, 12 mo 0.7-1.2%
- Mean onset age 20, but can start under age 10
- CBT and ERP are effective first line options – equivalent or superior to pharmacotherapy
- Group or individual , self-help, books, telephone, internet based
- Maintained over 5 years of follow up
- Combo pharmacotherapy and psychotherapy > pharm alone but = CBT
- Begin with SSRI – cipralex, fluoxetine, fluvox, paroxetine, sertraline → if response to optimal doses is inadequate or agent not tolerated, therapy should be switched to another first line agent before second line.
- Second line = citalopram, clomipramine, mirtazapine, venlafaxine XR
- Adjuncts may be important early in treatment
- Not recommended = clonazepam, clonidine, desipramine, bupropion, naltrexone
- Clomipramine similar efficacy to SSRIs but more poorly tolerated
- Symmetry/hoarding symptoms may have a poorer response to SSRI therapy (more dopamine system?)

Ottawa Review Course

- Compulsive eating, gambling, or sexual behavior may feel out of control and patients recognize their behaviors are harmful
- Unlike OCD, at least some of the time these acts are gratifying
- **BOCS, YBOCS**
- Psyched Ups OCD suggestions = escitalopram, sertraline, fluoxetine, desvenlafaxine, duloxetine, levomilnacipran, vortioxetine, vilazodone, mirtaz (2nd line)

London Review Course

- YBOCS scale, response is >25% reduction
- 90% have another disorder, most anxiety
- 4% delusional
- 80% O, 55% C in gen pop
- OCPD only in 25%
- Worries less egodystonic

- See compulsions with harm avoidance or attaining just right feeling
- YBOCS best scale, response is >25% reduction, remission is less than 8
- Rate level of insight
- 90% have another psychiatric disorder – most another anxiety disorder
- 4% have absent or delusional insight
- 80% of non-clinical samples have obsessions, 55% get compulsions
- Core symptoms seem independent of culture, religion or geography
- Mental compulsions – praying, reviewing, analyzing, replacing, re-thinking, mentally reorganizing
- Know difference between a mental compulsion and an obsession
- Comorbid with OCPD is less common 25% than most think
- Worries are more often triggered by internal or external event, less intrusive, related to experiences of everyday life, ego-syntonic, almost always just a thought (OCD – images, impulses)

London Review Course

- BDD focused solely on appearance, behaviors more likely to increase distress – mirror checking
- OCPD – ego syntonic obsessions, less distressed by behavior – if people would just do things their way, world would be a better place, see other symptoms – trouble spending money on self, trouble delegating, trouble throwing out old clothes
- Neuroanatomy – decreased caudate size, increased activity in orbito-frontal lobes, caudate, basal ganglia, anterior cingulate cortex, thalamus
- Genetics – more in childhood onset
- Serotonin, dopamine, glutamate
- Childhood onset – high severity, more significant Os and Cs, higher rates of tic disorders, less chance of response to SRI than adult, may be secondary to PANDAs
- Hypofunction at cortico-striatal-thalamo-cortical circuit (inhibitory), leads to hyperfunction at orbito-fronto-thalamic circuit (excitatory)
- Hyperactivity at DL PFC, supplemental motor areas, orbitofrontal thalamic circuit (deficits in inhibition of irrelevant info – concerns about danger, order, violence, hygiene, sex)
- MZ concordance = 80-87%, ½ variance due to genetics, 4x more likely if first degree relative
- Ordering and hoarding compulsions more genetic
- Genes in 5HT and glutamate regulation
- 21% of patients with OCD had childhood onset of their condition

- Corticostriatalthalamocortical circuit has hypofxn
- Decreased caudate size
- Childhood – severe, more tics, less response to SSRI
- 4 x more likely in first degree, 80-87% MZ concordance
- More genes in ordering and hoarding
- 21% have childhood onset

London Review Course

- Higher dose SSRIs, 8-12 weeks
- Try 2 SSRIs before clomipramine
- 6 mo – 2 years at least
- Fluvox, 2D6, clomipramine
- 10% tx refractory

- Treatments = CBT (ERP), meds, combo, psychosurgery, DBS, TMS
- First line meds = ESP, fluvox and fluoxetine, second = clomipramine, venlafaxine XR, citalopram, mirtazapine, third line = IV citalopram, IV clomipramine, duloxetine, tramadol, MAOIs
- Adjunct with risperidone and abilify, second line adjuncts = memantine, quetiapine, topiramate
- Therapeutic dose often higher than AD doses, length should be 8-12 weeks
- Try two SSRIs first, if no response then clomipramine (equal effectiveness but less tolerability)
- If lack of insight, consider antipsychotic SSRI combo
- If response, continue meds 6 mo to 2 years, lifelong for some
- Fluvox inhibits the conversion of clomipramine (more sertonergic) to desmethylclomipramine (more adrenergic) allowing for greater serotonin effect through 2D6
- CBT uses habituation and new learning
- Target family to improve outcomes
- At least 10% are treatment refractory – 3 failed SSRIs trials, failed augmentation x 2, failed CBT and meds

London Review Course

- Psychosurgery – cingulotomy or anterior capsulotomy, 25-30% response rate; seizures, EF defects, memory impairment, apathy, disinhibition as SE; may respond to meds post-surgery that were unresponsive to surgery
- DBS = still experimental, targets ventral capsule, can be adjusted
- TMS = stimulation of supplementary motor, low frequency more effective (inhibits cortical activity), daily for weeks
- ECT not recommended for OCD uncomplicated by co-morbidities – poor evidence, lack of controlled studies, lack of outcome measures
- Waxing and waning course better prognosis, constant unremitting course worth
- Poorer outcomes in = **early age of onset, yielding to compulsions, bizarre compulsions, hospitalization, comorbid depression, lack of insight (delusions, overvalued ideas, schizotypal PD)**
- **60-90%** have at least one other psychiatric diagnosis – bipolar, SAD, MDD, phobia, panic, GAD, tic, somatoform
- In bipolar – mood stabilization is most important goal, a minority of patients require SSRIs too, **OCD symptoms more in depressive phase** and often remit in mania
- **Clozapine 20-28%** have de novo OCD symptoms or exacerbation of pre-existing, 11-20% of olanzapine
- **5-20% of bipolar** have OCD → poorer QOL, episodic course, rapid cycling, greater disability, increased suicide risk, eating disorders, substance abuse
- Shared pathophysiology with OCD and bipolar – **more sexual, aggressive, religious obsessions, ordering, checking, repeating compulsions**

- Surgery = cingulotomy, ant capsulotomy, 25-30% response
- Not much for ECT
- Waxing, waning better than unremitting
- Poor prognosis: early age onset, yielding to compulsions, bizarre compulsions, depression, lack of insight
- 60-90% comorbidity
- Clozapine – 20-28% de novo OCD
- 5-20% in bipolar – more rapid cycling, disability, suicide

Toronto Review Course

- **Highest comorbidity with anxiety disorders**, then depressive or bipolar disorders, then SUDs, then OCPD, tics 30% lifetime
- **Checking most common compulsion, then washi**ng
- **Aggressive obsessions most common, then contamination**
- **No to clonazepam, clonidine, desipramine, buspar**
- Strongest evidence for adjunctive therapy is **risperidone**
- Avoid benzos
- **Combo > meds but not > CBT alone**
- Therapist guided better than self guided
- Group and individual CBT has evidence
- Family accommodation = poorer response

K and S

- 2-3% prevalence
- M=F, but childhood M>F
- Onset earlier in males
- Dysregulation of serotonin
- PET shows increased activity in frontal lobes, basal ganglia, cingulum
- **Bilaterally smaller caudates**
- Onset of OCD over 30 unusual – investigate
- 60% of Tourette's has OCD
- >50% have sudden onset, often stressful event like pregnancy
- 1/3 have MDD
- Good prognostic factors = **episodic, precipitating event, good social fxn**
- **BDD highly comorbid with depression**
- In BDD compulsions increase distress rather than OCD – decreases it temporarily

- Hoarding in 2-5% as high as 14%
  - *Early adolescence*
  - *30% OCD has hoarding behavior*
  - *Some comorbidity with ADHD*
  - *Also seen in neurocog disorders*
  - *For anxiety disorders, most associated with GAD*
  - *Less responsive to therapy and meds (only 18% respond)*
- Hair pulling disorder
  - *35-40% swallow it*
  - ***Earlier onset remits more readily, later onset more chronic****
- Excoriation disorder
  - *1-5%, 12% in adolescents*
  - *More F>M*
  - *38% have trichotillomania, 38% have SUDs*
  - *Prader Willi – 97%*
  - *High rates comorbid OCD*
  - *Picking can coincide with menstrual cycle*

PANDAS Guidelines

- **Pediatric Acute Onset Neuropsychiatric Syndrome (PANS)**
  - *Lightning like onset of **OCD or eating restrictions** and comorbid symptoms, two of the following:*
    - Anxiety (particularly **separation anxiety)**
    - Emotional lability or depression
    - Irritability, aggression, oppositional behaviors
    - **Deterioration in school performance** related to ADHD like behaviors, cognitive changes
    - Sensory or motor abnormalities
    - Somatic signs and symptoms including **sleep disturbances, enuresis and urinary frequency**
- **Education, supportive and behavioral therapies, and psychoactive medications are the mainstays** of symptomatic treatment
- School accommodation often required
- First address safety – need for hospitalization
- Family support
- **CBT and ERP and minimizing family accommodation most effective interventions** for pediatric OCD; highly effective in PANS; initiate tx as soon as possible to max benefits
- **Tx with same pharmacotherapy as in OCD**, may be more sensitive to adverse effects, start low and go slow, **benzos may help as well**
- **SSRIs preferred medication – fluoxetine, fluvoxamine, sertraline, clomipramine**

PANDAS Guidelines

- From International OCD Foundation Fact Sheet: PANS usually younger age of onset than childhood OCD (3-14 vs 9-10), do throat swab, if negative do ASO titer.
- ASO at sx onset less than 2 weeks and again 4-8 weeks later will provide support of strep trigger if fourfold rise in titers observed
- Not diagnostic
- Other illnesses can cause acute OCD onset – Lyme, thyroid, Celiac, lupus, Kawasaki's, etc.

- **70% develop tics – CBIT, HRT, clonidine, guanfacine**
- Irritability and aggression – benzos may be safest and most effective, antipsychotics maybe, Benadryl
- Stimulants if ADHD
- Sleep disturbances – **REM sleep behavior disorder in PANS** – use good sleep hygiene, then Benadryl, melatonin, clonidine, zolpidem
- Depression – CBT, SSRI
- Psychosis – atypicals
- Pain – physical therapy
- **For mild PANS – most appropriate is tincture of time with CBT and supportive therapies**
- **For moderate to severe, oral or IV steroids; IVIG**
- For more severe or chronic presentations – prolonged steroids with taper or repeated high dose steroids
- For PANS with **extreme and life threatening impairment, therapeutic plasma exchange is first line**, alone of in combo with IVIG, high dose IV steroids, rituximab
- **Initial course of anti-streptococcal treatment proposed for all newly diagnosed PANS cases**
- Chronic secondary antimicrobial prophylaxis for PANDAS with severe neuropsych symptoms or recurrent group A strep associated exacerbations
- Closely monitor PANS for strep pharyngitis, diagnose and treat promptly
- Standard immunizations and attention to vitamin D encouraged
- **Limited utility of adenotonsillectomy and probiotics**
- **If new PANS → do throat swab, if positive, treat with Amoxil**
- PANDAS diagnosis needs strep documentation
- Initial course of antibiotics is recommended for cases of PANS with or without evidence for strep, but long-term antibiotics not recommended

Resources

- DSM V
- K and S
- Canadian Anxiety Guidelines 2014
- Journal of Child and Adolescent Psychopharmacology 2019 – Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part I – Psychiatric and Behavioral Interventions
- IOCDF.ORG Fact Sheet on PANDAS
- Ottawa Review Course
- Toronto Review Course
- London Review Course