

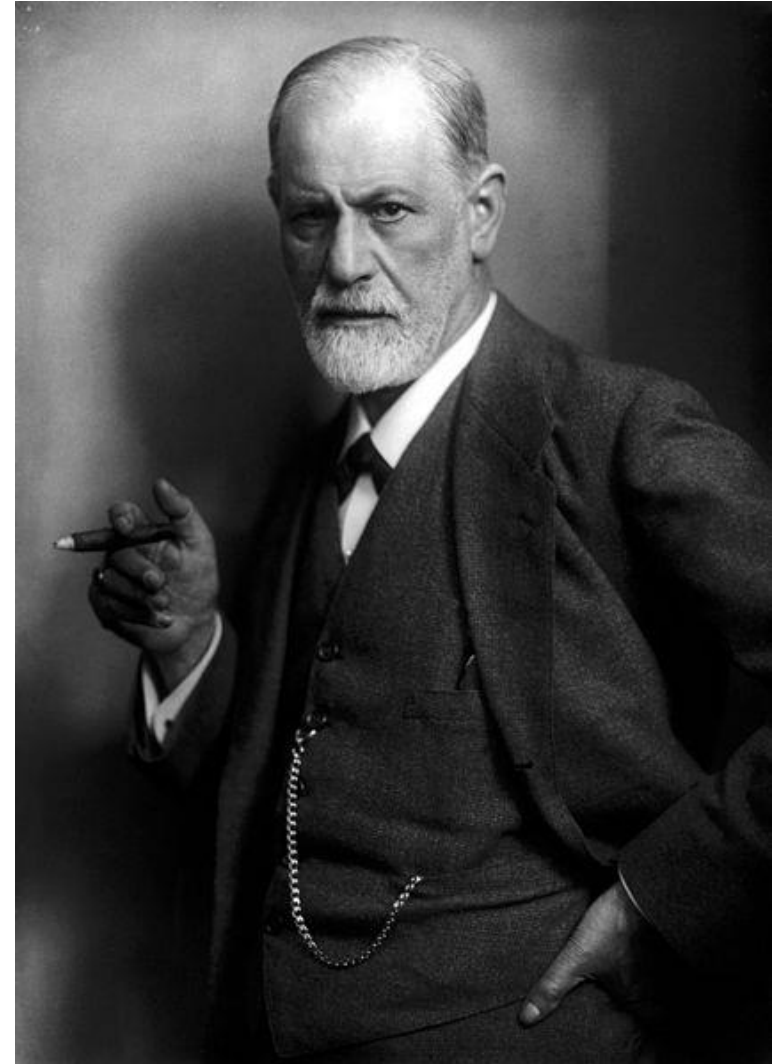
Defense Mechanisms

Jason Ryan, MD, MPH



Freudian Psychology

- Id - desire
- Superego – societal rules, morality
- Ego - mediator between id and superego



Wikipedia/Public Domain

Ego Defenses

- **Unconscious** adjustments in reality perception
- Resolve/manage conflict between id and superego
- Minimize anxiety
- Adaptation to stressful circumstances

Acting Out

- Avoiding emotions by **bad behavior**
- Attention seeking, socially inappropriate behavior
- Examples:
 - Child with sick parents misbehaves at school
 - Adolescent engages in promiscuous sex during parents' divorce



Denial

- **Refusing to accept** unpleasant reality
- Examples:
 - Patient thinks doctor is wrong about diagnosis
 - Heavy drinker believes she drinks socially



Projection

- Attributing feelings/emotions to others
- A cheater accuses a classmate of cheating off him



Clipart/Public Domain

Regression

- Reverting to behavior of younger person/child
- Stressed adult watches cartoons from childhood
- Sick adult wants parent to stay in hospital with them
- Hospitalized older child begins to wet his bed



Clipart/Public Domain

Displacement

- Directing emotions to another person
- Examples:
 - Patient angry at doctor after injury
 - Mother angry at husband yells at child



Reaction Formation

- Turning feelings into opposites
- Goes beyond denial
- Man who craves alcohol preaches abstinence
- Woman despises mother, throws birthday party
- Parent despises child shows extreme love/affection



Clipart/Public Domain

Intellectualization

- Avoiding emotions through reasoning
- Spouse going through divorce cites divorce statistics to friends to avoid admitting sadness



Rationalization

- Distorting events so outcome is positive
- “I’m glad I got fired, I needed a change.”

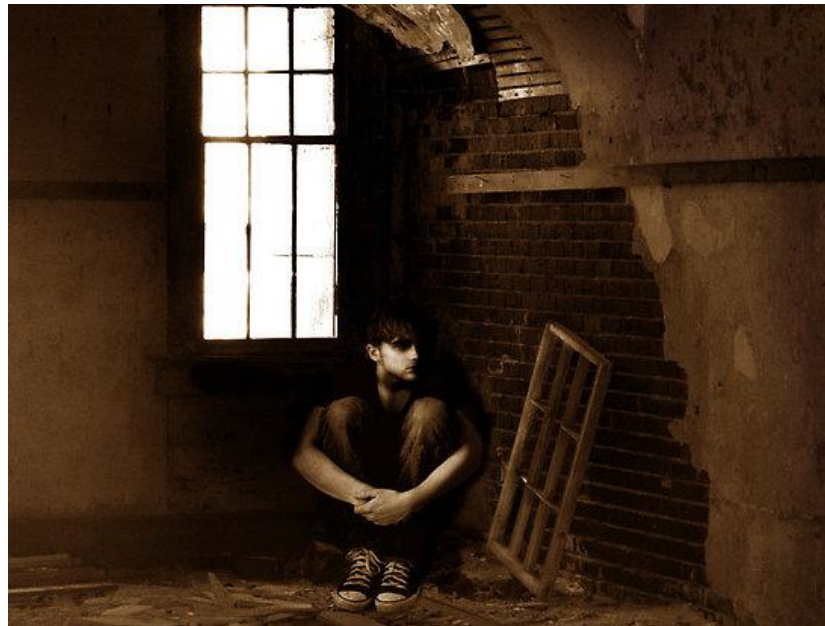


Repression

- “Motivated forgetting”
- Usually **forgetting** one particular memory/fact
- Often something that happened long ago
 - Example: difficult period of childhood
- First defense mechanism described by Freud
- Thoughts repressed to avoid guilt

Isolation of Affect

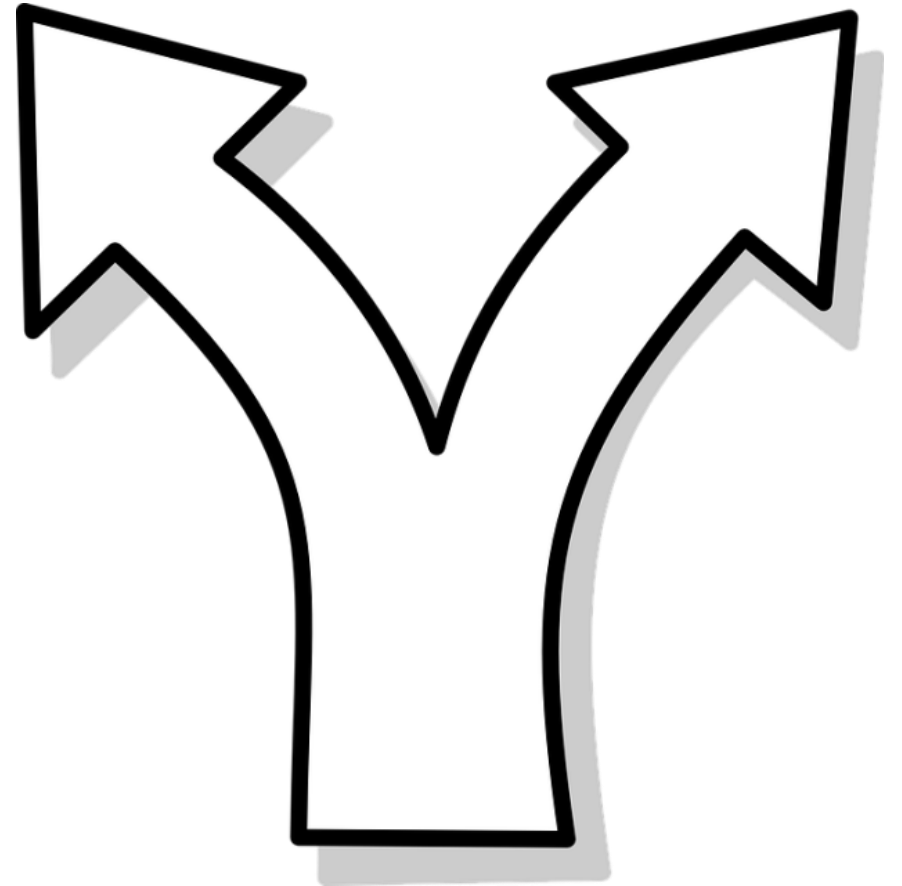
- Isolating a distressing memory/event
- Failing to experience emotions of event
- Person describes rape without expressing sadness



Clipart/Public Domain

Splitting

- Categorizing others at extremes
- “Wonderful” or “horrible” people
- Patient loves her doctor but hates nurse
- Common in borderline personality disorder



Clipart/Public Domain

Undoing

- Reaction to an unhealthy or destructive thoughts or acts
- **Engaging in contrary behavior**
- Trying to make things “unhappen”
- Example:
 - Patient thinks about hurting someone
 - Acts overly nice to person in response

Altruism

- Practice of concern for others
- Caring for others to reduce stress/anxiety
- Cancer survivors help others with same disease



Clipart/Public Domain

Humor

- Relief of anxiety with jokes/laughter
- Medical student jokes about board studying



Sublimation

- Using negative emotions in a positive way
- Anxious person becomes a security guard
- Aggressive person becomes a boxer

Suppression

- **Conscious** defense mechanism
- Done intentionally to relieve stress/anxiety
- Ignoring stressful thoughts/feelings to cope
- “I’m not going to think about that now”
- Contrast with repression (unconscious)

Mature Defenses

- Sublimation
- Altruism
- Suppression
- Humor

Psychotic Disorders

Jason Ryan, MD, MPH



Psychosis

- Loss of perception of **reality**
- Occurs in medical and psychiatric disorders
 - Delirium
 - Schizophrenia
 - Drug-induced (illicit and prescription)
- Three main manifestations
 - Delusions
 - Disorganized thought
 - Hallucinations

Delusions

- Strongly held **beliefs** that conflict with reality

Delusion	Example
Persecutory	Someone is after me!
Grandiose	I am a millionaire!
Erotomantic	Brad Pitt is in love with me.
Somatic	There are worms in my chest!
Delusions of Reference	The television news caster is talking about me.
Delusions of control	My body is controlled by aliens! I can control the sun!

Disorganized Thought

- Shown by **patterns of speech**
- Alogia (speech poverty)
- Thought blocking
 - Sudden, abrupt stop while talking
- Loosening of association
 - Ideas discussed that do not follow each other
- Tangentiality
 - Diverging from topic under discussion to another



Nevit Dilmen/Wikipedia

Disorganized Thought

- Clanging
 - Using words that rhyme but do not make sense
 - “The cow said how he had to bow”
- Word salad: incoherent words that make no sense
- Perseveration: repeating words or ideas persistently



Clipart/Public Domain

Hallucinations

- Sensory perceptions without external stimuli
- **Visual**
 - Seeing things that are not there
 - Common in hospitalized patients with delirium
 - Usually has an “organic” cause – drugs, disease
- **Auditory**
 - Hearing voices or sounds
 - Classic feature of schizophrenia
- Rarely olfactory (smell), gustatory (taste) or tactile (bugs crawling on skin)

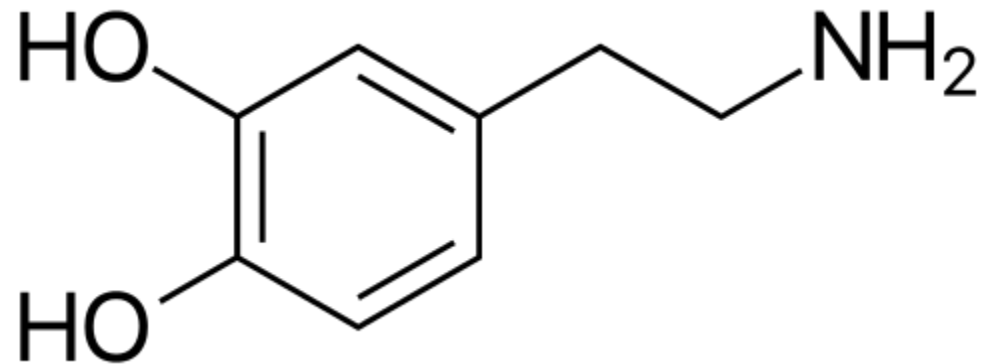
Schizophrenia

- Chronic psychiatric syndrome
- Recurrent episodes of psychosis
- Cognitive dysfunction
- Negative symptoms

Schizophrenia

Pathology

- Excess central **dopamine** activity
- Dopamine antagonists used for therapy
- Also hypofunction of the **NMDA glutamate receptor**

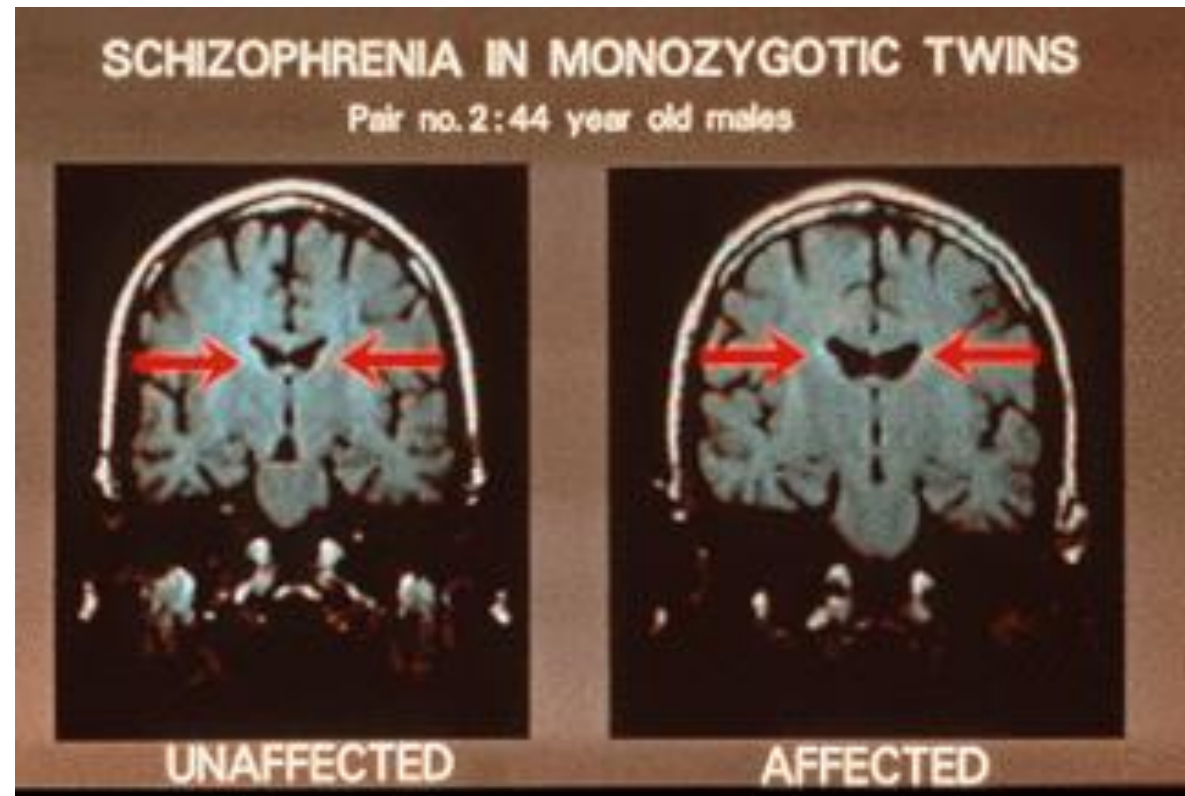


Dopamine

Schizophrenia

Pathology

- MRI/CT:
 - **Lateral ventricular enlargement**
- PET scan:
 - Hypoactivity frontal lobe
 - Hyperactivity basal ganglia



Schizophrenia

Epidemiology

- Lifetime prevalence about 1% adults globally
- Slight male predominance
- Occurs in **adolescence/young adulthood**
 - Men: 18 to 25
 - Women: 25 to 35



Brenkee/pixabay

Schizophrenia

Risk Factors

- Living in **urban areas** (cities)
- Immigration
 - UK study: immigrants ten times more risk



Schizophrenia

Risk Factors

- **Obstetric complications**
 - Hemorrhage
 - Preterm labor
 - Blood-group mismatch
 - Fetal hypoxia
 - Maternal infection



Øyvind Holmstad/Wikipedia

Schizophrenia

Risk Factors

- **Cannabis use**
- Usually in adolescence
- Unclear if cause-effect
- Mild symptoms may lead to cannabis use

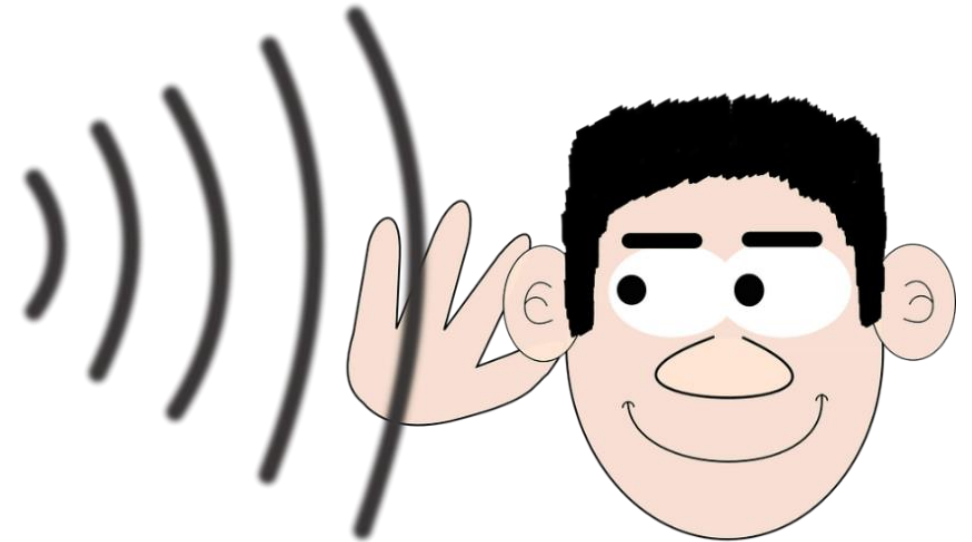


Chuck Grimmett/Wikipedia

Schizophrenia

Hallucinations and delusions

- Main manifestation: **auditory hallucinations**
 - Hearing voices
 - Strange sounds
- **Delusions**



Pixabay/Public Domain

Schizophrenia

Disorganized speech

- Most commonly tangential or circumstantial speech
- **Tangential speech**
 - Changes topic frequently
 - May not answer questions
- **Circumstantial speech**
 - Long, round-about answers to questions

Schizophrenia

Cognitive impairment

- Difficulty processing information
- Poor attention
- Poor learning and memory

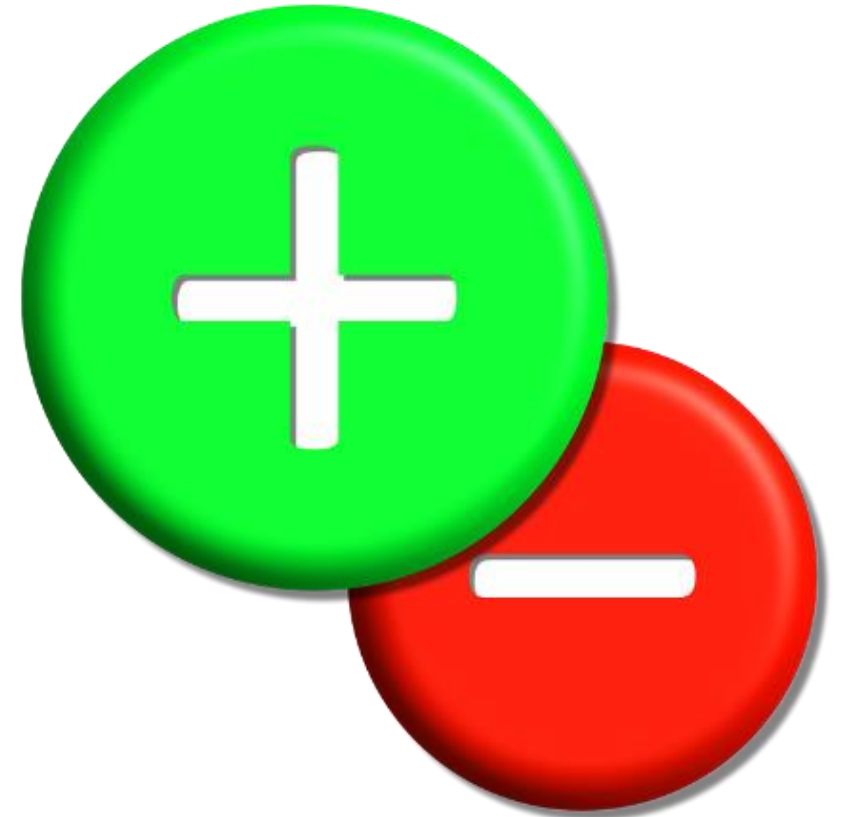


[Onlineassignmenthelps/Wikipedia](https://en.wikipedia.org/wiki/Schizophrenia)

Schizophrenia

Positive Symptoms

- Abnormal behaviors
- Hallucinations, delusions, disorganized thought
- Related to dopamine activity
- Respond to antipsychotics

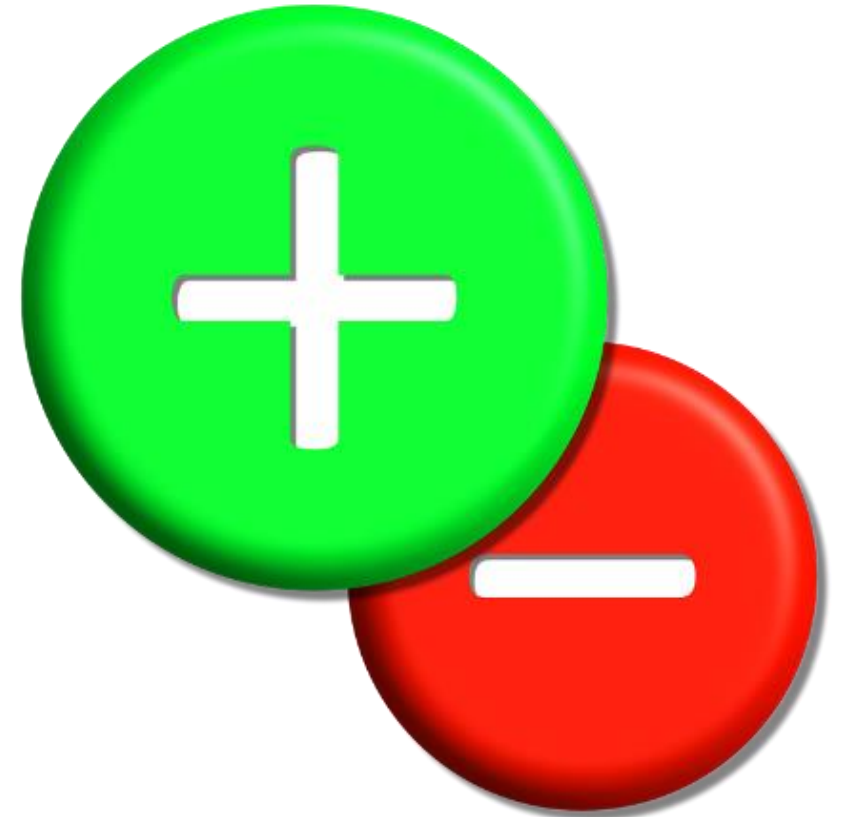


Pixabay/Public Domain

Schizophrenia

Negative Symptoms

- Absence of normal behaviors
- Flat affect
- Poverty of speech (alogia)
- Cannot engage in social interactions (asociality)
- Lack of motivation/cannot complete tasks (avolition)
- Cannot feel pleasure (anhedonia)
- Often persist despite therapy



Pixabay/Public Domain

Schizophrenia

Complications

- High risk of **suicide**
- 5% schizophrenics commit suicide
- 10% all suicides occur in schizophrenics

Le Suicidé

Édouard Manet, 1877



Schizophrenia

Diagnosis

- At least **one month** of two or more:
 - Delusions
 - Hallucinations
 - Disorganized speech
 - Disorganized or catatonic behavior
 - Negative symptoms
- Must have either delusions, hallucinations or disorganized speech
- Continuous signs for at least **six months**

Schizophrenia

Treatment

- Antipsychotic drugs
- Psychotherapy



Wallpaper Flare.com/Public Domain

Schizophreniform Disorder

- Meets criteria for schizophrenia
- Duration **one to six months**

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
28	29	30	31 <small>New Year's Eve</small>	1 <small>New Year's Day</small>	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19 <small>Martin Luther King Day</small>	20	21	22	23	24
25	26	27	28	29	30	31

Brief Psychotic Disorder

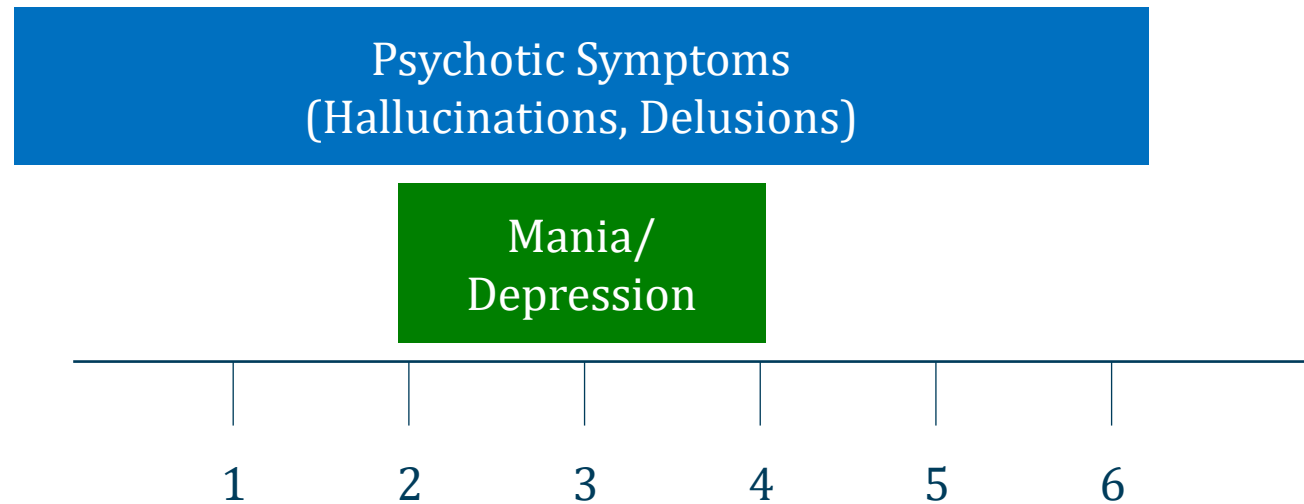
- Psychotic symptoms
- Sudden onset
- **Full remission within one month**
- More common in women than men
- Commonly follows **stressful life events**
 - Death in family
 - Loss of job

Schizophrenia with Mania/Depression

- Schizoaffective Disorder
 - Schizophrenia with mania or depression
 - **Must have some episodes psychosis alone**
 - **Some psychosis in absence of mania/depression**
 - DSM-V: Two or more weeks with psychosis alone
- Mania or depression with psychotic features
 - All psychotic episodes occur with mania/depression

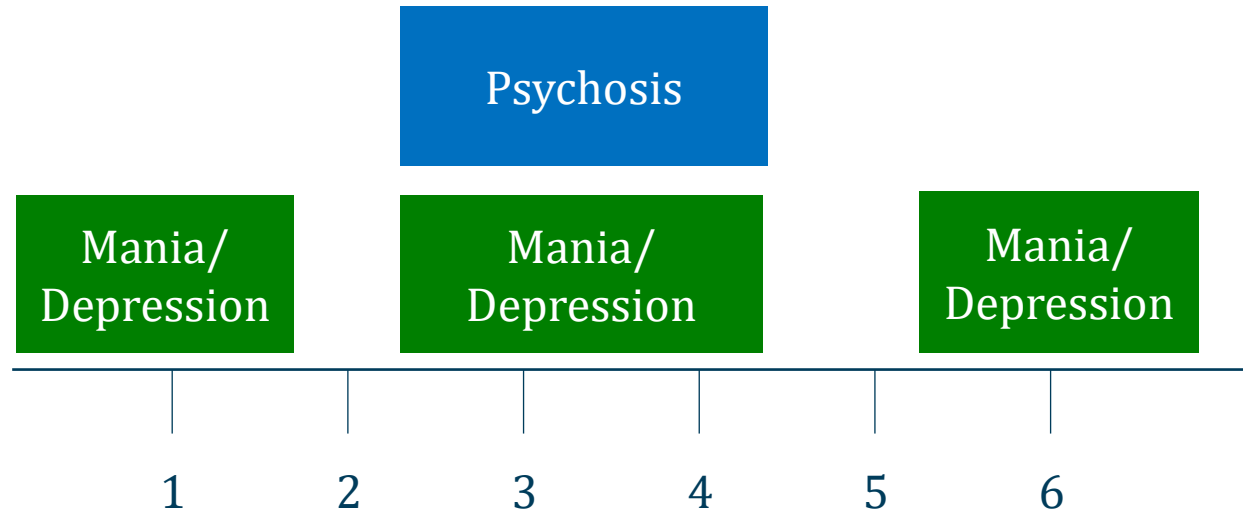
Schizoaffective Disorder

Possible Course



Mood Disorder with Psychosis

Possible Course



Delusional Disorder

- One or more delusions
- Lasts **one month or longer**
- Otherwise, **no abnormal behavior**
 - Man believes he is being followed for past two months
 - Frequently checks for someone behind him
 - Cannot be persuaded he is safe
 - No hallucinations, disorganized thought, negative symptoms
- Folie a deux (madness of two)
 - Close friend shares delusions

Psychotic Disorders

Disorder	Features	Time Frame
Schizophrenia	Psychosis, Learning Disability, Negative Symptoms	> 6 months
Schizophreniform	Psychosis, Learning Disability, Negative Symptoms	1 to 6 months
Brief Psychotic Disorder	Psychosis	< 1 month
Delusional Disorder	Delusions only	> 1 month
Schizoaffective	Psychosis Alone and Mood Symptoms	--
Mood with Psychosis	Mood Symptoms with Psychosis	--

Mania

Jason Ryan, MD, MPH



Mood Disorders

- Abnormal emotional state
- Sadness (depression)
- Extreme happiness (mania)



Wikipedia/Public Domain

Depression

Mania



Manic Episode

- Abnormally elevated **mood** and **energy level**
- Talking fast, pressured speech
- Decreased need for sleep
 - But not tired
 - Different from insomnia (tired but cannot sleep)
- Psychomotor agitation (pacing, fidgeting)
- Flight of ideas



Clipart/Public Domain

Manic Episode

- **Disinhibition** and irresponsibility
 - Waste money, wearing no clothes
- **Grandiosity**
 - Increased self-esteem, confidence
 - “I can do anything!”
- Typical case:
 - Change in mood to elevated state
 - Not sleeping
 - Altered behavior
 - Disruption of social functioning



Public Domain

Manic Episode

Diagnosis

- Symptoms for **at least one week**, most of the day
 - **D**istractibility
 - **I**rrresponsibility
 - **G**randiosity
 - **F**light of ideas
 - **A**gitation
 - Less **S**leep
 - **T**alking too much, pressured speech

DIG FAST

Hypomanic Episode

- Similar to those of mania but **less severe**
- Key feature: **little/no impairment in functioning**
- Inflated self-esteem but no delusions of grandeur
- More organized thought than mania
- More energy but leads to productive activity
 - Contrast with mania: unproductive
- Milder risk-taking behavior

Hypomanic Episode

- Lasts **at least 4 days**
- **No psychotic symptoms**
 - By definition psychotic symptoms = mania
- Typical case:
 - Change in mood to elevated state
 - Continued social functioning
 - Resolves in few weeks

Bipolar Disorder

Manic Depression

- Symptoms of mania and depression
- Can present with mania, hypomania or depression
 - Treatment with antidepressants may cause mania
- Bipolar I
 - **Manic episode** +/- depression +/- hypomania
 - Manic episodes = bipolar I
- Bipolar II
 - **Hypomania** and depression
 - No manic episodes



Clipart/Public Domain

Psychotic Features

- Often hallucinations or delusions
- Associated with severe forms of mood disorders
- May occur in bipolar disorder or depression
- Always occur **together with mood symptoms**
- Psychosis without mood symptoms: schizoaffective



Ingela Hjulfors Berg/Flickr

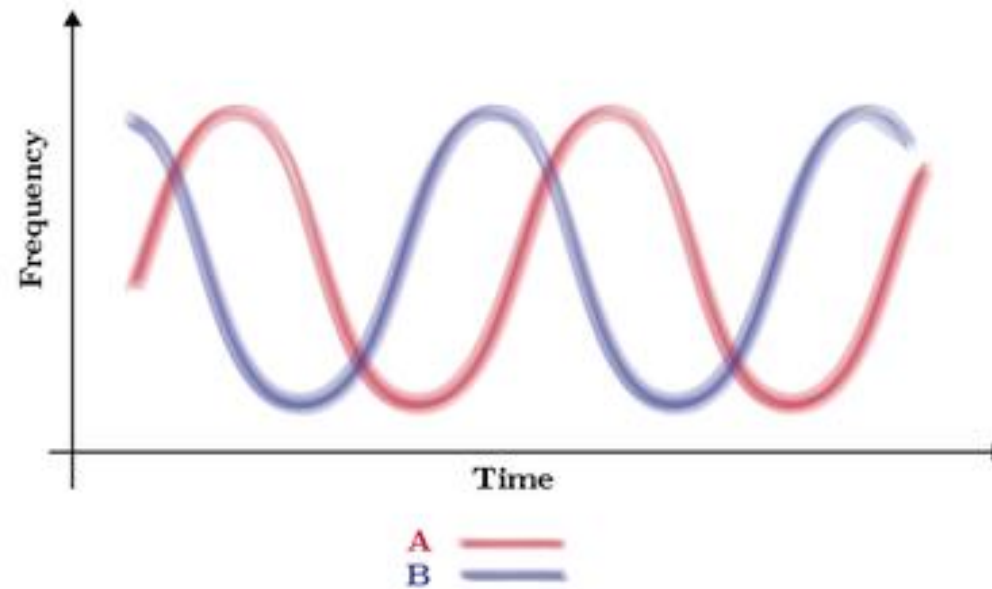
Cyclothymic Disorder

- Mild mania symptoms
- Mild depressive symptoms
- Do not meet criteria for hypomania or MDD
- Symptoms come/go over **at least two years**
 - Come/go with ups and downs
 - Occur at least half of the time
 - Never absent for more than two consecutive months

Bipolar Disorder

Course

- Fluctuation: mania-hypomania-depression
- May have periods of euthymia (normal mood)



Bipolar Disorder

Treatment

- Mood stabilizers
 - Lithium
 - Valproic acid (anticonvulsant)
 - Lamotrigine (antipsychotic)
 - Carbamazepine (antipsychotic)
- Antipsychotics
- Electroconvulsive therapy (ECT)
- Antidepressants may cause mania
 - Bipolar depression treated with mood stabilizers

Bipolar Disorder

Treatment

- Patients with new-onset acute mania:
 - **Lithium plus antipsychotic**
 - Alternative: Valproic acid plus antipsychotic
- Antipsychotics:
 - Aripiprazole
 - Haloperidol
 - Olanzapine
 - Quetiapine
 - Risperidone

Lithium

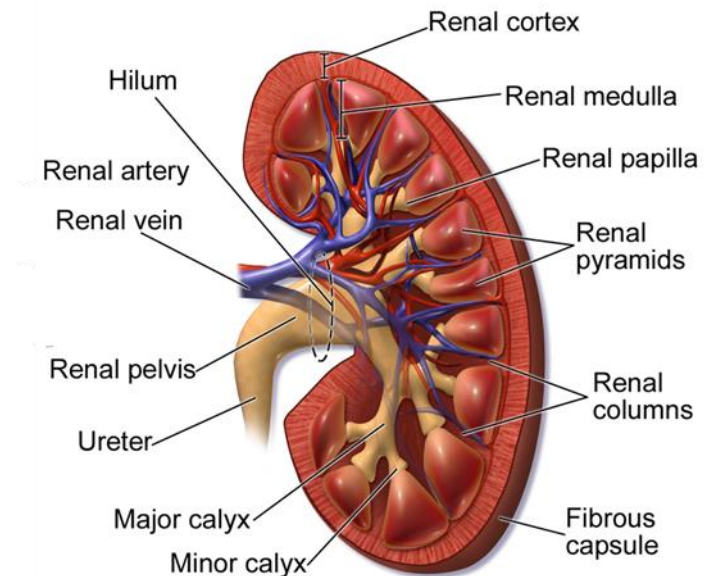
- Chemical element/cation
- First medical therapy of **bipolar disorder** (1949)
- Mechanism poorly understood
- Many toxicities
- Narrow therapeutic index
- Serum level monitored to titrate dose
- Therapeutic range 0.8 to 1.2 mEq/L

1 H			
3 Li	4 Be		
11 Na	12 Mg		
19 K	20 Ca	21 Sc	22 Ti
37 Rb	38 Sr	39 Y	40 Zr

Lithium

Elimination

- Primarily **renal** excretion
- Mostly reabsorbed in proximal tubule (like Na)
- Contraindicated with significant renal impairment
- Toxicity with acute renal failure



Lithium

Adverse Effects

- Acute effects
 - Occur when starting drug
 - Tremor
 - Nausea
 - Diarrhea
- Toxicity/poisoning
- Chronic effects



PublicDomainVectors.org

Lithium Toxicity

Lithium Poisoning

- Gastrointestinal: nausea, vomiting, and diarrhea
- Neurologic
 - Confusion
 - Tremors
 - Seizures
- Treatment: stop drug +/- dialysis
 - Dialysis for level > 5.0 mEq/L
 - Or > 2.5 mEq/L with symptoms



Lithium Tremor

- Occurs when drug is started or dose increased
- Symmetric
- Usually limited to hands or arms
- Often resolves over time
- **Most common symptom of lithium toxicity**
- Persistent tremor treatment: propranolol



Lithium Toxicity

Risk Factors

- Renal insufficiency
 - Volume depletion
 - Elderly patients (low glomerular filtration rate)
- Drug interaction

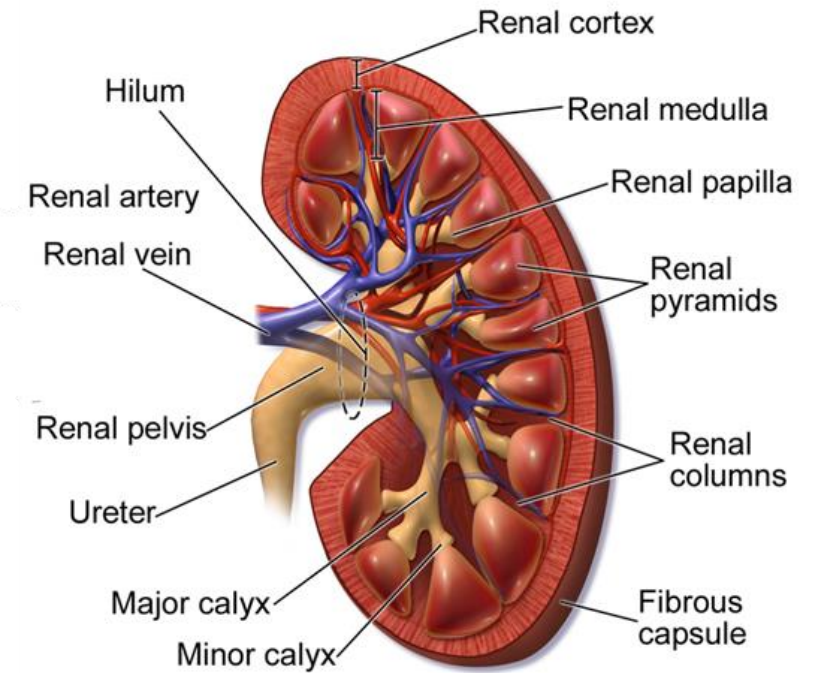
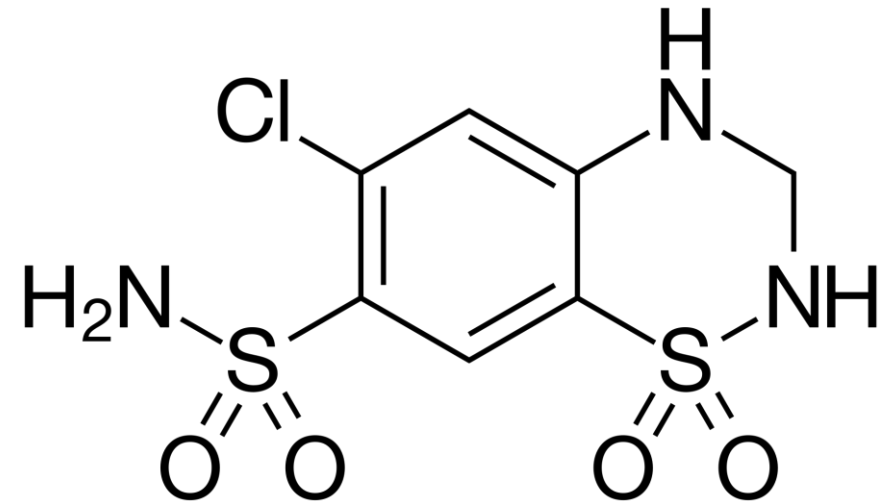


Image courtesy of BruceBlaus

Lithium Toxicity

Drug Interactions

- Increased lithium level (↓ renal excretion)
 - **Thiazide diuretics**
 - NSAIDs
 - ACE inhibitors
 - Metronidazole
 - Tetracycline
- Decreased lithium level
 - Potassium-sparing diuretics
- Varying effects: loop diuretics



Hydrochlorothiazide

Lithium

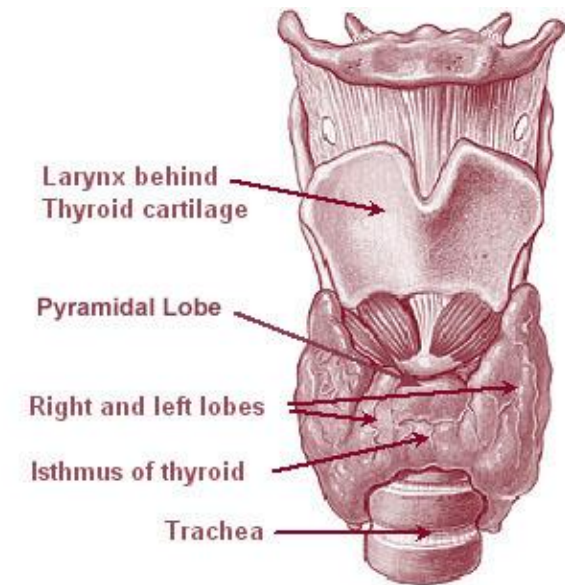
Adverse Long-term Effects

- Hypothyroidism
- Hyperparathyroidism
- Nephrogenic diabetes insipidus
- Cardiac
- Fetal effects
 - Ebstein's anomaly
- Mild leukocytosis
 - Increased neutrophils

Thyroid Effects

- Lithium: goitrogen
- Inhibits hormone release
- Commonly causes **goiter** (enlarged thyroid)
 - 40-50% of patients on lithium
- May cause **hypothyroidism**

Thyroid Gland



Wikipedia/Public Domain

Parathyroid Effects

- May elevate parathyroid hormone levels
- May cause mild hypercalcemia
- Usually asymptomatic

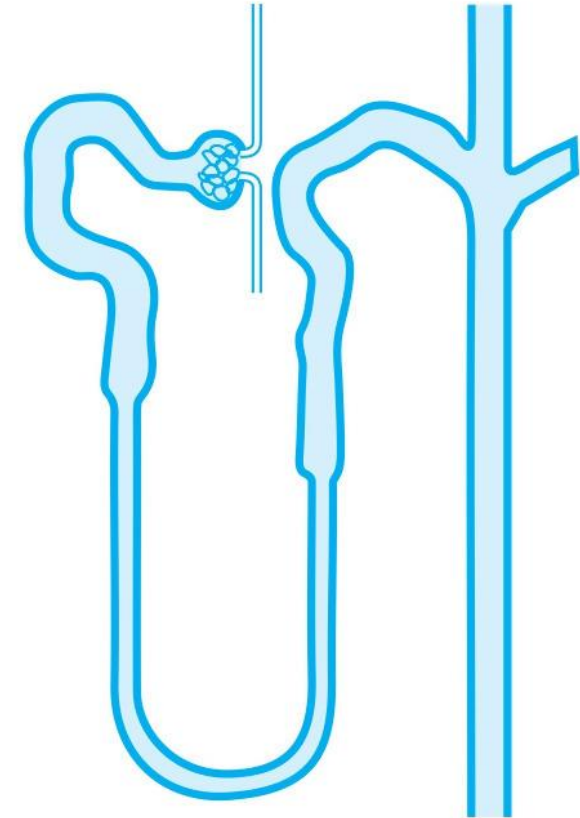
Parathyroid Glands



[Busca tu equilibrio/Wikipedia](#)

Diabetes Insipidus

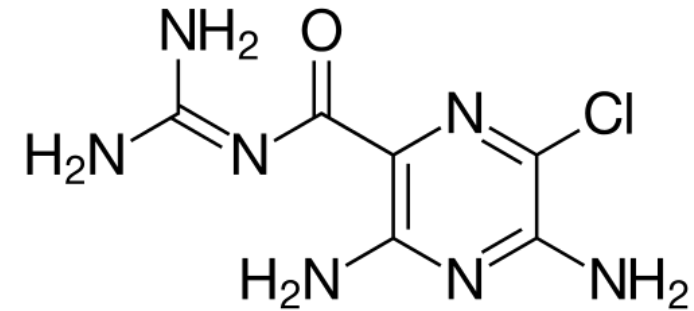
- “Chronic tubulointerstitial nephropathy”
 - Loss of tubule urine concentrating ability
- Tubules do not respond to ADH
- Dilute urine (low Uosm)
- **Polyuria and polydipsia**
- Serum sodium normal or increased



Diabetes Insipidus

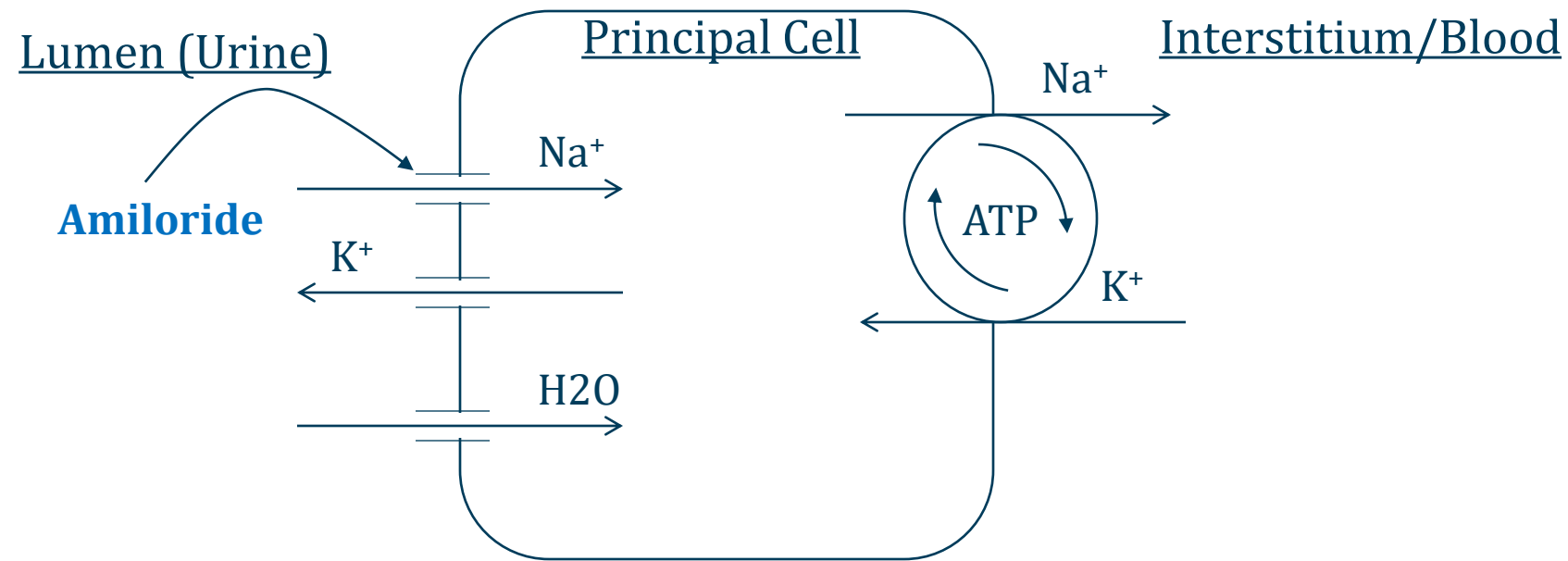
Treatment

- Discontinue lithium (if possible)
- **Amiloride**
 - Potassium-sparing diuretic
 - Blocks lithium entry into renal cells
- Vasopressin: no response
 - No change U_{osm}
 - Nephrogenic DI



Amiloride

Amiloride



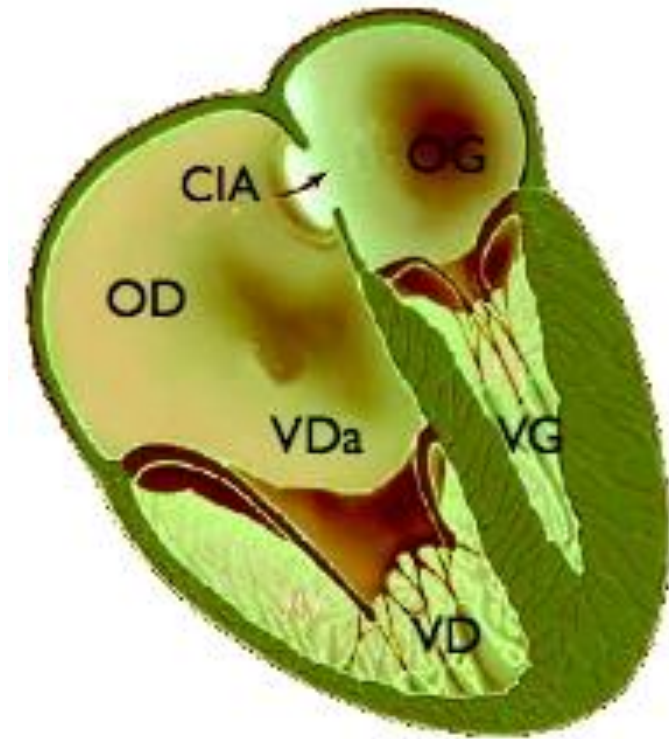
Cardiac Effects

- Suppression of **sinus node**
- Make cause sinus node dysfunction
- Bradycardia
- Pauses
- Syncope



Maternal Lithium

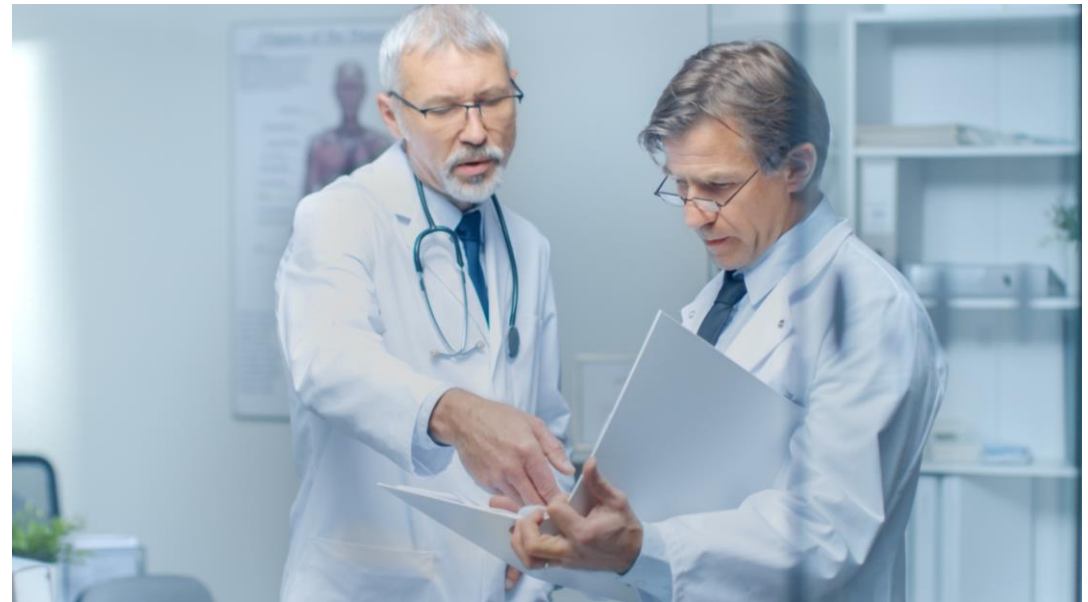
- Teratogen
- Completely equilibrates across the placenta
- Teratogenic effects primarily involve heart
- **Ebstein's anomaly** most common



Ebstein

Lithium Management

- Prior to start:
 - EKG (sinus rate)
 - Chemistries (BUN, Cr, Ca)
 - TSH
 - Pregnancy test
 - Urinalysis
- Blood levels
 - At day 5, then every 2-3 days
 - Once therapeutic every 6-12 months
- Check Cr and TSH q3-6 months



Shutterstock

Depression

Jason Ryan, MD, MPH



Mood Disorders

- Abnormal emotional state
- Sadness (depression)
- Extreme happiness (mania)



Wikipedia/Public Domain

Depression

Mania



Major Depressive Disorder

- Depressed mood
- Loss of interest in activities (anhedonia)
- **Appetite/weight changes**
- Feeling worthless or guilty
- Inability to concentrate, make decisions
- Fatigue/loss of energy
- Psychomotor agitation/retardation
- **Sleep disturbances**
- Suicidal ideation/attempts



Public Domain

Major Depressive Disorder

Psychomotor agitation/retardation

- **Psychomotor agitation**
 - Excessive motor activity
 - Often repetitious
 - Feeling of inner tension
 - Fidgeting, pacing
- **Psychomotor retardation**
 - Slowing of movements, thinking, or speech
 - Slow to answer questions
 - Low voice
 - Few words



Pixabay/Public Domain

Major Depressive Disorder

Sleep Disturbances

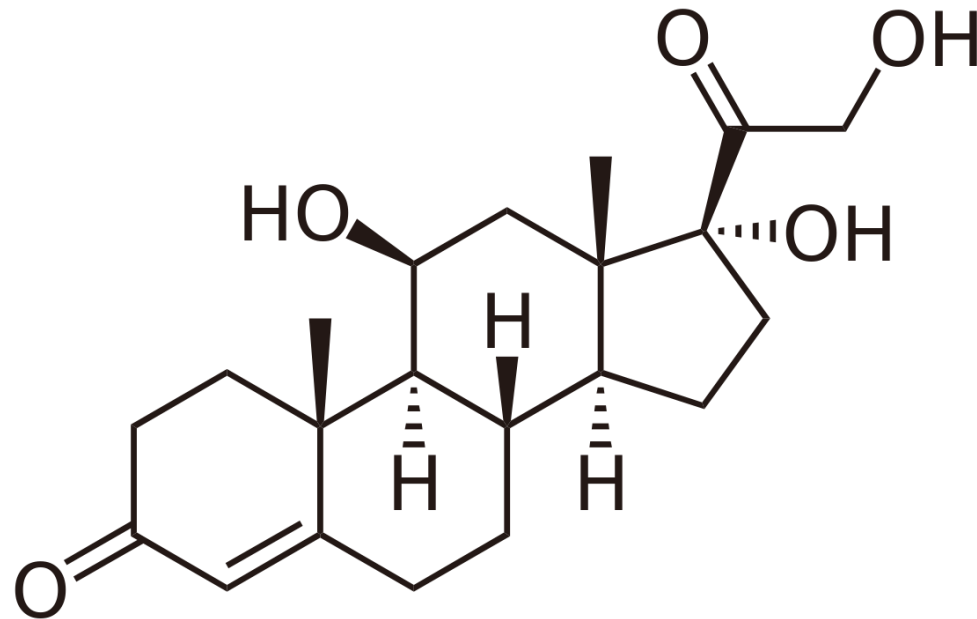
- Difficulty getting to sleep (initial insomnia)
- Waking in the night (middle insomnia)
- Waking earlier than usual (terminal insomnia)
- Hypersomnia: excessive sleeping
- Altered **sleep rhythms**
 - REM starts quicker after sleep onset (↓ **REM latency**)
 - ↑ total REM sleep
 - ↓ slow-wave sleep
 - Sleep rhythms normalize on anti-depressant drugs



Pexels.com/Public Domain

Cortisol

- Severe depression: elevated serum cortisol



Depression-Related Cognitive Impairment

Pseudodementia

- DSM-V: Difficulty thinking and concentrating and/or making decisions

	Dementia	Pseudodementia
Mood	Variable	Depressed
Onset	Slow	Rapid
Progression	Slow	Rapid
Disability	Diminished by patient	Emphasized by patient
Answers to Questions	Tries but unable	"I don't know"
Suicide Risk	Low	High

Major Depressive Disorder

Diagnosis

- At least **5 symptoms** (of 9) for **2 weeks**
 - Depressed mood
 - **S**leep disturbance
 - Lack of **I**nterest
 - **G**uilt
 - **E**nergy loss and fatigue
 - **C**oncentration problems
 - **A**ppetite/weight changes
 - **P**sychomotor symptoms
 - **S**uicidal ideation
- No evidence of mania

SIG E CAPS

Psychotic Features

- Often hallucinations or delusions
- Associated with severe forms of mood disorders
- May occur in depression or bipolar disorder
- Always occur **together with mood symptoms**
- Psychosis without mood symptoms: schizoaffective

Persistent Depressive Disorder

Dysthymic Disorder

- Low grade form of depression
 - Less severe but more chronic
 - Depressed mood most of the time
- Lasts **at least two years**
- No symptom free periods lasting >2 months



Flickr/Public Domain

Persistent Depressive Disorder

Dysthymic Disorder

- At least two of the following:
 - Hopelessness
 - Decreased appetite
 - Sleep problems
 - Low energy
 - Low concentration
 - Low self-esteem



Flickr/Public Domain

Major Depressive Disorder

Subtypes

- Atypical
- Melancholic
- Catatonic
- Psychotic
- Mixed features
- Anxious
- Seasonal



Public Domain

Atypical Depression

- **Mood reactivity** (core unique feature)
 - Able to react to pleasurable stimuli
 - Feels better when good things happen
- Eating and sleeping all the time
 - Increased appetite or weight gain
 - Increased sleep (hypersomnia)
- Heavy or leaden feelings in limbs
- Sensitive to rejection
 - History of interpersonal rejection sensitivity

Atypical Depression

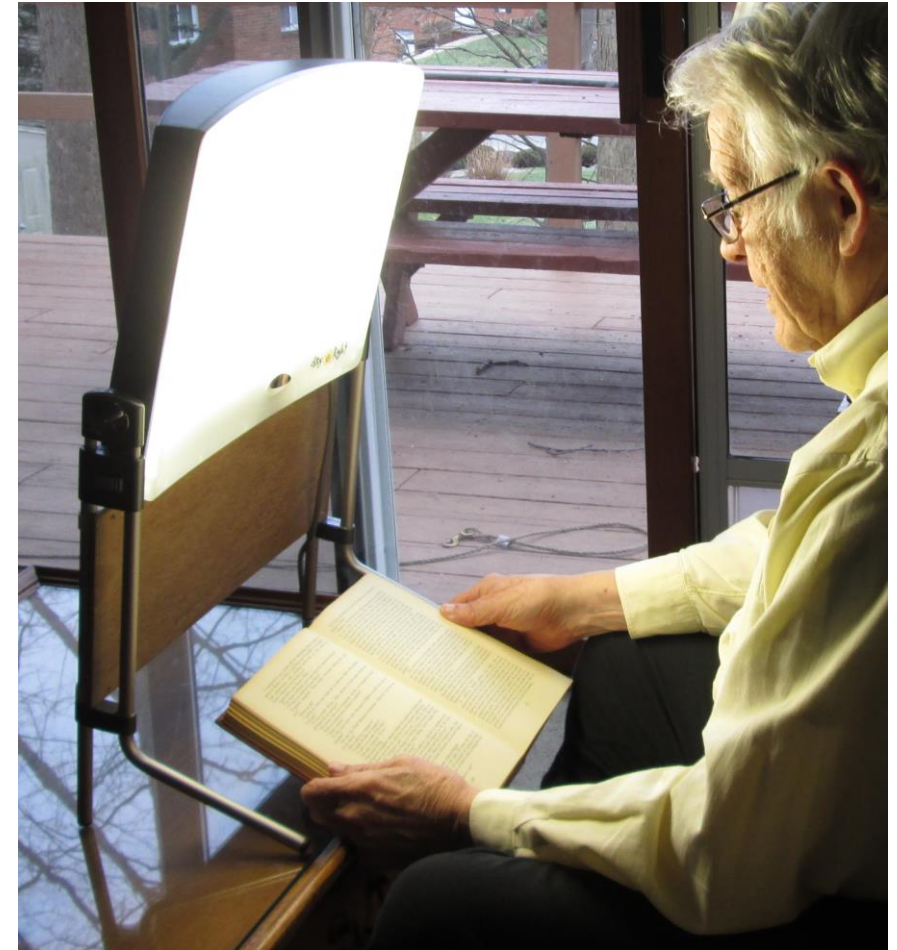
- Most common subtype in some studies
- Older studies: increased response MAOi drugs
- SSRIs also effective
- Usually treated with SSRIs (fewer side effects)



Tom Varco/Wikipedia

Seasonal Depression

- Worsening depression in fall and winter
- Treatment: **phototherapy**
 - In addition to other therapy



Wikipedia/Public domain

Major Depressive Disorder

Treatments

- Psychotherapy
 - Cognitive behavioral
 - Interpersonal
- Antidepressants
 - Usually SSRIs and SNRIs
 - Need 4 to 6 weeks to assess efficacy
 - If still symptomatic, increase dose, add/switch drugs
 - Few head-to-head trials of SSRI or SNRI
 - Fluoxetine most widely studied in adolescents
- Electroconvulsive therapy (ECT)
- Hospitalization if high suicide risk

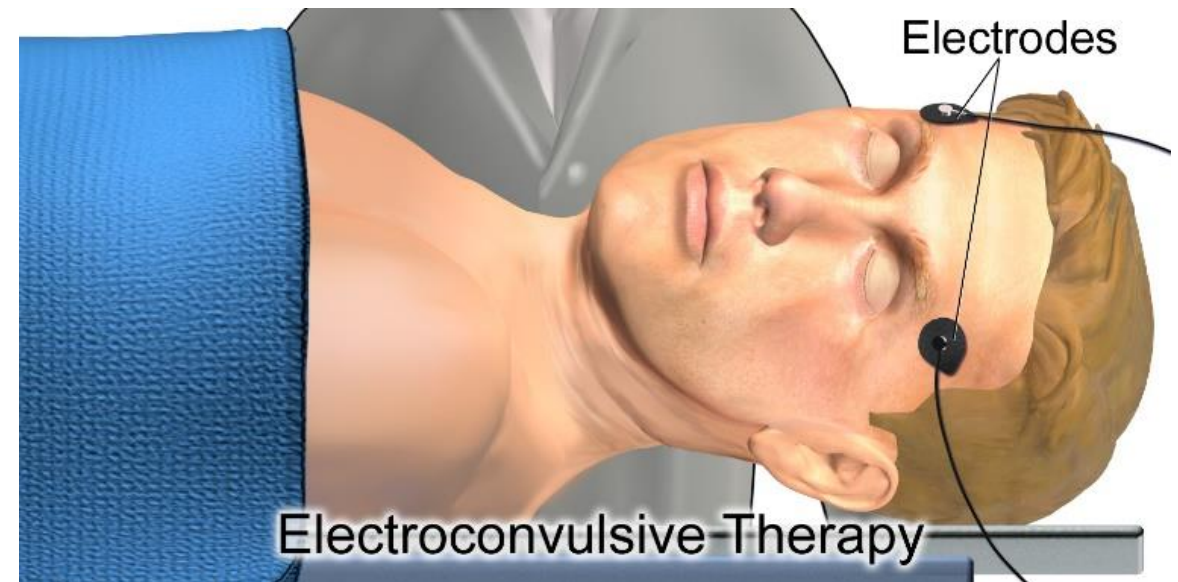


Shutterstock

ECT

Electroconvulsive Therapy

- Performed under general anesthesia
- Electricity administered → **seizure**
- *Highly effective* in treating depression
- Reserved for severe depression due to risks
- Can be used in pregnancy
- Persistent suicidal intent
- Depression with psychosis
- Catatonia
- Food refusal



Wikipedia/Public Domain

ECT

Electroconvulsive Therapy

- May cause **amnesia**
 - Retrograde amnesia (memories before procedure)
 - Anterograde amnesia (few weeks after)
 - Often resolves over several months
- Lithium held before procedure
 - Can worsen memory impairment
- Benzodiazepines avoided
 - Anticonvulsant drugs
- Most other psychiatric drugs safe



Wikipedia/Public Domain

Suicide

- Seen in depression and bipolar disorder
- 95% successful attempts have psychiatric diagnosis
 - Depression, bipolar, substance abuse, schizophrenia
- Women: more attempts, less successful
- Men: fewer attempts, more successful
- Most common method: **firearms**
- Increased risk with access to guns



Augustas Didžgalvis

Suicide

Risk Factors

- **Sad person scale** (0-10pts)
 - **S**ex (male)
 - **A**ge (young adults or elderly)
 - **D**epression
 - **P**rior attempt (higher risk group)
 - **E**thanol or drugs
 - **R**ational thinking loss (psychosis)
 - **S**ickness (medical illness)
 - **O**rganized plan
 - **N**o spouse (or lack of social support)
 - **S**tated intent

SAD PERSONS

0-4: Low risk

5-6: Medium risk

7-10: High risk

Suicide

Risk Assessment

- Ideation (common – 60% depressed patients)
- Plan
- Intent
- High risk if all three present
- Hospitalization for highest risk patients



KOMUNews/Flickr

Catatonia

- Behavioral syndrome
- **Inability to move normally**
- Occurs in patients with mental and medical illness
 - Depression
 - Bipolar
 - Schizophrenia
- Treatment:
 - Benzodiazepines (first-line)
 - ECT
 - Avoid antipsychotics



Pixabay/Public Domain

Catatonia

Clinical Features

- Immobility
- Stupor or mutism (decreased alertness of speech)
- Negativism (resistant to instructions)
- Catalepsy (remains in fixed position)
- Posturing (resistant to movement)
- Echolalia (meaningless repetition of another person's words)
- Echopraxia (meaningless imitation of movements of others)

Typical Acute Grief

- Normal response to **loss of loved one**
- Five stages (Kübler-Ross model)
 - Denial (“He can’t be gone there must be a mistake”)
 - Anger (“This is your fault!”)
 - Bargaining (“I’ll do anything if she could be alive again”)
 - Depression
 - Acceptance
- Visions/voices of dead person may occur
- Usually resolves within 6 months



PickPic/Public Domain

Typical Acute Grief

- **Depression** can occur within 6 months of loss
- Symptoms more severe than grief
 - Unable to be comforted by others
 - Worthlessness
 - Anhedonia
 - Weight loss
 - Suicidal ideation



PickPic/Public Domain

Complex Grief

- Lasts longer than 6 months
- Interferes with functioning
- May lead to major depressive disorder



Tim Green/Flickr

Anxiety Disorders

Jason Ryan, MD, MPH



Panic Attack

- Sudden onset of intense fear
 - Often occur with no trigger
 - Sometimes triggered by stressful event
- Brief: lasts for **minutes to an hour**



Nclm/Wikipedia/Public Domain

Panic Attack

- **Physical symptoms** caused by panic
 - Palpitations, racing heart
 - Sweating
 - Trembling or shaking
 - Chest pain or discomfort



Shutterstock

Panic Attack

Diagnosis

- Four or more of the following:
 - Palpitations, pounding heart, or accelerated heart rate
 - Sweating
 - Trembling or shaking
 - Sensations of shortness of breath or smothering
 - Feelings of choking
 - Chest pain or discomfort
 - Nausea or abdominal distress
 - Feeling dizzy, unsteady, light-headed, or faint
 - Chills or heat sensations
 - Paresthesias (numbness or tingling sensations)
 - Fear of losing control or "going crazy"
 - Fear of dying
 - Derealization
 - Depersonalization

Panic Attack

Diagnosis

- Derealization
 - Items in room look foggy, unreal
 - Feel like in a foreign place despite being at home
 - Often intensely scary
- Depersonalization
 - “Out of body” experience
 - Detached, looking at self from above



Shutterstock

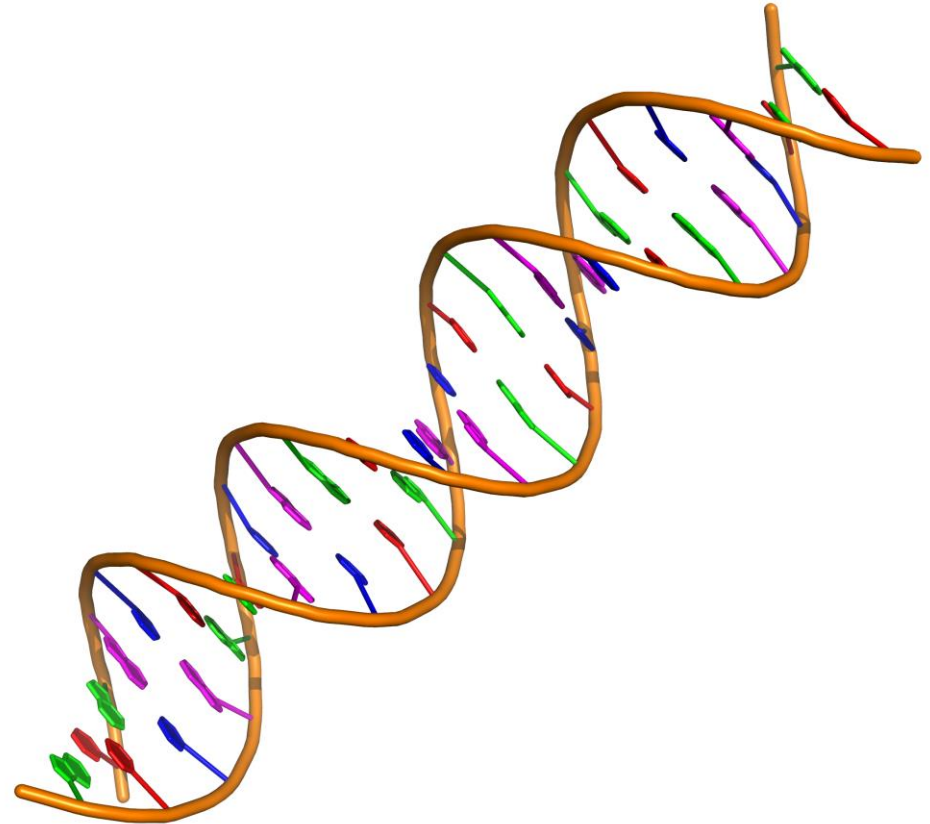
Panic Disorder

Diagnosis

- Recurrent **unexpected** panic attacks
 - No obvious trigger
 - Not post-traumatic
 - Not in response to phobia
- Attacks followed by **1 month or more:**
 - Persistent concern or worry about panic attacks
 - Change in behavior to avoid attacks

Panic Disorder

- Median age: 24 years
- Twice as common in women vs. men
- Risk factors
 - **Genetic component**
 - 1st degree relative with PD increases risk
 - History of physical or sexual abuse
 - Life stress
- Treatments:
 - Cognitive behavioral therapy
 - Antidepressants (SSRIs)
 - Benzodiazepines



Specific Phobias

- Fear of a **specific object or situation**
- Leads to **avoidance behavior**
- Persists for > 6 months
- Common: flying, dental procedures, blood draw



Flickr/Delmar Clemmons

Specific Phobias

- Social anxiety disorder
 - Specific phobia of social settings
 - Excessive fear of **embarrassment** in social settings
 - Fear of being humiliated or judged
- Agoraphobia
 - Agora = public space (Greek)
 - Fear of leaving a safe place (home) for **public setting**
 - Fear of needing to flee with no help available
 - NOT fear of scrutiny and embarrassment
 - Example: Fear of empty bus (no people)
 - Often co-occurs with panic disorder
 - Often patients fear panic attack in public setting

Specific Phobias

Treatments

- Medications
 - Benzodiazepines for infrequent exposure
 - Beta-blockers (blunt physical symptoms)
 - SSRIs for frequent exposure



Tom Varco/Wikipedia

Specific Phobias

Treatments

- Often responds to **behavioral therapy**
- Systematic desensitization
 - Imagining exposure to feared stimulus
 - Relaxation
- Exposure therapy
 - Confrontation of feared stimulus in safe/controlled manner
 - Fear reduced over time (extinction learning)

Generalized Anxiety Disorder

- **Chronic, persistent anxiety**
- About many different events/activities
- **Lasts \geq 6 months**
 - More days than not for at least six months



Generalized Anxiety Disorder

- Three or more of the following:
 - Restlessness
 - Fatigue
 - Difficulty concentrating
 - Irritability
 - Muscle tension
 - Sleep disturbance
- Treatment:
 - Cognitive behavioral therapy + SSRIs
 - Combination most effective

OCD

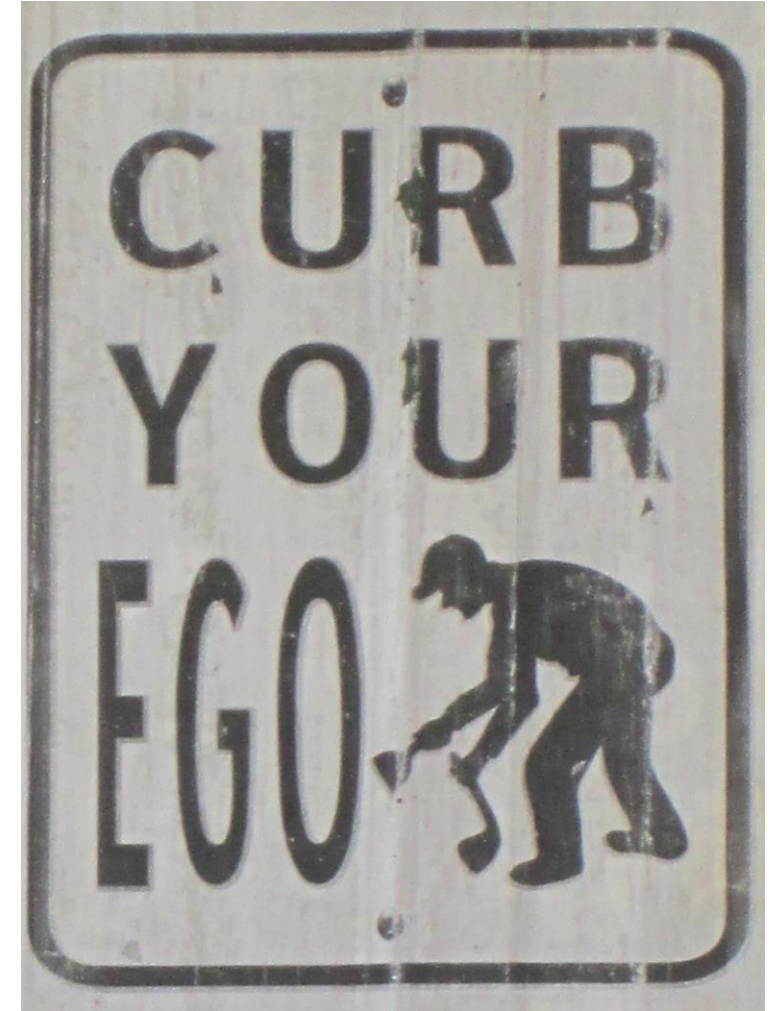
Obsessive-Compulsive Disorder

- Obsessions
 - Recurrent, persistent thoughts, urges, or images
 - Intrusive and unwanted
 - Patient attempts to ignore or suppress
 - Causes distress
- Compulsions
 - Repetitive behaviors or mental acts
 - Done to relieve obsessions
 - Hand washing, checking stove
 - Praying, counting, repeating words
 - Patient feels driven to perform in response to obsessions

OCD

Obsessive-Compulsive Disorder

- Ego
 - Mediates id (desire) and super-ego (rules, society)
- Egosyntonic
 - Behaviors that achieve goals of the ego
 - Obsessions/compulsions used to achieve goals
 - Seen in obsessive-compulsive personality disorder
- **Egodystonic**
 - Behaviors that conflict with goals of the ego
 - Obsessions/compulsions are barriers to goals
 - Seen in obsessive-compulsive disorder



Public Domain

OCD

Obsessive-Compulsive Disorder

- Commonly co-occurs with:
 - Schizophrenia or schizoaffective disorder
 - Bipolar disorder
 - Eating disorders (anorexia/bulimia)
 - Tourette's disorder
- Treatment: cognitive behavioral therapy
 - “Exposure and response” therapy
 - Expose patient to obsessive thoughts/image
 - Respond with non-compulsive behavior
- SSRIs

PTSD

Post Traumatic Stress Disorder

- Follows traumatic event
 - Rape, physical assault, war
- Thoughts, nightmares, flashbacks
- Avoidance of reminders
- Hypervigilance
 - Anxious, alert, scanning
- Sleep problems
 - Restless, can't fall or stay asleep
- Leads to social dysfunction



Public Domain

PTSD

Diagnosis

- Exposure to traumatic event
- Trauma persistently re-experienced
 - Thoughts, nightmares, flashbacks
- Avoidance of trauma-related stimuli
- Negative thoughts or feelings after trauma
- Trauma-related arousal and reactivity
- Symptoms last for **more than 1 month**



Public Domain

PTSD

Treatments

- Cognitive behavioral therapy
- SSRIs or SNRIs
- **Prazosin**
 - Alpha-1 blocker
 - Reduces nightmares and improves sleep
 - May cause orthostatic hypotension
- Avoid benzodiazepines or opioids
 - Addiction potential



Tom Varco/Wikipedia

Acute Stress Disorder

- Exposure to threatened death, injury, sexual assault
- Recurrent, intrusive memories
- Recurrent distressing dreams
- Dissociative symptoms
 - Altered sense of reality
 - In a daze, time is slow
 - Cannot remember aspects of trauma (dissociative amnesia)
- **Lasts less than one month**
- Treatment: CBT (no drugs)

Adjustment Disorder

- Behavioral or emotional symptoms
- Develop within **3 month of stressful life event**
- Distress in excess of expected/usual
- Impairment of daily functioning
- Does not meet criteria for another disorder
- Usually resolves within 6 months
- Treatment: psychotherapy (various forms)



Piqsels

Body Dysmorphic Disorder

- Occurs in physically normal patients
- Preoccupation with physical appearance
- Focus on nonexistent or minor defects
- Patient believes they look abnormal, ugly, deformed
- Leads to repetitive behavior
 - Checking mirror
 - Combing hair
- Treatment: CBT plus SSRIs



Needpix.com

Personality Disorders

Jason Ryan, MD, MPH



Personality Traits

- Fixed patterns of behavior
- Way of interacting with environment
- No significant distress or impaired function
- Positive traits: kind, confident
- Negative traits: lazy, rude
- Person often aware of own traits

Personality Disorders

- Fixed patterns of behavior
- Way of interacting with environment
- **Cause distress or impaired function**
- **Person often unaware**
- All treated with psychotherapy
- Difficult to treat (“enduring”)
- Often strains doctor-patient relationship

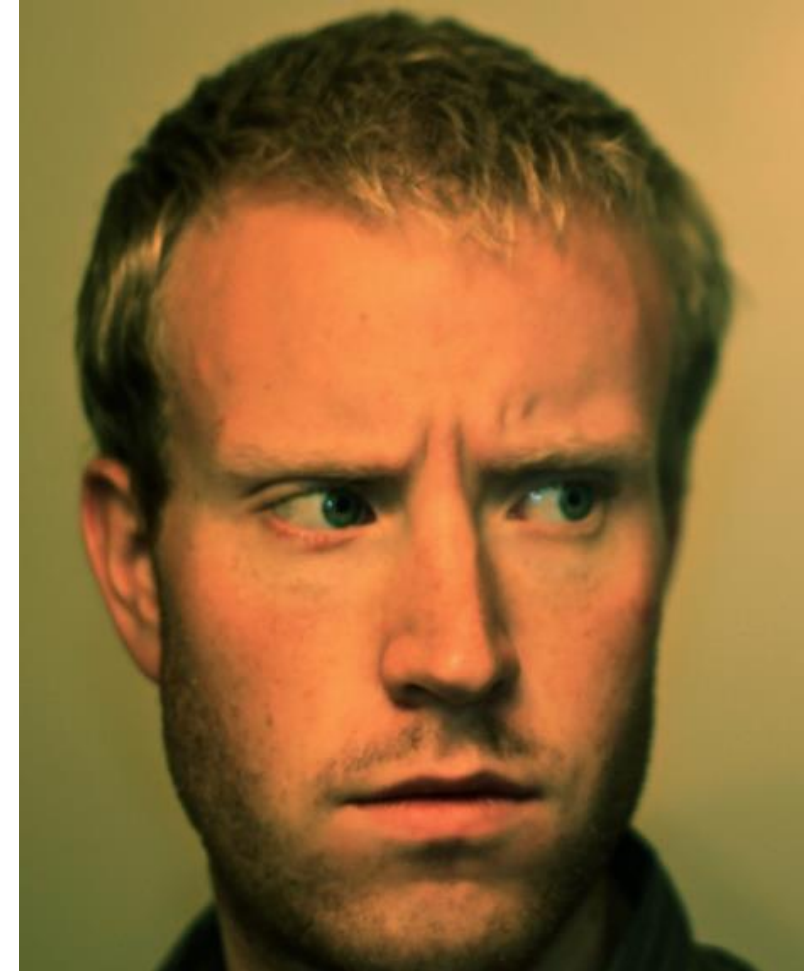
Personality Disorders

- Cluster A (Weird)
 - Paranoid, schizoid, schizotypal
 - Odd and eccentric behavior
- Cluster B (Wild)
 - Antisocial, borderline, histrionic, narcissistic
 - Dramatic, erratic behavior
- Cluster C (Wacky)
 - Avoidant, obsessive-compulsive, dependent
 - Anxious, fearful behavior

Paranoid

Personality Disorder

- **Distrust** of others, even friends/family
- Guarded
- Suspicious
- Struggles to build close relationships
- Hallmark ego defense: projection
 - Attributing unacceptable thoughts to others
 - Often accuses others of being suspicious

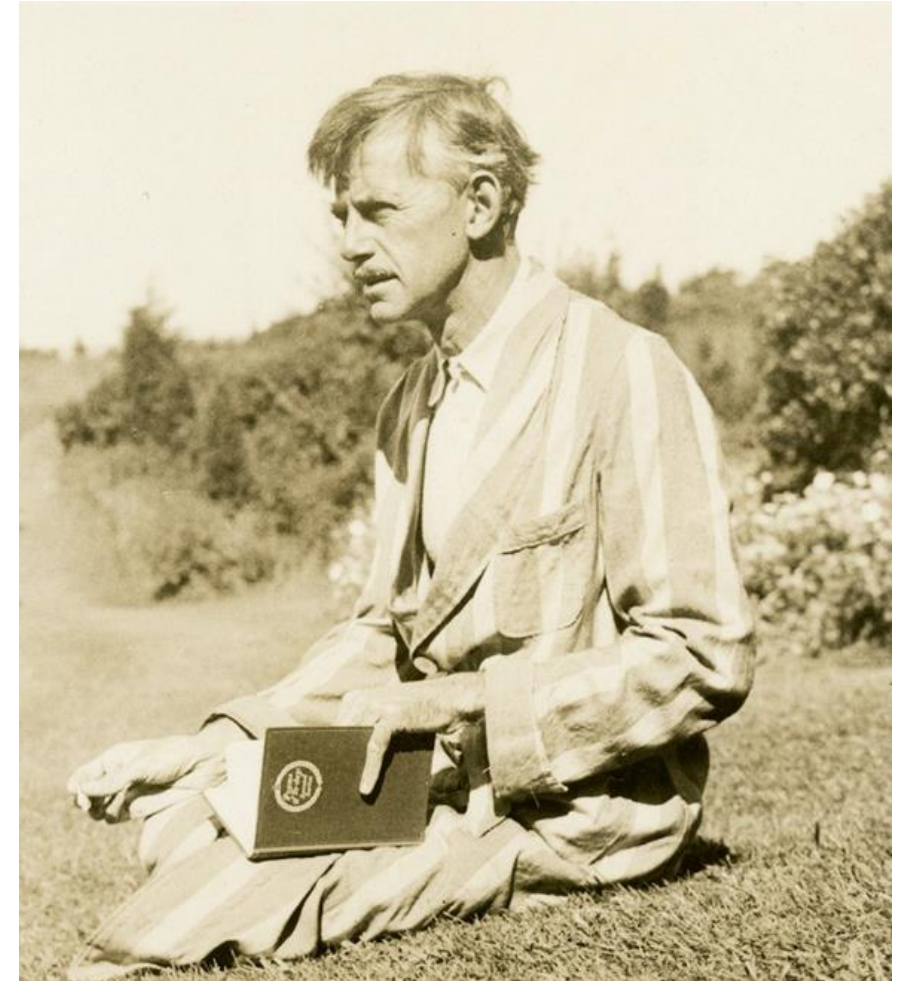


Aaron Tait/Flickr

Schizoid

Personality Disorder

- **Chooses** social isolation
 - More comfortable alone
- Does not enjoy close relationships
- Little/no interest in sexual experiences
- Few/no pleasure activities (hobbies)
- Lacks close friends
- Detachment
- Flat affect



Public Domain

Schizotypal

Personality Disorder

- Fear of social interactions and few close friends
- **Odd beliefs or magical thinking**
 - Superstitious
 - Believes in telepathy, sixth sense
- Ideas of reference
 - Believe events and happenings somehow related to them
- Key feature: open to challenges to beliefs
 - May reconsider superstitions, etc.
 - Contrast with delusions in schizophrenia
 - Also no hallucinations, cognitive impairment



Shutterstock

Antisocial

Personality Disorder

- More common in men
- Disregard for rights of others
- Often breaks the law
- Impulsive and lacks remorse
- Child (< 18) version: conduct disorder
 - 25% girls and 40% boys with CD → ASPD
- Must be at least age 18 years old
- Must have evidence of conduct disorder before 15



Public Domain

Borderline

Personality Disorder

- More common in women
- Unstable personal relationships
 - **All people are very good or very bad**
 - Stormy relationships
 - “My boyfriend is the greatest guy in the world!”
 - “My boyfriend is the devil!”
- Fear of abandonment
 - May accuse others of abandoning them



Ingela Hjulfors Berg/Flickr

Borderline

Personality Disorder

- Impulsivity
 - Spending sprees, sex with strangers, reckless driving
- Self mutilation
 - Cutting, burning
- Suicide gestures or attempts
 - Relates to fear of abandonment
 - “You don’t care about me, so I’ll kill myself”

Splitting

- Major defense mechanism in borderline PD
- Black and white thinking (always-never)
- Cannot hold opposing views
- Patient's physician may be great or terrible
- All people/things/events wonderful or horrible



Pathfinder257/Pixabay

Dialectical Behavior Therapy

- Form of cognitive behavioral treatment
- Designed to treat chronic suicidality
- **Gold standard** for borderline personality disorder
- Weekly therapy for 1-2 years
 - Mindfulness
 - Distress tolerance
 - Emotion regulation

Histrionic

Personality Disorder

- Wants to be the **center of attention**
 - Talks loudly, tells wild stories, uses hand gestures
- Inappropriate sexually provocative behavior
 - Often wears provocative clothing
 - Touching others frequently
- Very concerned with physical appearance
 - Exotic outfits, shoes, hats

Narcissistic

Personality Disorder

- **Inflated sense of self**
 - Brags, thinks everything they do is great
- Lacks empathy for others
 - Other people are competitors
- Wants to hear they are great
- Overreacts to criticism with anger/rage



Shutterstock

Avoidant

Personality Disorder

- Avoids social interactions
- “Social inhibition”
- Feels inadequate
- Afraid people won’t like them
- Afraid of embarrassment
- Struggles with intimate relationships
 - “Maybe he/she doesn’t like me”
- Different from schizoid: wants to socialize but can’t
 - Schizoid prefers to be alone (aloof)



Public Domain

Dependent

Personality Disorder

- Clingy
- Low self-confidence
- Struggle to care for themselves
- Depend on others excessively
 - Rarely alone, always in a relationship
- Hard to make decisions on their own
 - Want someone to tell them what to do
- Difficulty expressing an opinion
- May be involved in abusive relationships



Francisco Carbajal/Flickr

Obsessive-Compulsive

Personality Disorder

- Preoccupied with **order and control**
 - Loves “To Do” lists
 - Always needs a plan
- **Inflexible** at work or in relationships
- Behaviors help to achieve goals (contrast with OCD)



Obsessive-Compulsive

Personality Disorder

- Ego
 - Mediates id (desire) and super-ego (rules, society)
- **Egosyntonic**
 - Behaviors that achieve goals of the ego
 - Obsessions/compulsions used to achieve goals
 - Seen in obsessive-compulsive personality disorder
- Egodystonic
 - Behaviors that conflict with goals of the ego
 - Obsessions/compulsions are barriers to goals
 - Seen in obsessive-compulsive disorder

Dissociative Disorders

Jason Ryan, MD, MPH



Dissociation

- Detachment from reality
- Feeling “like I was outside my own body”
- Extreme cases: becoming another person
 - New name, age, job, etc.
- Often associated with psychological trauma
- May allow victim to cope with trauma



Shutterstock

Dissociative Amnesia

Psychogenic Amnesia

- Inability to recall **autobiographical** memories
 - Past events
 - Job
 - Where they live
- Usually follows major trauma/stress
- Potentially reversible (memories may come back)
- Patient not bothered by lack of memory
- Amnesia not explained by another cause

Dissociative Amnesia

Psychogenic Amnesia

- Different from other forms of amnesia
 - Large groups of memories: name, job, home
 - Caused by overwhelming stress
- Different from repression
 - Loss of autobiographical information: name, job, home



Dissociative Amnesia

Psychogenic Amnesia

- Example:
 - Woman attacked in elevator
 - Does not recall her job, where she lives, etc.
- Usually self-limited
- Treatment: psychotherapy



Dissociative Fugue

- Subtype of dissociative amnesia
 - Fugue = Latin for flight or flee
- **Sudden travel/wandering** in dissociated state
- Example:
 - Manager fired from work goes missing
 - Found in another town
 - No recollection of prior job



Wikipedia/Public Domain

DDD

Depersonalization/Derealization Disorder

- **Depersonalization**
 - Feeling detached or estranged from one's self
 - "Like in a dream"
 - "Like I am watching myself"
 - Loss of control over thoughts, actions
- **Derealization**
 - Detachment from surrounding world
 - Objects seem unreal, foggy, visually distorted

DDD

Depersonalization/Derealization Disorder

- Often triggered by **trauma**
- Must cause significant distress/impairment
- **Intact reality testing**
 - Differentiates from psychosis
 - Patient aware that sensations are not real
- Treatment: psychotherapy



Public Domain

Dissociative Identity Disorder

- Multiple personality disorder
- More common in women
- Associated with **childhood trauma/abuse**
- Especially sexual abuse, often before age 6



Shutterstock

Dissociative Identity Disorder

- **Two or more distinct identities**
 - “Personality states”
 - Alterations in behavior, memory, thinking
 - Observed by others or reported by patient
- Gaps in memory about events
- Symptoms cause distress or problems in functioning
- Treatment: psychotherapy



Alan Levine/Flickr

Comorbidities

-
- A word cloud centered around PTSD. The largest word is 'PTSD'. Other large words include 'flashbacks', 'fear', 'anxiety', 'hypervigilance', 'trauma', 'cognitive', 'avoidance', 'survivors', 'risk', 'anxious', 'trigger', 'arousal', 'accidents', 'death', 'hypocampus', 'diagnostic', 'counselling', 'acute', 'treatments', 'psychological', 'family', 'intervention', 'loose', 'drugs', 'chemical', 'brain', 'emotional', 'numbing', 'loss'. Smaller words include 'post traumatic stress disorder', 'neuroendocrinology', 'numbing disturbance', 'veterans', 'biochemical', 'health problems', 'occupational', 'drug addiction', 'symptom', 'event', 'behavioural', 'cognitive', 'Feeling', 'memories', 'criteria', 'avoidance', 'distressing dreams', 'alternative help', 'worse', 'survivors', 'diagnose', 'risk', 'individuals', 'traumatic', 'abuse', 'alcohol', 'reducing', 'diagnostic', 'counselling', 'accidents', 'death', 'hypocampus', 'diagnostic', 'counselling', 'acute', 'treatments', 'psychological', 'family', 'intervention', 'loose', 'drugs', 'chemical', 'brain', 'emotional', 'numbing', 'loss'.



Boards & Beyond[®]
STUDY SMARTER[™]

Dissociative Identity Disorder

Comorbidities

- **Somatoform conditions**
- Physical symptoms not explained by medical condition



Pixabay/Public Domain

Somatic Disorders

Jason Ryan, MD, MPH



Somatization

- Physical expression of stress or emotions
- Symptoms not explained by medical disease
- Not consciously created for gain (factitious)
- Associated with anxiety and depression
- Risk factors
 - Female gender
 - Less education
 - Minority status
 - Low socioeconomic status

Somatization

- Pain symptoms
 - Headache, back pain, joint pain
- Gastrointestinal symptoms
 - Nausea, abdominal pain, bloating, gas
- Cardiopulmonary symptoms
 - Chest pain, dizziness, palpitations
- Neurologic symptoms
 - Fainting, muscle weakness, blurred vision
- Dyspareunia, dysmenorrhea

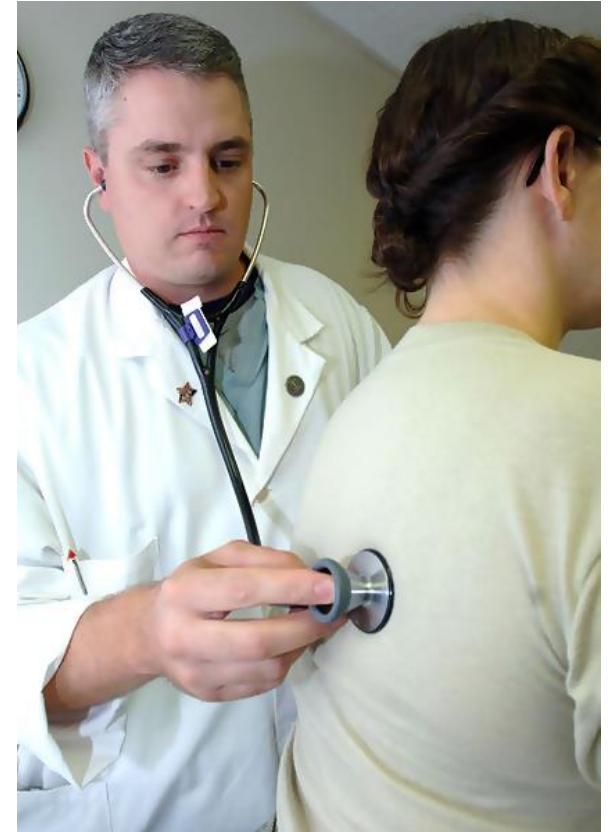


Pixabay.com

Somatization

Management

- Avoid debating if symptoms are psychiatric or medical
- Do not challenge belief that symptoms are medical
- **Regular visits with same physician**
- Limit tests and referrals
- **Reassure patient that serious diseases are ruled out**
- Set goals of functional improvement
- Address psychiatric issues gently
- Psychotherapy



Wikipedia/Public Domain

Somatic Symptom Disorder

DSM-V Diagnosis

- **Somatic symptoms** that cause distress
- Persistent thoughts about seriousness of symptoms
- Anxiety about symptoms
- Excessive time and energy devoted to symptoms
- Persistent (usually more than six months)

Conversion Disorder

Functional neurologic symptom disorder

- Sudden onset usually following stressor
- Voluntary motor or sensory **neurologic symptoms**
 - Inability to speak or move
 - Blindness
 - Seizures
- Neurologic work-up normal
 - Positive findings incompatible with disease
 - Example: absence plantar flexion but can stand on toes
- **La belle indifference**
 - Patient shows lack of concern (indifference) about symptoms



Flickr/Public Domain

Illness Anxiety Disorder

DSM-V Diagnosis

- Preoccupation with having **undiagnosed illness**
- **Mild or no somatic symptoms**
- Anxiety about health
- Excessive health-related behaviors
 - Repeatedly checking for signs of illness
- Present for at least six months

Factitious Disorder on Self

Munchausen syndrome

- **Falsified** medical or psychiatric symptoms
- Done **consciously** out of desire for attention
- Patient may feign illness
- May aggravate genuine illness
- Patient often willing to go for tests/surgeries

Factitious Disorder on Self

Munchausen syndrome

- Done for primary (internal) gain from illness
 - Patient feels better in sick role
 - Sick role solves internal conflict
 - Example: patient is afraid of work or afraid to be alone
- Chronic, persistent
- Risk factors:
 - **Female gender**
 - Unmarried
 - Prior or current **healthcare worker**



Pixabay/Public Domain

Factitious Disorder on Another

Munchausen by proxy

- Falsified medical symptoms by caregiver
- Often parent of **child** or caretaker of **elderly**



Public Domain

Malingering

- Consciously falsified medical symptoms
- Done for **secondary (external) gain**
 - Allows patient to miss work but get paid
 - Obtain workman's compensation
- Self-limited
- Ends when secondary gain achieved
- Not a DSM-V psychiatric disorder

Eating Disorders

Jason Ryan, MD, MPH



Eating Disorders

- Abnormal eating patterns
- Disrupt health or psychosocial functioning
- More common in women
- Usually present in adolescence or young adulthood
- DSM-V Disorders
 - Anorexia nervosa
 - Bulimia nervosa
 - Binge eating disorder

Anorexia Nervosa

- Diet and exercise that leads to **low body weight**
 - World Health Organization: $\text{BMI} < 18.5 \text{ kg/m}^2$
- Intense fear of gaining weight
- Distorted perception of body weight
- **Increased mortality** from malnutrition
- Two subtypes:
 - Restricting (low calorie intake/exercise)
 - Binge-purging



Wikipedia/Public Domain

Anorexia Nervosa

- Often **co-exists** with other disorders
 - Depression
 - Anxiety
 - Obsessive-compulsive disorder
 - Posttraumatic stress disorder
 - Substance abuse
- Often secondary to eating disorder
- Improve with weight restoration
 - Especially depression

Anorexia Nervosa

Endocrine Effects

- Reproductive hormones
 - ↓ GnRH secretion
 - ↓ LH/FSH
 - **Amenorrhea**
 - “Functional hypothalamic amenorrhea”
- Thyroid
 - “Sick euthyroid” pattern of thyroid function tests
 - Low T3
 - High rT3
 - Normal or low TSH/T4

Anorexia Nervosa

Electrolytes

- **Hyponatremia**
 - Low solute intake
 - Tea and toast diet
- **Creatinine low** (↓ muscle mass)
- If purging: hypokalemia



Wikipedia/Public Domain

Anorexia Nervosa

Bones

- **↓ bone density**
 - Low estrogen
 - High cortisol
- Osteopenia
- Osteoporosis

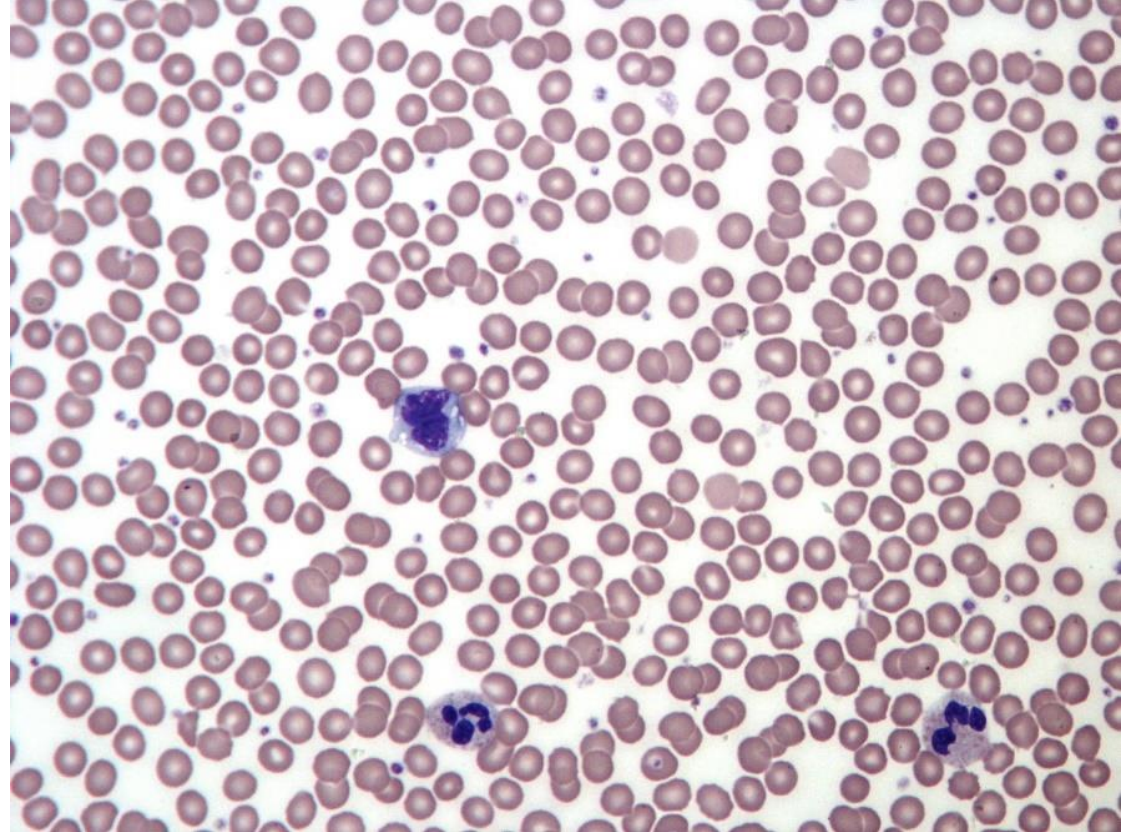


Hellerhoff/Wikipedia

Anorexia Nervosa

Hematology

- Bone marrow suppression
- Anemia
- Leukopenia
- Thrombocytopenia

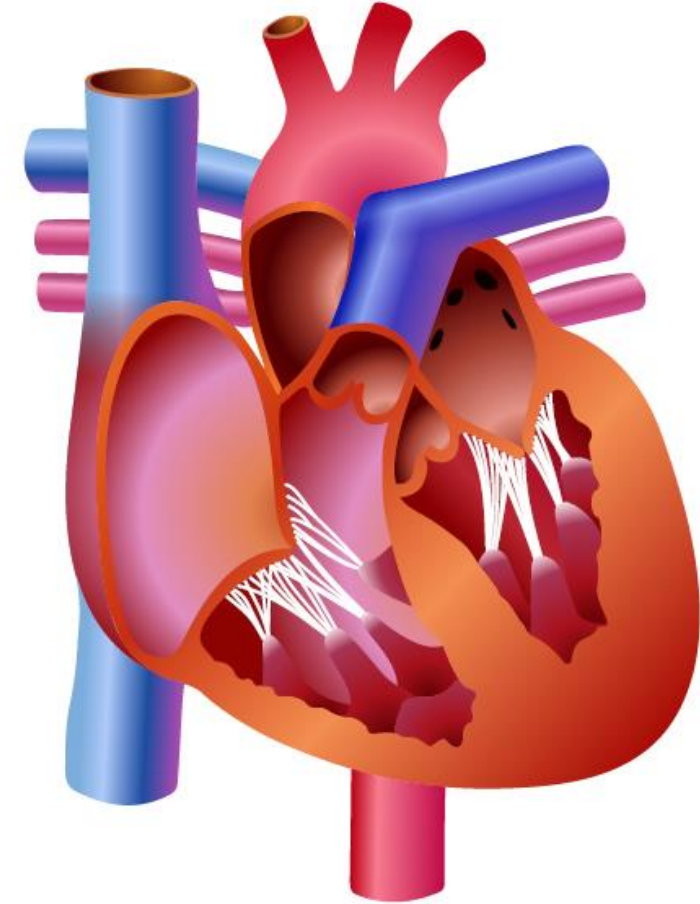


Keith Chambers/Wikipedia

Anorexia Nervosa

Cardiac

- Decreased cardiac mass
- May lead to cardiomyopathy
- May cause arrhythmias



Anorexia Nervosa

Physical Exam

- Low body mass index ($< 18.5 \text{ kg/m}^2$)
 - Mild: 17 to 18.5
 - Moderate: 16 to 16.99
 - Severe: 15 to 15.99
 - Extreme: < 15



Public Domain

Anorexia Nervosa

Physical Exam

- Bradycardia
- Hypotension
- ↓ bowel sounds
- Dry, scaly skin (xerosis)
- Hair loss
- Lanugo hair growth
 - Soft, fine hair



Wikipedia/Public Domain

Anorexia Nervosa

Treatment

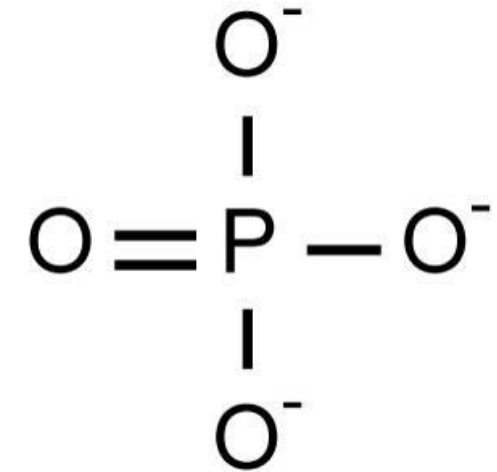
- **Nutritional rehabilitation**
 - Structured meals with observation
 - Calorie goals
- **Psychotherapy**
- Olanzapine (antipsychotic)
- Hospitalization indications
 - Very low body weight
 - Hemodynamic instability
 - Volume depletion
 - Refusal to eat



Shutterstock

Refeeding Syndrome

- Hallmark: **hypophosphatemia**
 - Low PO₄ from poor nutrition
 - Glucose → ↑ insulin → ↑ metabolism
 - Further ↓ PO₄ from cellular uptake
 - Loss of ATP → cardiac and respiratory failure
- Most fatalities: **cardiac**
 - Poor contractility, low stroke volume
 - Heart failure, arrhythmias
- Prevention: slow refeeding (gentle ↑ calorie intake)



Phosphate

Bulimia Nervosa

- Binge eating
- Inappropriate compensation to avoid weight gain
 - Vomiting (purging)
 - Laxatives, diuretics, enemas
 - Excessive exercise
 - Fasting
 - Severely restrictive diets

Bulimia Nervosa

- Occurs at least once a week for **three months**
- Weight usually normal (contrast with anorexia)
- Commonly coexists with other disorders
 - Anxiety
 - Depression
 - Posttraumatic stress disorder
 - Substance abuse

Bulimia Nervosa

Purging Complications

- Increased bicarbonate
 - Vomiting
 - Contraction alkalosis
- Hypokalemia
 - Loss of potassium
- Hypochloremia
 - Urinary chloride is low (<20)

Na	Cl	BUN	Glucose
K	CO ₂	Cr	

Urinary Chloride

- Useful in metabolic alkalosis unknown cause
- Low (< 20) in vomiting
 - Loss of Cl in gastric secretions
- High (> 20) in many other forms of alkalosis
- Classic scenario:
 - Young woman with unexplained metabolic alkalosis
 - Urinary chloride low

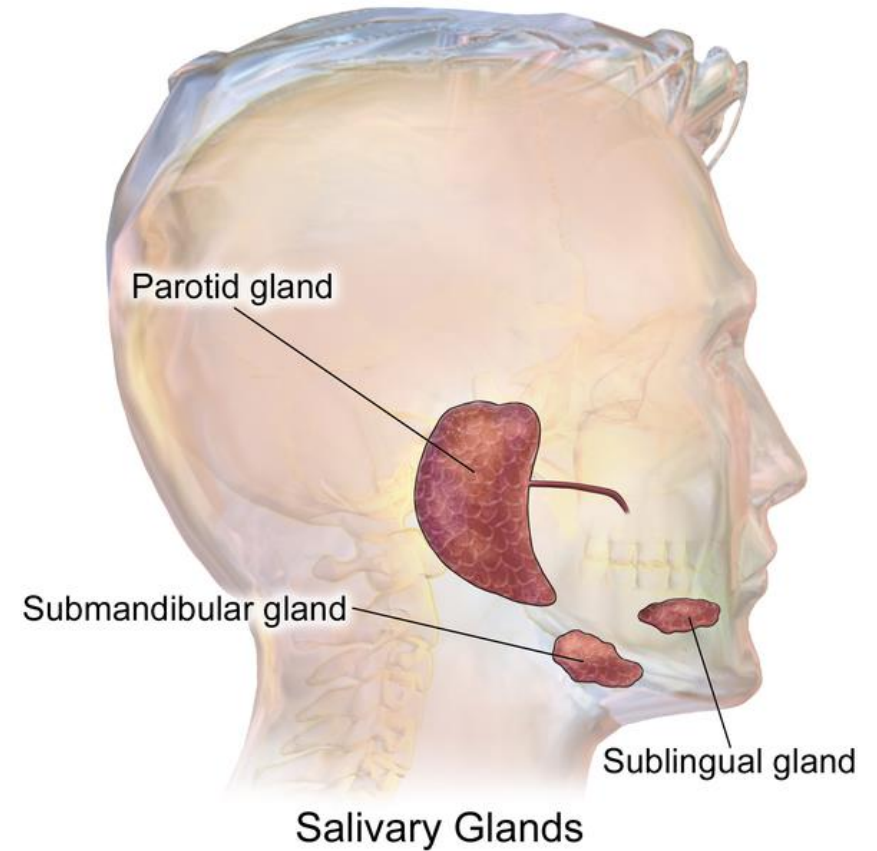


Wikipedia/Public Domain

Bulimia Nervosa

Purging Complications

- Parotid swelling
 - “Parotid gland hypertrophy”
 - Sialadenosis
- Erosion of dental enamel



Russell's Sign

- Scars on knuckles from induced-vomiting



Wikipedia/Public Domain

Bulimia Nervosa

Treatment

- Nutritional rehabilitation
- Psychotherapy
- SSRIs

Binge Eating Disorder

- Binge eating
 - Compulsive overeating
 - Excessively large amounts of food
 - Often eaten quickly
 - Patient feels they lack control
 - Patient feels shame/embarrassment
- No inappropriate compensation
- Weight gain
- Occurs at least once a week for **three months**

Binge Eating Disorder

- Often occurs with other disorders
 - Anxiety, depression
- Studies show high risk of type II diabetes
- First-line treatment: **psychotherapy (CBT)**
 - Large clinical effect in trials
 - Greater than medication effect
- SSRIs used but less effective

Binge Eating Disorder

- **Lisdexamfetamine**
 - ADHD stimulant
- **Topiramate**
 - Seizure medication
- Clinical trials: ↑ abstinence from binge episodes
- Both lead to reduced weight

Alcohol Use Disorder

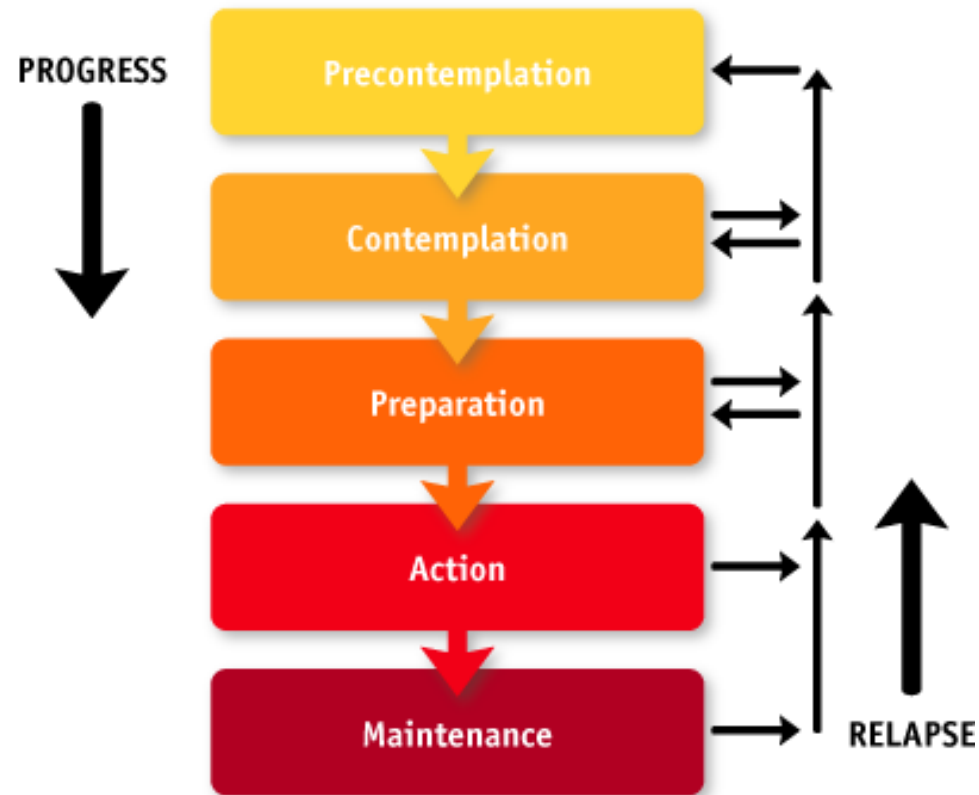
Jason Ryan, MD, MPH



Substance Use Disorder

- DSM-V: Two or more during 12-month period
 - Tolerance
 - Withdrawal
 - Taken in larger amounts or over a longer period
 - Unsuccessful efforts to cut down or control use
 - Lots of time spent to obtain, use, or recover from
 - Craving or a strong desire or urge to use
 - Failure to fulfill obligations at work, school, home
 - Continued use despite social or interpersonal problems
 - Social/occupational activities given up or reduced
 - Use in situations in which it is physically hazardous
 - Use despite knowledge of having a problem

Stages of Change

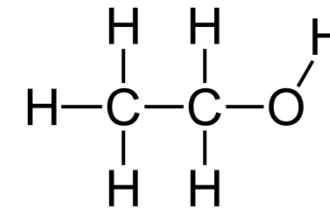


Stages of Change

- Precontemplation
 - No intention of behavior change
 - May not recognize/acknowledge problem
- Contemplation
 - Aware problem exists
 - Not yet willing to change
- Preparation
 - Intending to take action
- Action
- Maintenance
- Relapse

Alcohol

- “Alcohol” = ethyl alcohol = **ethanol**
- Found in alcoholic beverages
- Commonly abused substance
- Metabolized by liver
- Activates GABA receptors
- Numerous biochemical effects



Ethanol



Wikipedia/Public Domain

Alcohol Intoxication

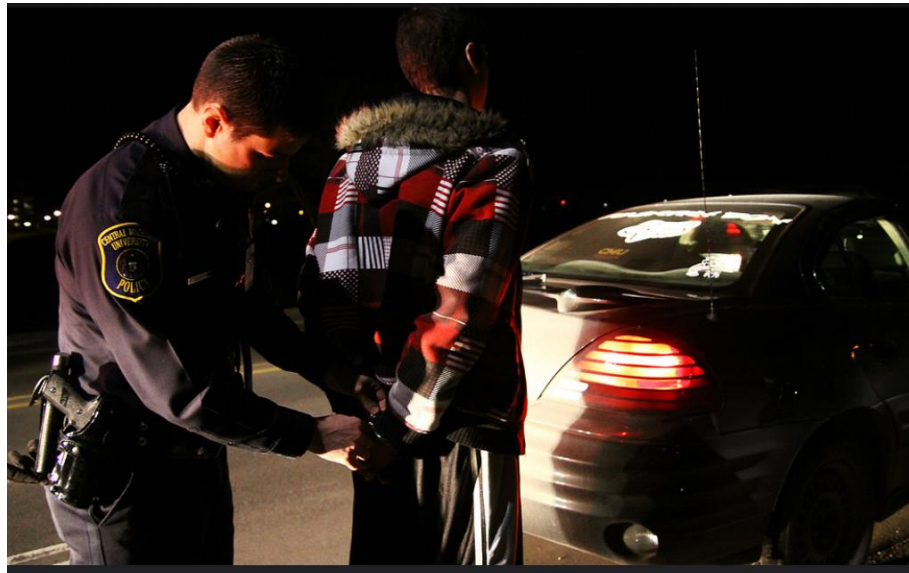
- CNS depressant
- Slurred speech
- Incoordination
- Unsteady gait
- Stupor
- Coma



Pixabay/Public Domain

Alcohol Intoxication

- Serum blood alcohol concentration (BAC)
- Most US states: legal limit **80 mg/dL**
 - “0.08 g/dL” or “0.08” or “8%”
- Number of drinks to reach limit varies with size



Jeffrey Smith/Flickr

Alcohol Biomarkers

- Markers of liver damage
- Used to screen for heavy, chronic use

Biomarker	Abstinence Time for Return to Normal
Gamma-glutamyltransferase (GGT)	2-6 weeks
Aspartate aminotransferase (AST)	7 days

Also seen in chronic use: **↑ MCV** and **hypertension**

Alcohol Poisoning

- Very high BAC → respiratory depression
- Can be fatal
- Treatment is mostly supportive
- May require ICU care



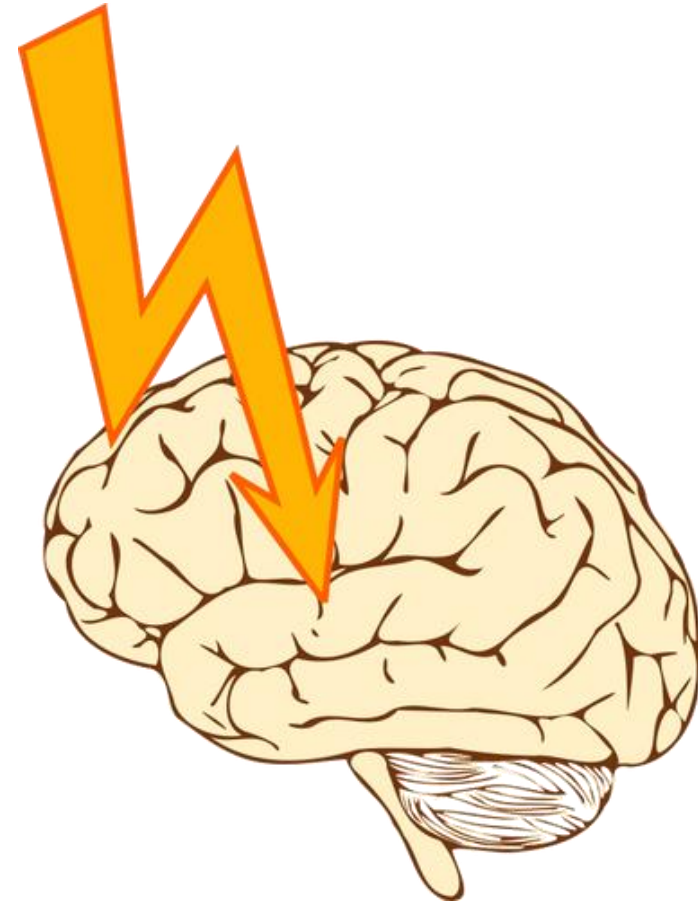
Pixabay/Public Domain

Alcohol Withdrawal

- Heavy drinkers after abrupt cessation
- 6 to 24 hours after last drink
 - **Tremors**
 - Anxiety
 - GI upset
 - Headache
 - Sweating
 - Palpitations
 - Mental status intact

Alcohol Seizures

- 24 to 48 hours after last drink
- Generalized tonic-clonic seizures
- Single or in clusters of two to three



Public Domain

Alcohol Hallucinosi

- 24 to 48 hours after last drink
- Often **visual** hallucinations
- Seeing insects or animals
- Hearing voices
- Tactile sensations



Steve Jurvetson/Flickr

Delirium Tremens

- Between 48 and 96 hours after last drink
- Most severe withdrawal manifestation
- **20% mortality** in some studies



Pixabay/Public Domain

Delirium Tremens

- Delirium
- Agitation
- Fever
- Drenching sweats
- **Autonomic hyperactivity**
 - Tachycardia, hypertension
- Death from:
 - Hyperthermia
 - Cardiovascular collapse
 - Arrhythmias
 - Fluid/electrolyte abnormalities



Shutterstock

Alcohol Withdrawal

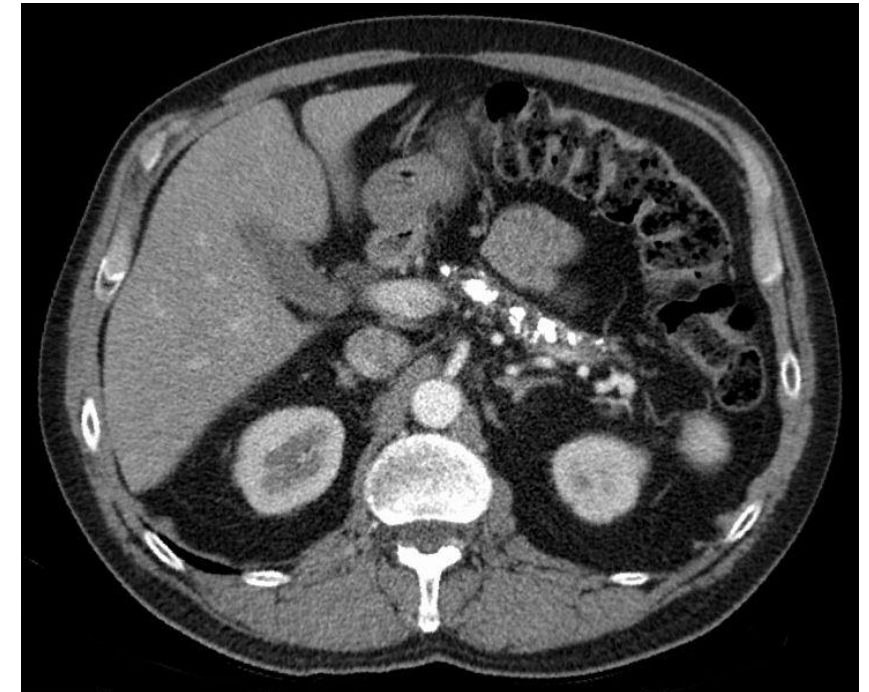
Treatment

- **Benzodiazepines**
 - Functional liver: diazepam or chlordiazepoxide (long-acting)
 - Cirrhosis or alcoholic hepatitis: lorazepam (short acting)
- Improve agitation and prevent progression
- CIWA scale
 - Symptom-triggered therapy
 - Clinical Institute Withdrawal Assessment for Alcohol
 - Point system for assessing withdrawal symptoms
 - Regular assessment of patient
 - Benzodiazepine given if score is high

Alcohol Use Disorder

- Recurrent drinking causing impaired social functioning
- Many medical complications
- **Gastrointestinal**
 - Gastritis, hepatitis, cirrhosis, pancreatitis
- Cardiac
 - Dilated cardiomyopathy, refractory hypertension
- Malignancy
 - Esophageal and oropharyngeal cancers

Chronic Pancreatitis



Hellerhoff/Wikipedia

Alcohol Use Disorder

Wernicke-Korsakoff

- Wernicke: acute encephalopathy
- Korsakoff: chronic neurologic condition
 - Usually a consequence of Wernicke
- Both associated with:
 - Thiamine (B1) deficiency
 - Alcohol use
- Atrophy of mammillary bodies common finding
 - 80% for both conditions
- Associated with damage to thalamic nuclei

Alcohol Use Disorder

Wernicke-Korsakoff

- **Wernicke Encephalopathy**
 - Visual disturbances/nystagmus
 - Gait ataxia
 - Confusion
 - Often reversible with thiamine
- **Korsakoff Amnesia**
 - Recent memory affected more than remote
 - Can't form new memories
 - Confabulation: Can't remember so makes things up
 - Lack of interest or concern (apathy)
 - Usually permanent



Shutterstock

Alcohol Use Disorder

Nutritional Deficiencies

- **Thiamine (vitamin B1)**
- Pyridoxine (vitamin B6)
- Folate (vitamin B9)
- **Magnesium**
- Calcium
- Phosphorus

Alcohol Use Disorder

Nutritional Deficiencies

- **Banana bag**
 - IV infusion to alcohol users
 - Thiamine, folate, and magnesium
- Wernicke precipitated by **glucose without thiamine**
 - Thiamine co-factor glucose metabolism
 - Glucose will worsen thiamine deficiency



Public Domain

Alcohol Use Disorder

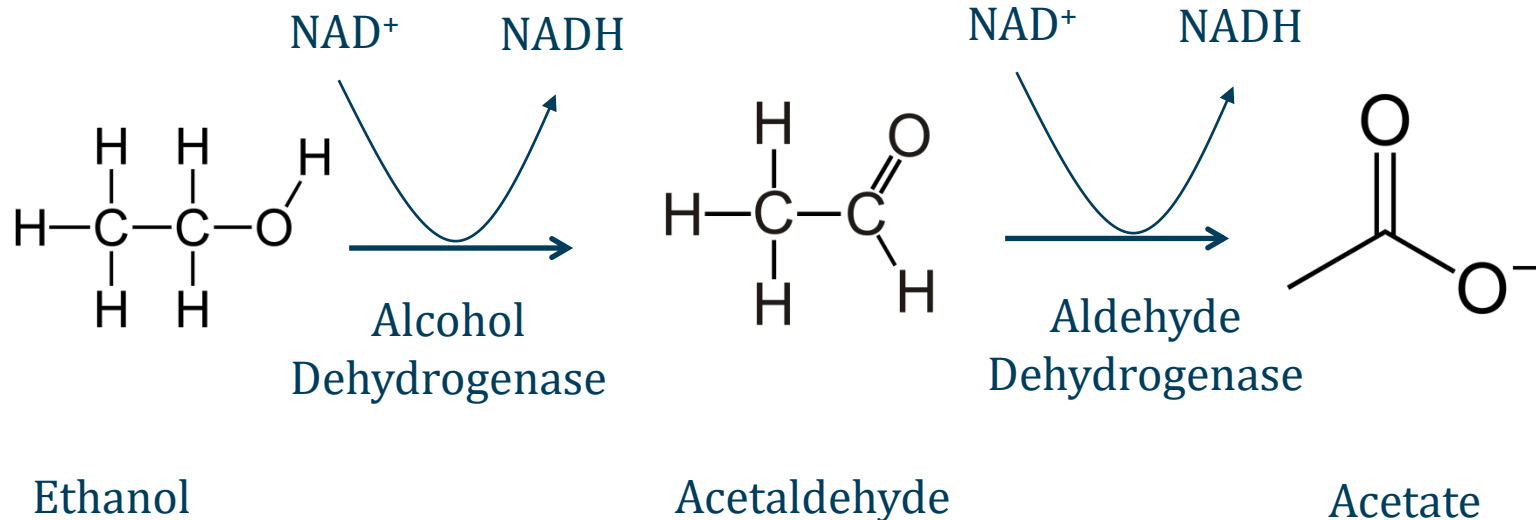
Treatment

- Support groups (Alcoholics Anonymous)
- Three FDA-approved drugs
 - Reduce risk of relapse
- Disulfiram (Antabuse)
- Naltrexone
- Acamprosate

Disulfiram

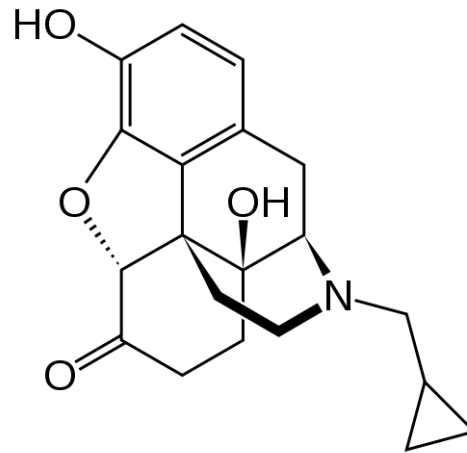
Antabuse

- Inhibits aldehyde dehydrogenase
- Acetaldehyde accumulates
- Triggers catecholamine release
- **Sweating, flushing**, palpitations, nausea, vomiting



Naltrexone

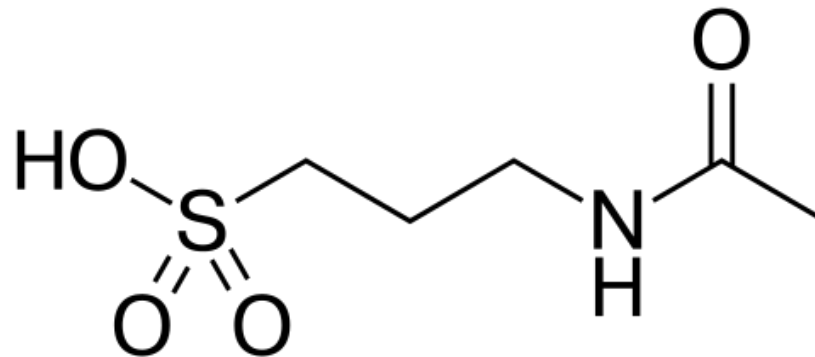
- Long acting **opioid antagonist**
- Endogenous opioids reinforce alcohol effects
- Given orally to prevent relapse
- Also used in opioid abuse



Naltrexone

Acamprosate

- Mechanism incompletely understood
- Modulates NMDA receptors
 - Alcohol disrupts CNS equilibrium
 - Excitatory glutamate activity (NMDA receptor)
 - Inhibitory GABA activity
- Common side effect (~15%): **diarrhea**



Acamprosate

Alcohol Use Disorder

Screening

- **CAGE questionnaire**
 - Have you ever felt you should **Cut** down on your drinking?
 - Have people **Annoyed** you by criticizing your drinking?
 - Have you ever felt bad or **Guilty** about your drinking?
 - Have you ever had a drink first thing in the morning as an **Eye opener**?
 - Score of 2 or greater is clinically significant
- Other tools
 - AUDIT (10 questions)
 - MAST (25 questions)



Pixabay

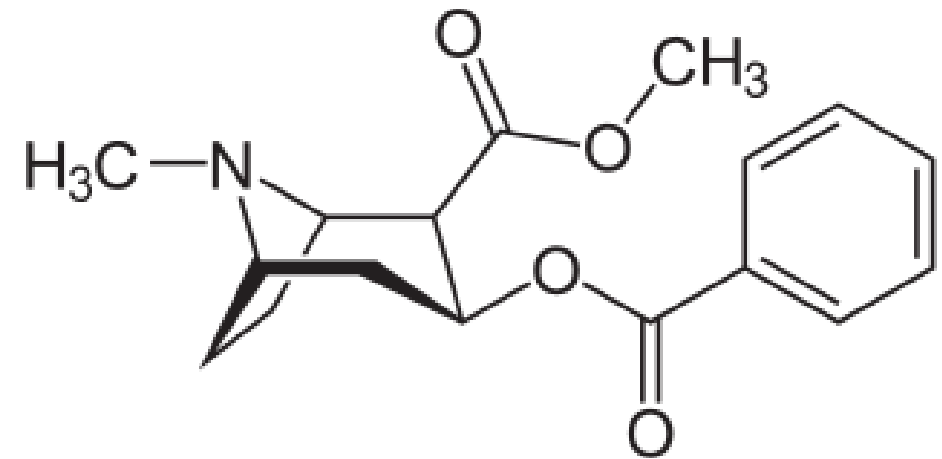
Substance Abuse I

Jason Ryan, MD, MPH



Cocaine

- Two key physiologic effects
 - #1: Local **anesthetic** (Na channel blocker)
 - #2: Inhibits **monoamine reuptake**
 - Monoamines: dopamine, serotonin, NE
- **Sympathetic activation**



Cocaine

Cocaine Intoxication

- Increased energy
- Decreased need for sleep
- Alertness
- Euphoria



Wikipedia/Public Domain

Cocaine Intoxication

- Hallucinations
 - Classically tactile
 - **“Bugs crawling on my skin”**
- Paranoia
- **Fever**
 - Increased muscle activity
 - Central dopamine release
- Anxiety
- May mimic psychosis
- Treatment: **benzodiazepines**



Michael "BuZZeR" Kadykov

Cocaine Intoxication

- Rhabdomyolysis
- Seizures
- Myocardial ischemia

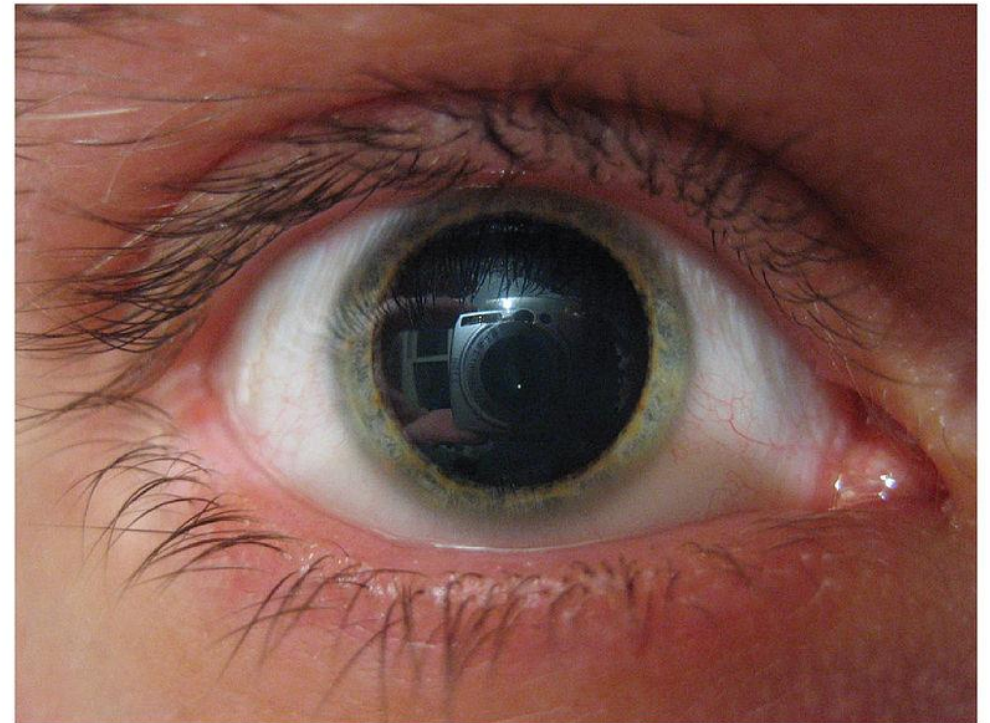


Free SVG

Cocaine Intoxication

Signs

- Sympathetic nervous system activation
- Stimulation of alpha and beta receptors
- **Dilated pupils**
- Tachycardia
- Hypertension



OpenStax College/Wikipedia

Cocaine Intoxication

Myocardial Ischemia

- Angina common among cocaine users
- ↑ O₂ demand (tachycardia, elevated BP)
- ↓ O₂ supply (coronary vasoconstriction)
- O₂ mismatch → angina
- May lead to thrombosis → myocardial infarction

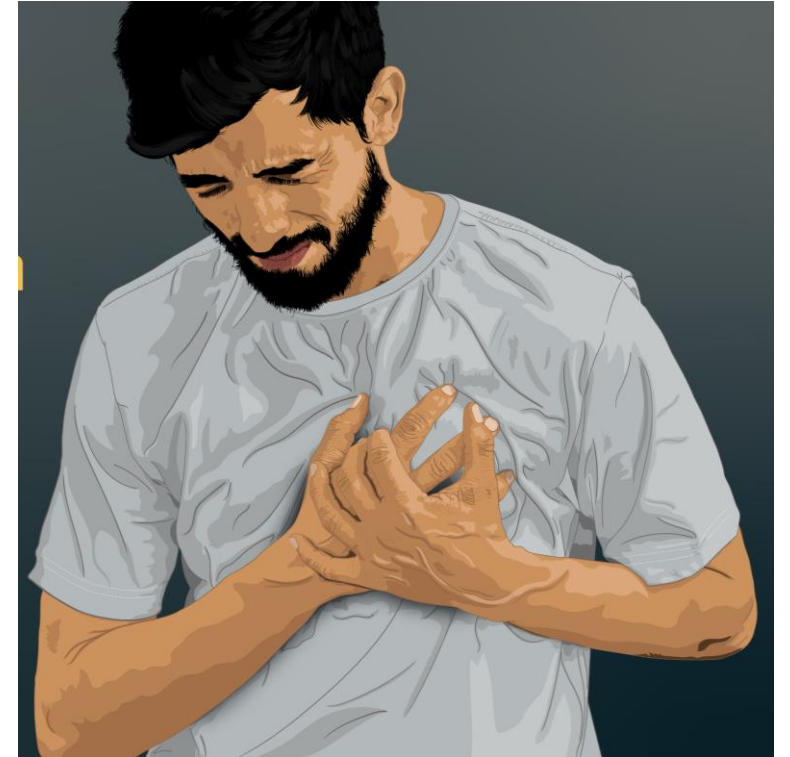


Freestocks.org

Cocaine Intoxication

Myocardial Ischemia

- Treatment: **benzodiazepines**
 - Sedating/calming
 - Diminish cocaine-related stimulating effects
- Aspirin
- Catheterization in severe cases
- **Avoid beta-blockers**
 - Increased alpha effects
 - Worsening of hypertension and chest pain



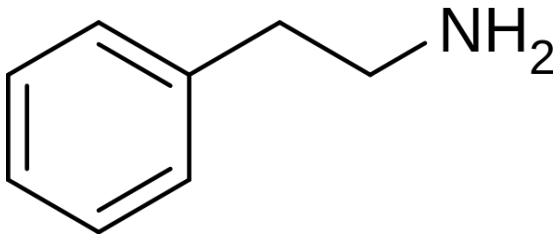
Wikipedia/Public Domain

Cocaine Withdrawal

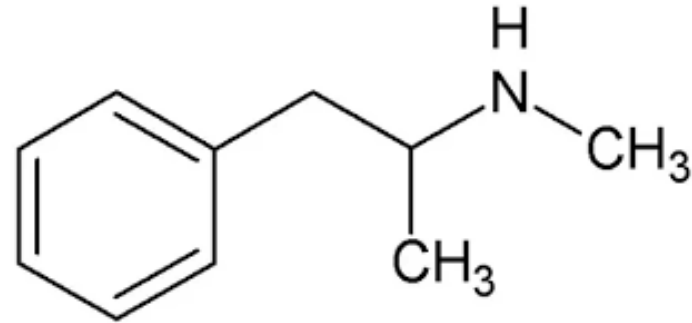
- Occurs with stopping after chronic, heavy use
- **Usually not life-threatening**
- Depression and anhedonia
- Anxiety
- Cravings
- Increased sleep

Amphetamines

- Modified phenethylamines
- **Stimulants**
- Indirect sympathomimetics
- Increase synaptic **dopamine/NE** levels



Phenethylamine



Methamphetamine

Amphetamine Intoxication

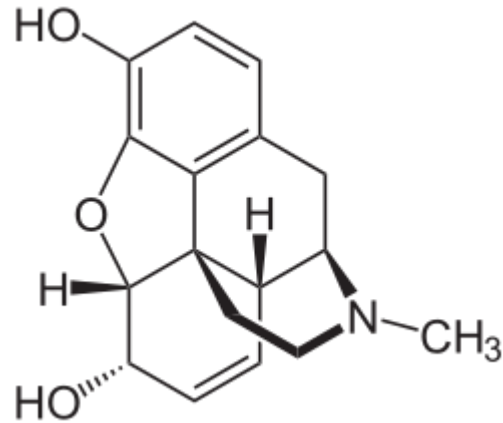
- Similar to cocaine
- Euphoria/fever
- Sympathetic stimulation
 - Tachycardia, hypertension
 - Pupillary dilation
- Rhabdomyolysis/seizures/ischemia
- Treatment: **benzodiazepines**
- Withdrawal syndrome similar to cocaine



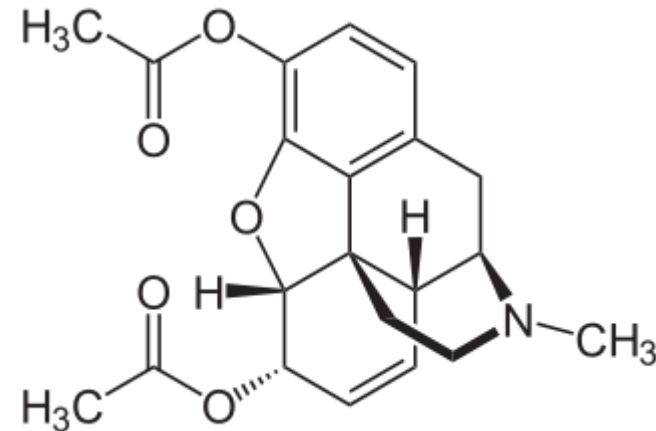
Wikipedia/Public Domain

Opioids

- Activate opioid receptors: mu, kappa and delta
- Prototype: **morphine**
- Also hydromorphone, meperidine, fentanyl, codeine
- Drug of abuse: **heroin** (diamorphine)



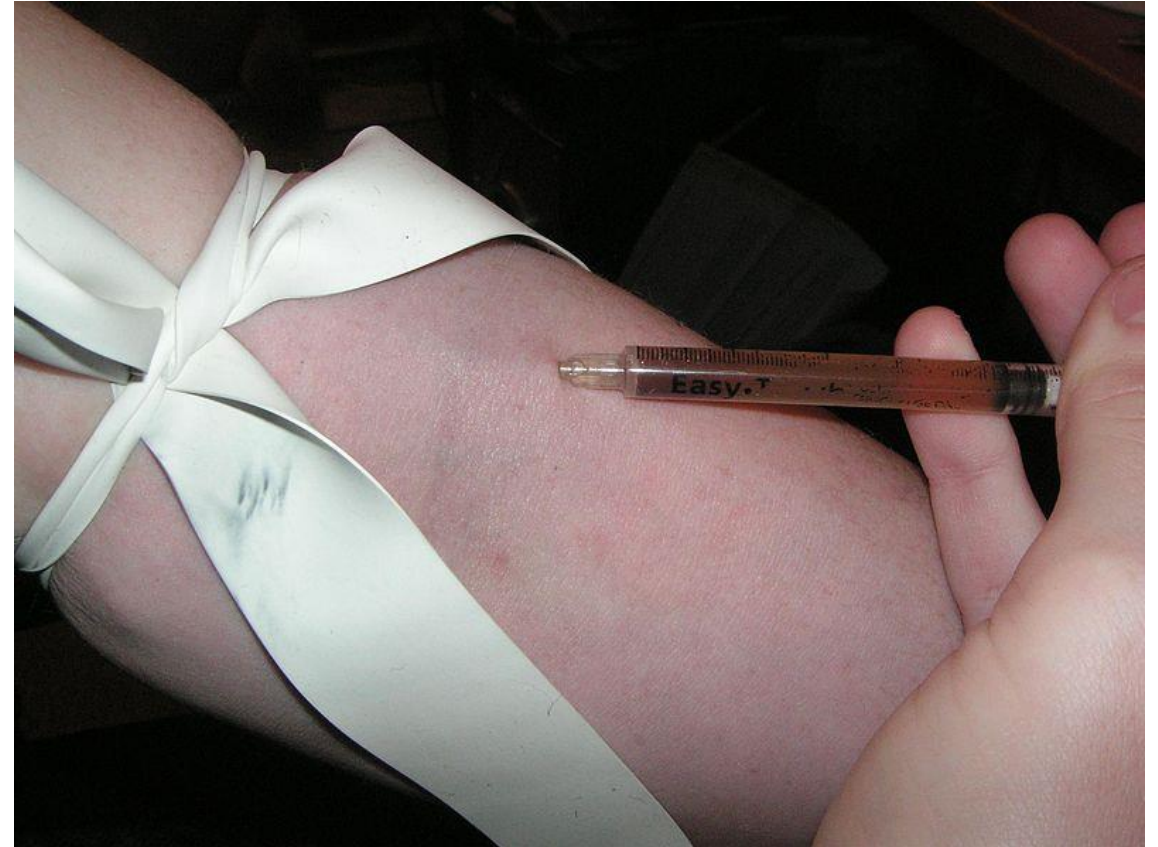
Morphine



Heroin

Heroin

- Usually **injected** into vein
- Contaminated needle or drugs:
 - Bacteremia → tricuspid endocarditis
 - Hepatitis B & C
 - HIV



Psychonaught/Wikipedia

Opioids

Central nervous system effects

- Pain relief (analgesia)
- Euphoria
- Sedation



Wikipedia/Public Domain

Opioids

Central nervous system effects

- Slurred speech
- Respiratory depression
- Cough suppression
- Miosis (small pupils)
 - Exception: meperidine



Wikipedia/Public Domain

Opioids

Peripheral nervous system effects

- Constipation
- Nausea
- Vomiting
- Skin warmth and flushing



John Johnson/Pexels

Opioids

Clinical Uses

- Pain control
- Acute pulmonary edema (IV morphine)
- Cough suppression (codeine)
- Diarrhea (loperamide)
- Shivering: (meperidine/Demerol)

Opioids

Addiction & Tolerance

- Highly addictive
- **Tolerance** develops
 - Less effect of drugs over time
 - Higher dosages required to achieve effects
 - **No tolerance to miosis and constipation**



Wikipedia/Public Domain

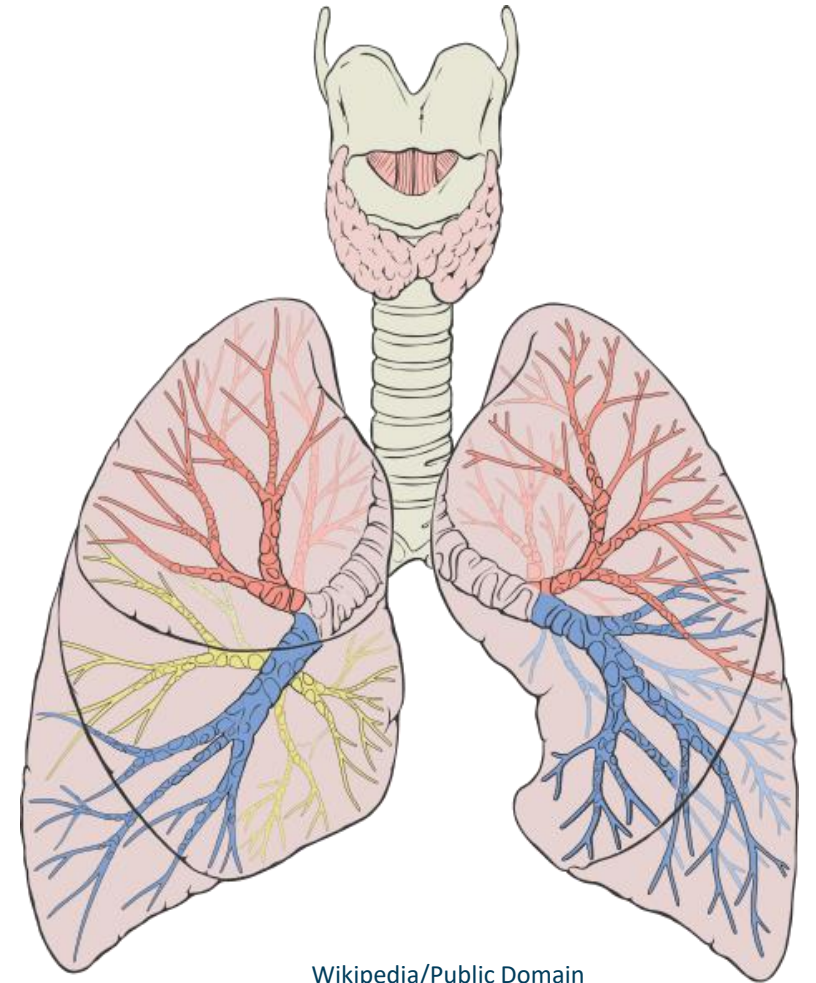


John Johnson/Pexels

Opioids

Acute Intoxication

- Most common cause of drug overdose death
- Euphoria to depressed mental status
- **Decreased respiratory rate**
- **Decreased bowel sounds**
- **Miotic (constricted) pupils**
- Seizures
 - Most common with tramadol or meperidine

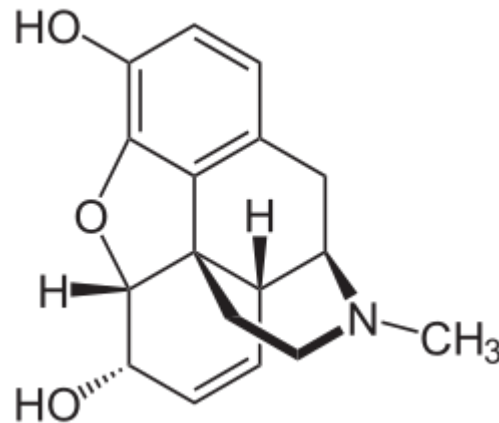


Wikipedia/Public Domain

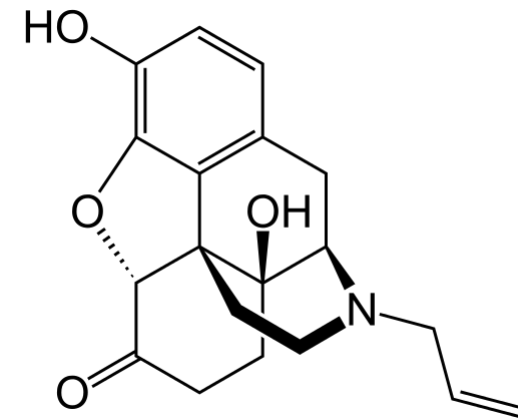
Opioid Intoxication

Treatment

- **Naloxone**
- Short-acting opioid antagonist
- May cause withdrawal if dose too high (“overshoot”)



Morphine



Naloxone

Opioid Withdrawal

Causes

- Iatrogenic
 - Caused by opioid antagonist
 - Potentially life-threatening
 - Surges in catecholamines
 - Hemodynamic instability
- Naturally-occurring
 - Usually not life-threatening
- Clinically Oriented Withdrawal Scale (COWS)
 - 11-item scale
 - Point system to assess symptoms
 - Mild, moderate, severe withdrawal

Opioid Withdrawal

Naturally-Occurring

- Occurs in opioid-dependent individuals
- Usually starts 6-12 hours after last dose
- Reversal of CNS, eye, skin, GI effects
- Restlessness
- **Yawning**
- **Rhinorrhea and lacrimation**
- **Piloerection**
- Nausea, vomiting, abdominal cramps
- Diarrhea



FreeSVG

Opioid Withdrawal

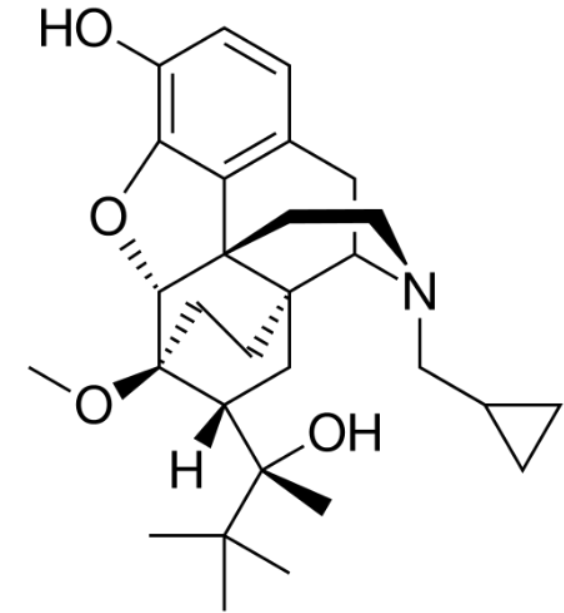
Medical Therapy

- Minimizes withdrawal symptoms
- Clonidine
 - Central alpha agonist
 - Blunts sympathetic activation
 - Sedating
- Opioid agonists
 - Buprenorphine
 - Methadone

Opioid Use Disorder

Treatment

- **Buprenorphine**
 - Partial agonist (agonist and antagonist effects)
 - Long duration of action
 - Sublingual tablet
 - DEA schedule III drug
 - May cause withdrawal (like naloxone)
- Combined with naloxone
 - Prevents abuse
 - Naloxone not absorbed sublingually
 - Crushed pill → IV injection → no effect

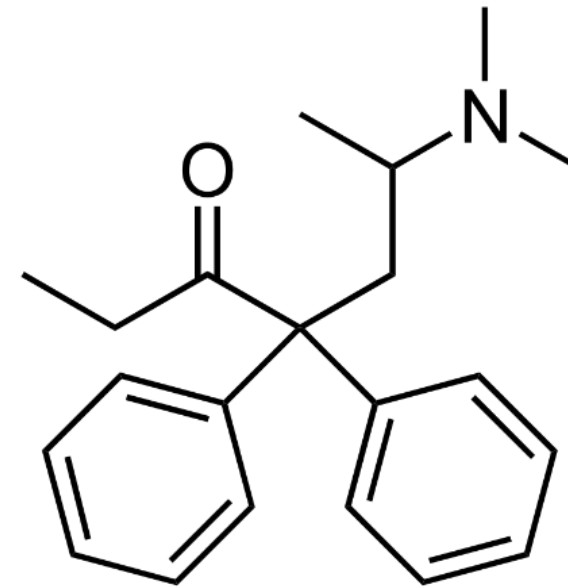


Buprenorphine

Opioid Use Disorder

Treatment

- **Methadone**
 - Long-acting oral opiate
 - Reduces cravings
 - Maintenance
 - Strictly regulated/controlled
 - DEA schedule II



Methadone

Controlled Substances Act

- Places drugs in categories based on abuse potential

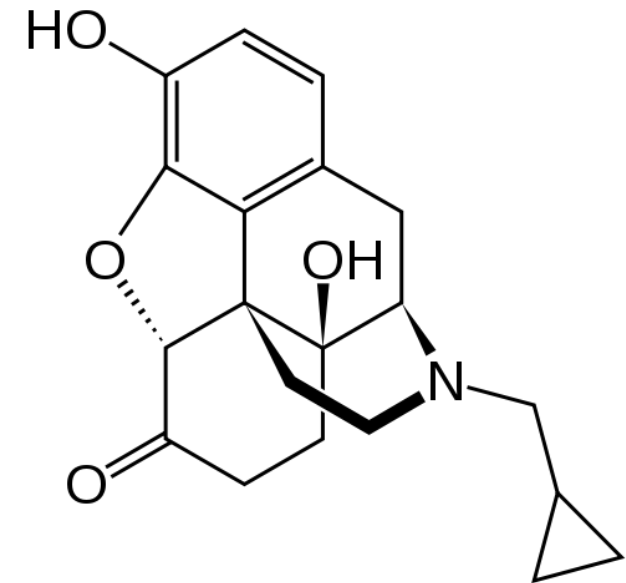
Schedule	Meaning	Examples
I	No medical indication	Heroin, LSD, ecstasy
II	High abuse potential	Cocaine, methadone, fentanyl, Ritalin
III	Moderate abuse potential	Buprenorphine, ketamine, anabolic steroids
IV	Low abuse potential	Benzodiazepines
V	Very low abuse potential	Cough medications with codeine

Opioid Use Disorder

Treatment

- **Naltrexone**

- Long-acting opioid antagonist
- Blocks effects of opioids if taken
- Administered to detoxified patients to prevent relapse
- Some data show prevention of relapse
- Also used in alcohol use disorder



Naltrexone

Substance Abuse II

Jason Ryan, MD, MPH



Barbiturates

Phenobarbital, pentobarbital

- Anti-seizure drugs
- GABA activators
- Used as sedatives in past
- Now largely replaced benzodiazepines
- Similar effects to alcohol (CNS depressants)
- Narrow therapeutic index
- Dangerous used **together with alcohol**

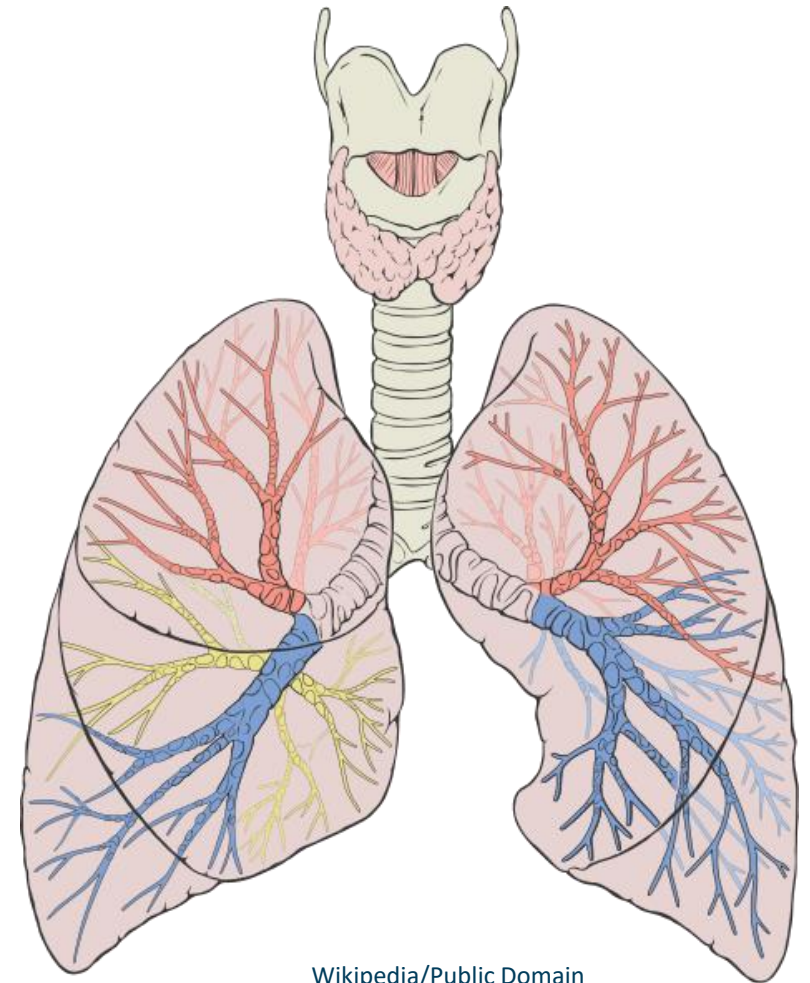


Wikipedia/Public Domain

Barbiturates

Phenobarbital, pentobarbital

- Overdose: **respiratory depression**
 - No antidote
 - Supportive care
- Heavy users must be weaned
- Abrupt withdrawal:
 - Delirium
 - Hallucinations
 - Seizures
 - Cardiovascular collapse → death



Wikipedia/Public Domain

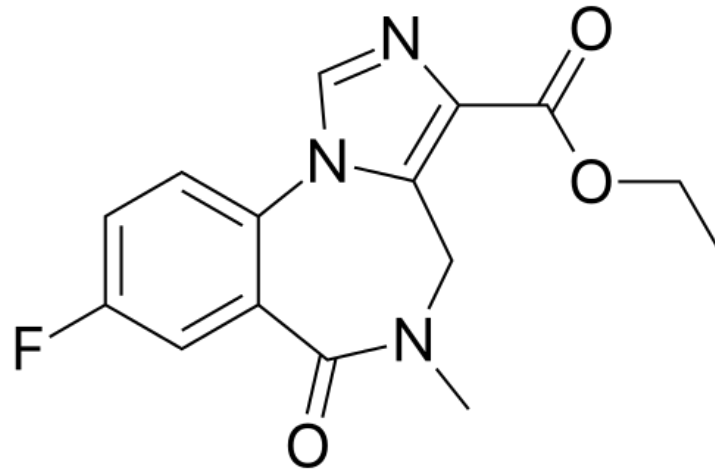
Benzodiazepines

Diazepam, oxazepam, lorazepam

- Many medical uses (seizures, anxiety, alcohol withdrawal)
- Increase GABA activity
- Rarely cause respiratory depression (safer drugs)
- Classic overdose presentation:
 - **CNS depression with normal vitals**
 - Altered mental status
 - Slurred speech
 - Ataxia

Flumazenil

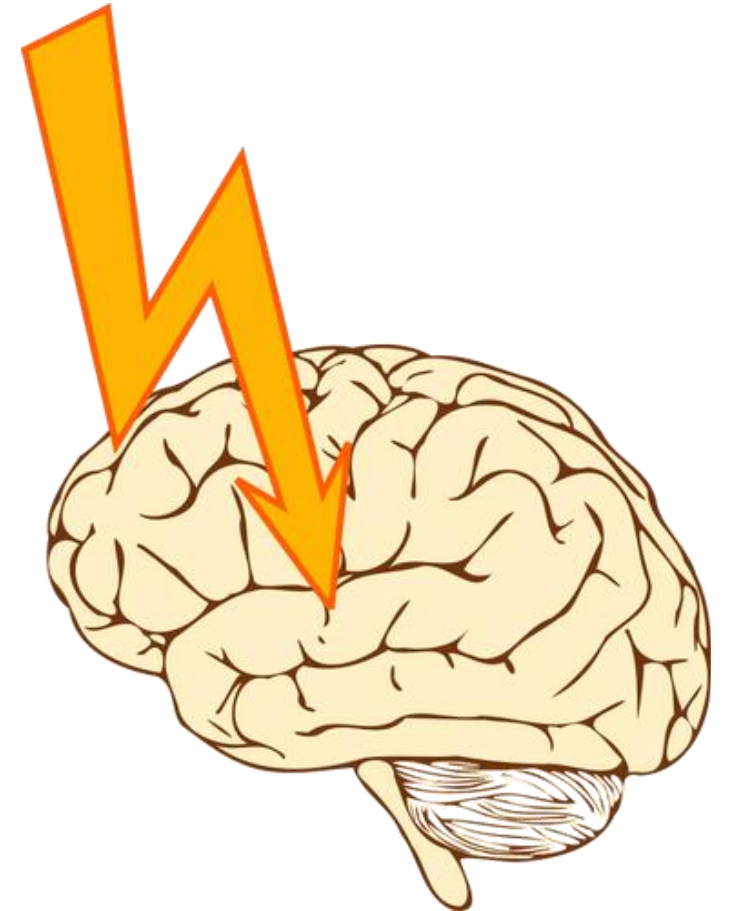
- **Antagonist** of benzodiazepine receptor
- Use to treat overdose controversial
- Overdose has low mortality rate
- Flumazenil may cause withdrawal seizures



Flumazenil

Benzodiazepine Withdrawal

- Occurs with abrupt cessation after chronic use
- Similar to alcohol withdrawal
- Tremors
- Anxiety
- Depressed mood (“dysphoria”)
- Hypersensitivity to sensations (noise, touch)
- Psychosis
- **Seizures**
- Can be life-threatening
- Treatment: benzodiazepines



Public Domain

Marijuana

- Derives from cannabis (plant)
- Psychiatric activity from **tetrahydrocannabinol (THC)**
 - Also called dronabinol
- Stimulates cannabinoid receptors in CNS



Wikipedia/Public Domain

Marijuana

- Euphoria
- Anxiety
- Impaired coordination
- Conjunctival injection
- Dry mouth
- Increased appetite
- Tachycardia
- Blood pressure fluctuations
- Rarely causes hallucinations or psychosis
- Usually not life-threatening



Wikipedia/Public Domain

Synthetic Cannabinoids

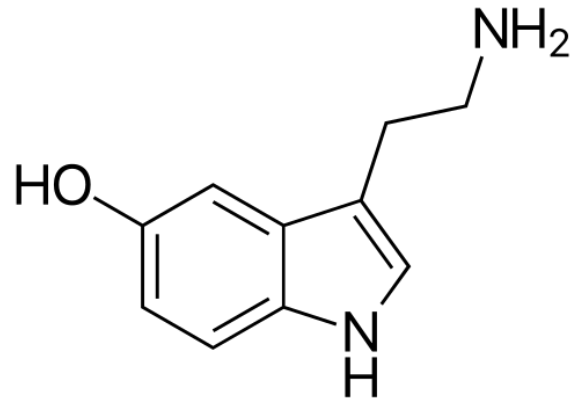
- Pharmaceutical forms of **dronabinol**
- Available in capsule form
- Cannabis withdrawal
- Chemotherapy-induced nausea and vomiting
- Appetite stimulation in wasting illnesses
 - Often end stage HIV/AIDS patients



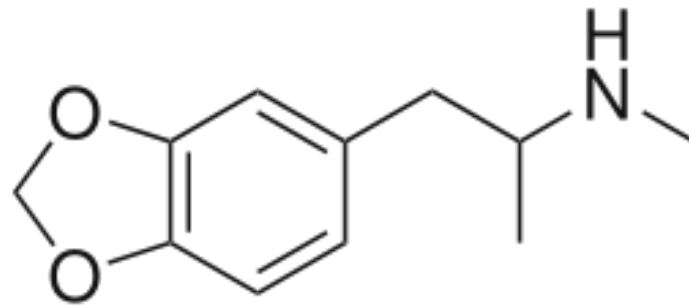
Ecstasy

Methylenedioxymethamphetamine (MDMA)

- Major effect on **serotonin**
 - Increased release of serotonin
 - Inhibition of serotonin reuptake



Serotonin



MDMA

Ecstasy

Methylenedioxymethamphetamine (MDMA)

- Euphoria
- Alertness
- Increased sociability
- Increased sexual desire
- **Bruxism** (grinding teeth)



Wikipedia/Public Domain

Ecstasy

Methylenedioxymethamphetamine (MDMA)

- Tachycardia and hypertension
- Hyperthermia
- **Hyponatremia**
 - Increased fluid intake
 - Secretion of antidiuretic hormone
 - Reports of **seizures and death**
- **Hepatotoxicity**
 - RUQ pain
 - Increased AST/ALT
- Can cause serotonin syndrome

hydrogen 1 H 1.0079	
lithium 3 Li 6.941	beryllium 4 Be 9.0122
sodium 11 Na 22.990	magnesium 12 Mg 24.305
potassium 19 K 39.098	calcium 20 Ca 40.078

Ecstasy Withdrawal

- “Crash” after using MDMA
- **Depression** and anxiety
- Fatigue and lethargy
- Difficulty concentrating
- Loss of appetite
- Jaw soreness (from grinding teeth while high)

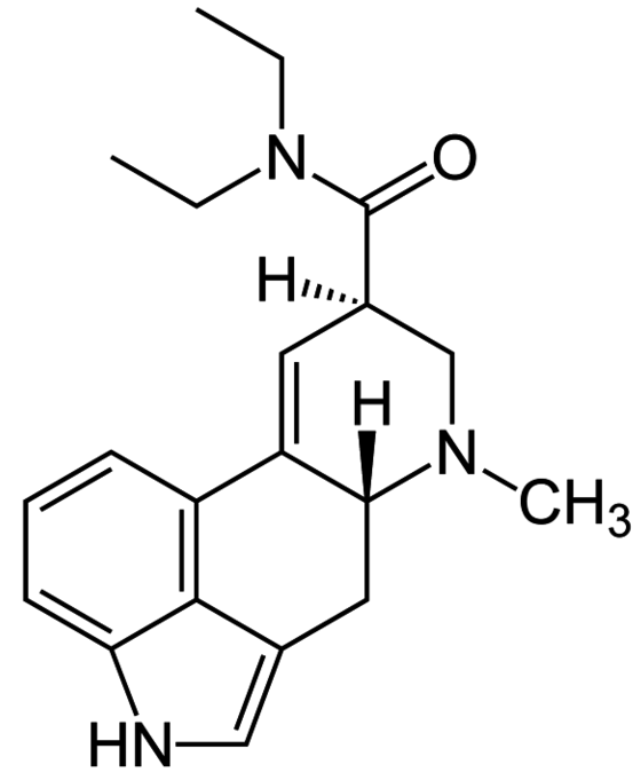


Public Domain

LSD

Lysergic acid diethylamide

- Hallucinogen
- Exact mechanism unknown
 - Binds **serotonin 5-HT2A receptors**



LSD

LSD

Lysergic acid diethylamide

- Causes LSD “trip”
 - Feeling of expanded consciousness
 - Can sense things beyond usual reality
- Synesthesia (a blending of the senses)
 - “Hearing” colors or “seeing” sounds
- Depersonalization
 - Feeling disconnected or detached from body
- “Bad trip”
 - Paranoia, anxiety



Shutterstock

LSD

Lysergic acid diethylamide

- May causes **“flashbacks”**
 - Return of hallucinogen effects after stopping drug
 - May occur days, weeks, even months later
- Intoxication management: supportive

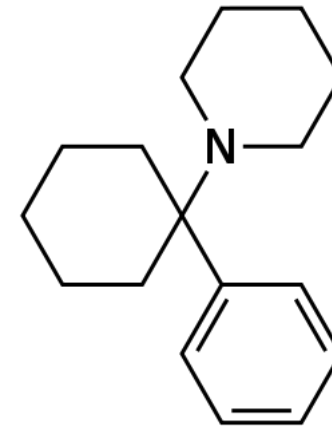


Pariroxy/Wikipedia

PCP

Phencyclidine

- “Angel dust”
- Antagonist of **NMDA** receptor in CNS
 - N-methyl-D-aspartate
 - Glutamate receptor
 - Blockade: hallucinations and psychosis
- Inhibits **reuptake** of dopamine, NE, 5HT
 - Increases sympathetic activity



Phencyclidine

PCP

Phencyclidine

- Stimulant
- Altered mental status
- Psychosis (with hallucinations)
- “Psychomotor agitation”
- Classically agitated, **violent** behavior
- Tachycardia, hypertension
- Nystagmus (repetitive involuntary eye movements)
- Rarely coma and seizures with overdose



Pxhere/public domain

PCP

Phencyclidine

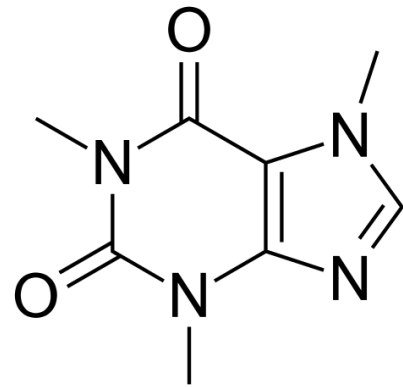
- Fatalities most commonly from **trauma**
 - Psychosis plus **loss of pain/sensation**
 - Patients may dissociate
 - Walk into traffic
 - Jump from buildings
- Treatment:
 - Benzodiazepines
 - Haloperidol (rapid-acting anti-psychotic)



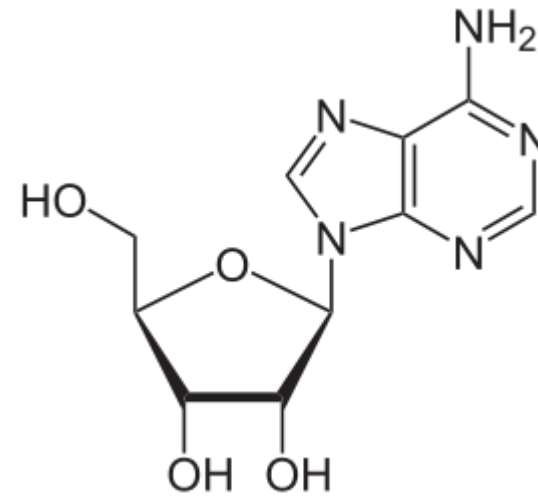
Alisha Vargas/Flickr

Caffeine

- Methylxanthine
- Antagonist of **adenosine receptors**
- Leads to release of dopamine/NE
- Renal adenosine blockade → diuresis



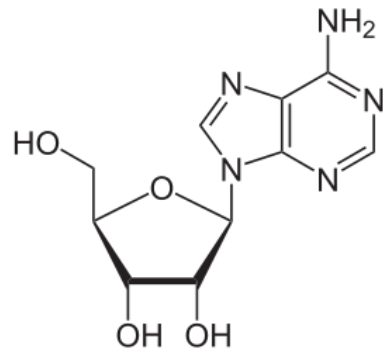
Caffeine



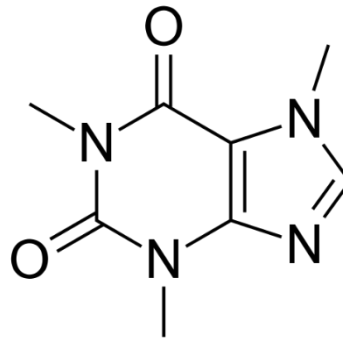
Adenosine

Chemical Stress Tests

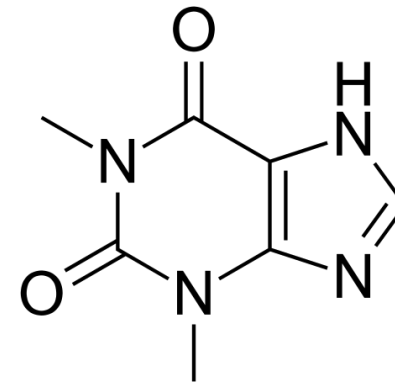
- Intravenous adenosine used as a **vasodilator**
- Induces coronary steal for chemical stress testing
- Effects **blocked by caffeine**
- Also blocked by theophylline (COPD drug)



Adenosine



Caffeine



Theophylline

Antidepressants

Jason Ryan, MD, MPH

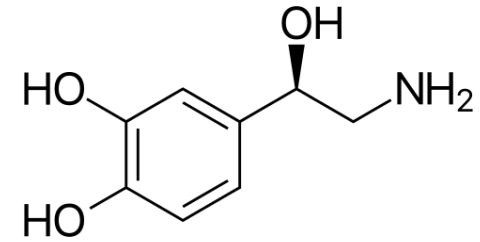


Antidepressants

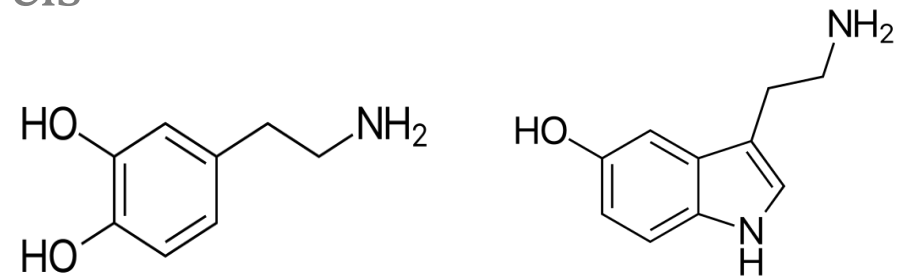
- Tricyclics
- MAO inhibitors
- SSRIs
- SNRIs
- Atypical antidepressants

Depression

- Associated with CNS neurotransmitter changes:
 - ↓ **serotonin**
 - ↓ **norepinephrine**
 - ↓ **dopamine**
- Improved symptoms with increased CNS levels
- Most antidepressant drugs increase synaptic levels
 - Block re-uptake
 - Inhibit breakdown

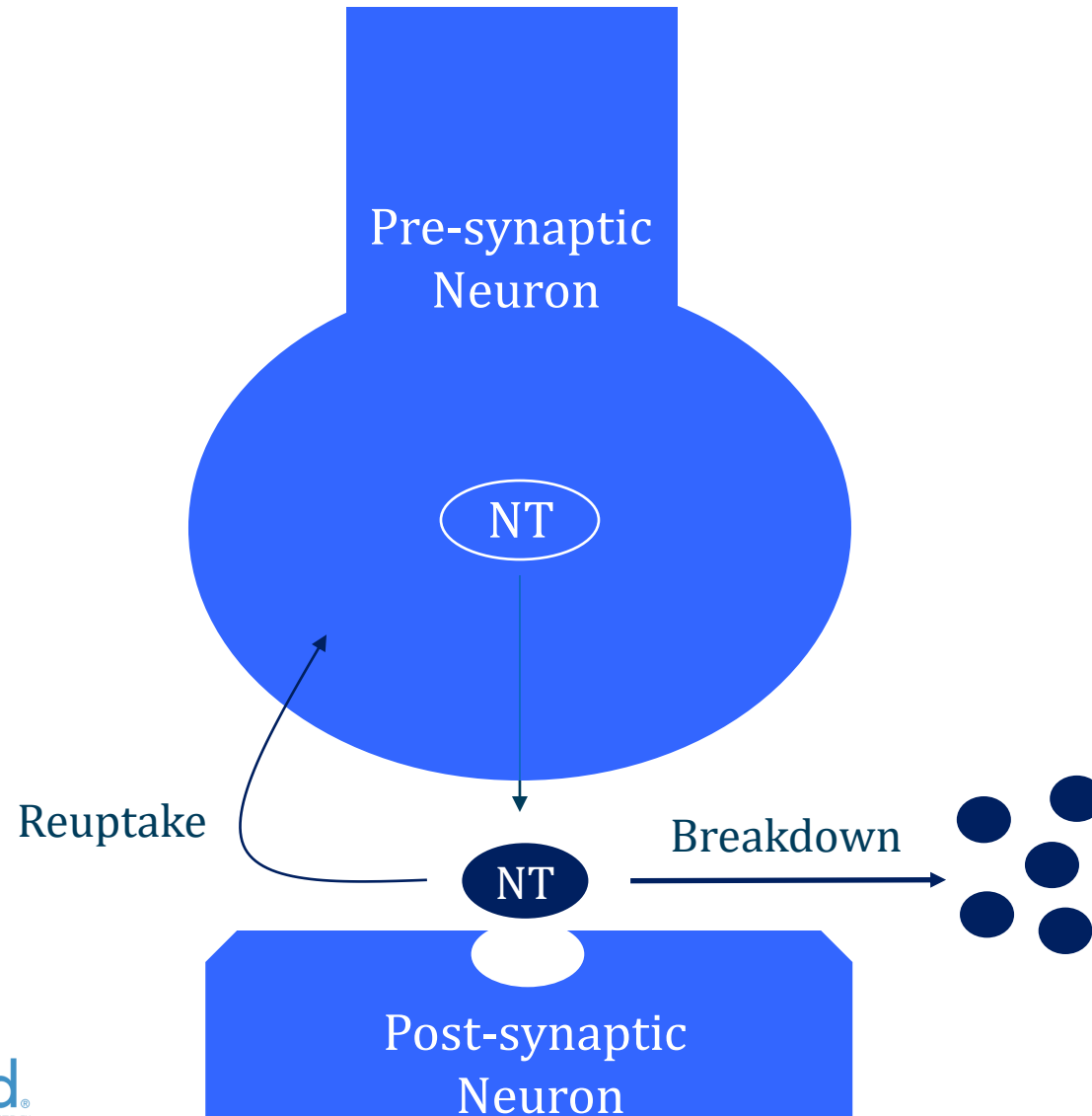


Norepinephrine



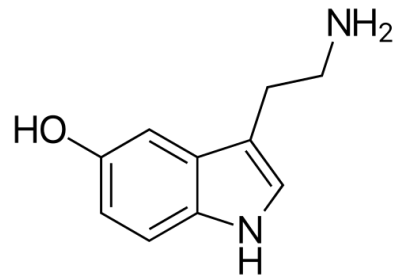
Dopamine

Serotonin
5-HT

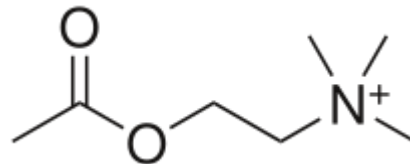


Monoamines

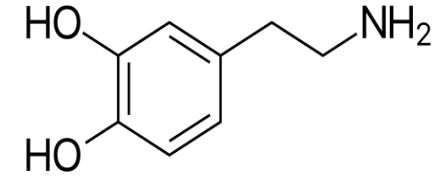
- Serotonin, norepinephrine, histamine, dopamine
- Most drugs affect more than one monoamine
- Anti-histamine: sedation, dry mouth
- NE blockade: hypotension (alpha-1)
- Muscarinic blockade: tachycardia, urinary retention



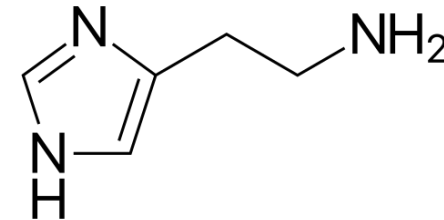
Serotonin
5-HT



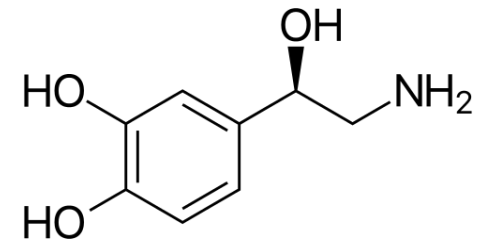
Acetylcholine



Dopamine



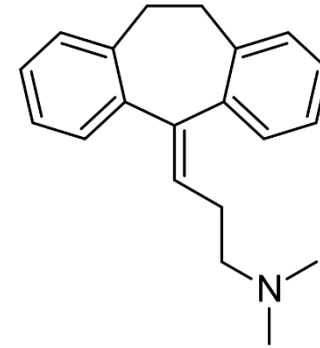
Histamine



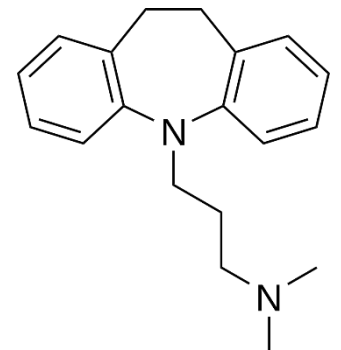
Norepinephrine

Tricyclic Antidepressants

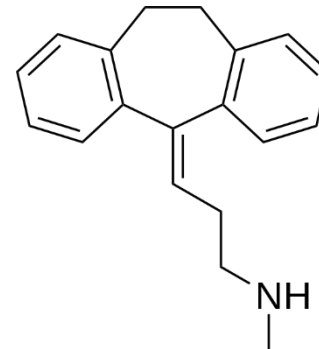
- Old antidepressants (1970s)
- Block re-uptake of **5-HT** and **norepinephrine**
- “Broad spectrum”
 - Anti-histamine
 - Anti-muscarinic
 - Block alpha-1 receptors
 - Many side effects



Amitriptyline



Imipramine



Nortriptyline

Tricyclic Antidepressants

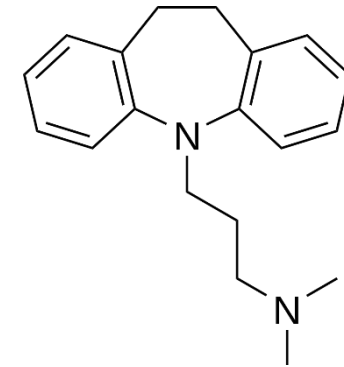
- Anti-histamine
 - Sedation, weight gain, confusion (especially elderly)
- Anti-cholinergic (muscarinic)
 - Blurry vision, constipation, dry mouth, urinary retention, sexual dysfunction
- Alpha-1 block
 - Orthostatic hypotension



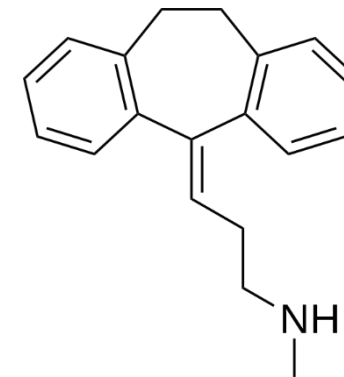
Shutterstock

Tricyclic Antidepressants

- **Tertiary amines** (3 nitrogen attachments)
 - Amitriptyline, imipramine, clomipramine, doxepin
 - More sedating (anti-histamine effects)
- **Secondary amines** (2 nitrogen attachments)
 - Desipramine, nortriptyline
 - More activating (norepinephrine effects)



Imipramine

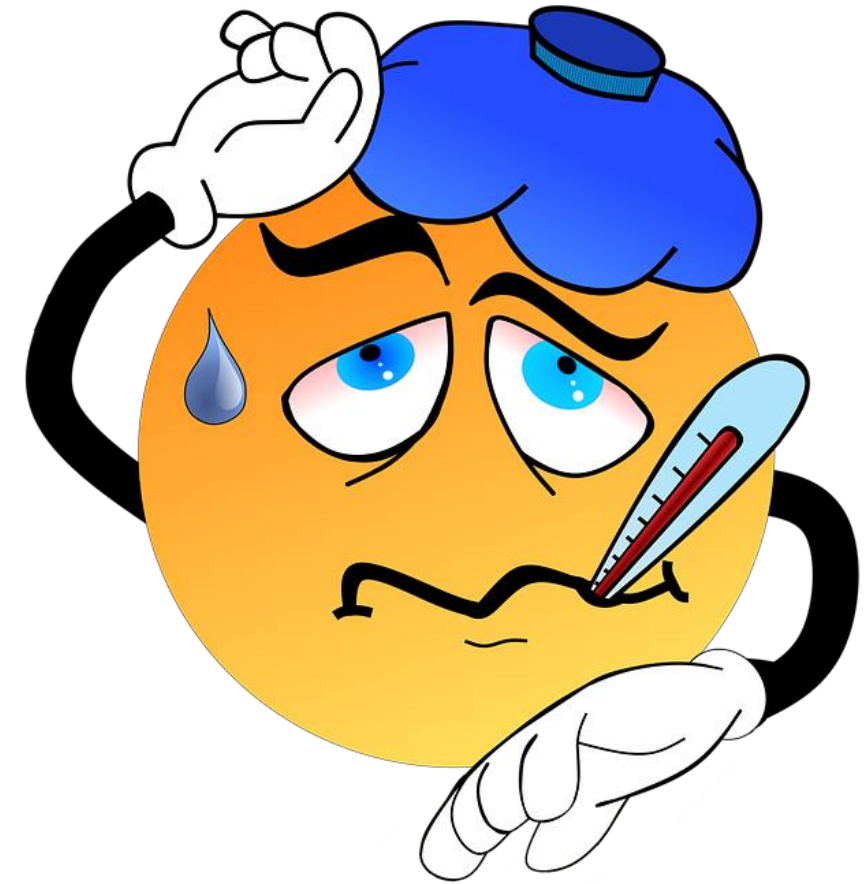


Nortriptyline

Tricyclic Antidepressants

Overdose

- Potentially fatal
- **Seizures** and coma
 - TCAs antagonize GABA receptors
- Anticholinergic toxicity
 - **Hyperthermia** (loss of sweating)
 - Skin flushing, dilated pupils
 - Ileus, urinary retention
- **Hypotension** (alpha blockade)
 - Major cause of death
- Prolongation of QT interval → arrhythmias

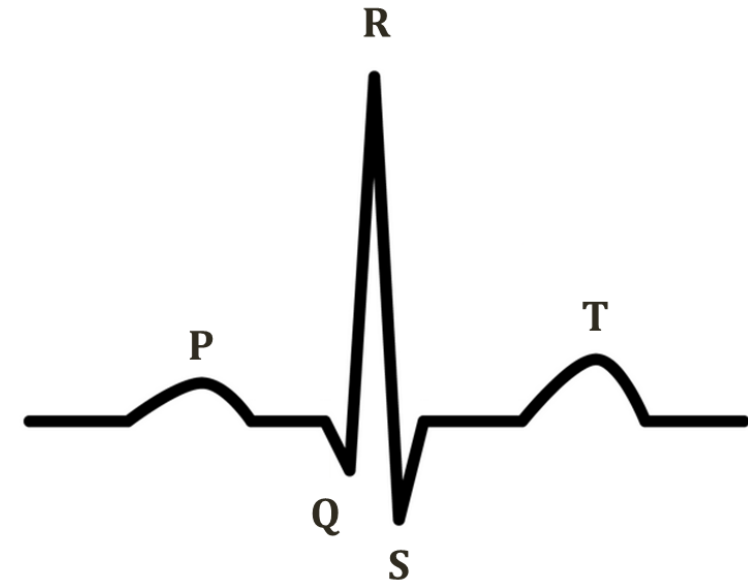


Pixabay.com

Tricyclic Antidepressants

Overdose

- Monitor ECG for **increased QRS interval**
 - Most prominent manifestation of toxicity
 - TCAs block cardiac sodium channels
- Treatment: **sodium bicarbonate**
 - Extra sodium overcomes TCA Na-channel blockade
 - Also \uparrow pH favors inactive form of drug



Tricyclic Antidepressants

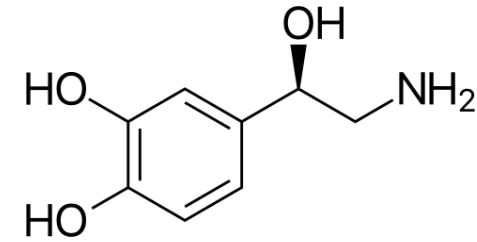
Non-depression uses

- Obsessive-compulsive disorder (clomipramine)
- Diabetic peripheral neuropathy
 - Amitriptyline, desipramine
- Chronic pain
 - Amitriptyline, doxepin, imipramine, nortriptyline, desipramine
- Prevention of migraine headaches
 - Amitriptyline
- Bedwetting (enuresis)
 - Not first-line therapy (desmopressin)
 - Imipramine, amitriptyline, and desipramine
- Insomnia (doxepin)

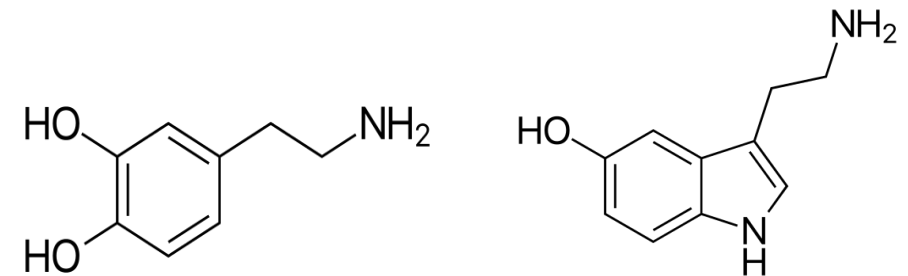
MAO Inhibitors

Monoamine Oxidase Inhibitors

- Inhibits monoamine oxidase
- **↓ breakdown of monoamines**
 - Serotonin, norepinephrine, dopamine
- MAO-A
 - Dopamine, serotonin, norepinephrine
- MAO-B
 - Dopamine



Norepinephrine



Dopamine

Serotonin
5-HT

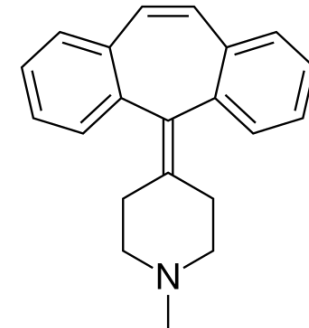
MAO Inhibitors

Monoamine Oxidase Inhibitors

- Non-selective MAO inhibitors
 - Tranylcypromine, phenelzine, isocarboxazid
- MAO-B selective: selegiline
 - Used in Parkinson's
- Rarely used as antidepressants in modern era
 - **Refractory depression**
 - Anxiety

Serotonin Syndrome

- Classic triad: Three As
- #1: Mental status changes
 - Agitation, restlessness, and disorientation
- #2: Autonomic hyperactivity
 - Diaphoresis, tachycardia, **hyperthermia**
- #3: Neuromuscular hyperactivity
 - Tremor, clonus, hyperreflexia, bilateral Babinski sign
- Treatment: **cypheptadine**
 - 5-HT antagonist



Cypheptadine

Serotonin Syndrome

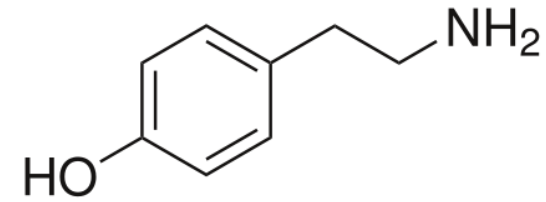
- Often caused by MAOI **plus another serotonin drug**
- Any drug that that ↑ serotonin activity
 - SSRIs, SNRIs, TCAs
 - MDMA (ecstasy)
 - Ondansetron (nausea; 5-HT₃ antagonist)
 - Tramadol (weak opioid; inhibits 5-HT reuptake)
 - Meperidine (opioid; inhibits 5-HT reuptake)
 - Triptans (migraines; 5-HT agonists)
 - Linezolid (antibiotic; weak MAO inhibitor)
 - Dextromethorphan (cough suppressant; weak SSRI)
 - St. John's wort (herbal supplement; increase 5-HT activity)

Serotonin Syndrome

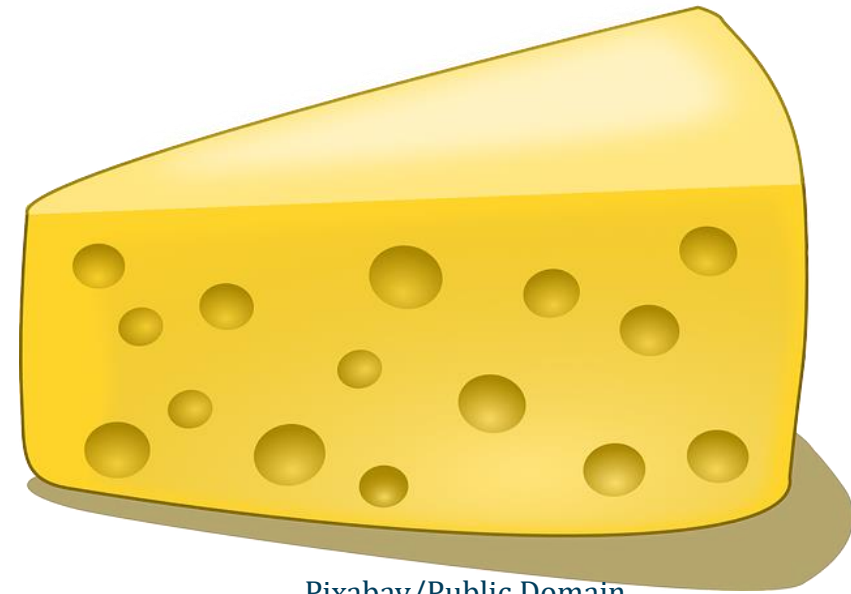
- When switching from MAOI to SSRI:
 - Two-week washout
- When switching from SSRI to MAOI:
 - Usually two-week washout
 - Fluoxetine: five weeks (long half life)

Tyramine

- Naturally occurring monoamine
- Sympathomimetic
- Causes sympathetic activation
- Normally metabolized GI tract
- Patients on MAOI → tyramine in blood
- Hypertensive crisis
- **“Cheese effect”**
 - Cheese, red wine, some meats



Tyramine



Pixabay/Public Domain

SSRIs

Selective serotonin reuptake inhibitors

- Inhibit **5-HT reuptake** by neurons
- Lead to ↑ 5-HT levels in synaptic cleft
- Take 4-8 weeks to have effects
- Used in many psychiatric disorders
 - Depression
 - Generalized anxiety disorder
 - Panic disorder
 - Obsessive-compulsive disorder
 - PTSD
 - Bulimia
 - Social anxiety disorder

Fluoxetine
Sertraline
Paroxetine
Citalopram
Escitalopram
Fluvoxamine

SSRIs

Selective serotonin reuptake inhibitors

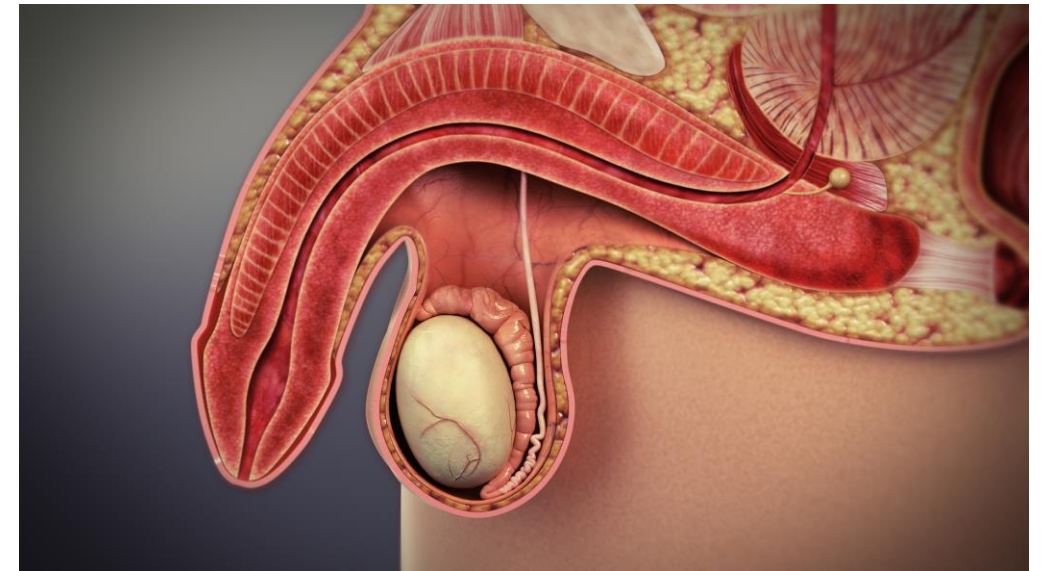
- Non-specific side effects that often subside with use
 - Headache
 - Insomnia
 - GI upset (nausea, diarrhea)
 - Drowsiness
- Rare, dangerous effects
 - SIADH and hyponatremia
 - QT prolongation
 - Serotonin syndrome
- Sexual dysfunction

1 H			
3 Li	4 Be		
11 Na	12 Mg		
19 K	20 Ca	21 Sc	22 Ti
37 Rb	38 Sr	39 Y	40 Zr

SSRIs

Selective serotonin reuptake inhibitors

- Common side effect: **sexual dysfunction**
- Increased serotonin effects in spinal cord
- Decreased libido (54 percent)
- **Anorgasmia**: difficulty achieving orgasm (36 percent)
- Erectile dysfunction in males (37 percent)
- Usually does not subside over time
- SSRIs can treat premature ejaculation



Wikipedia/Public Domain

Discontinuation Syndrome

- Abrupt discontinuation of antidepressant
- Can occur with any antidepressant
- Most common with **SSRIs**
 - Exception: fluoxetine (long half life)
- Dizziness
- Fatigue
- Headache
- Nausea
- Avoid by **slowly tapering off drug**



SNRIs

Serotonin-norepinephrine reuptake inhibitors

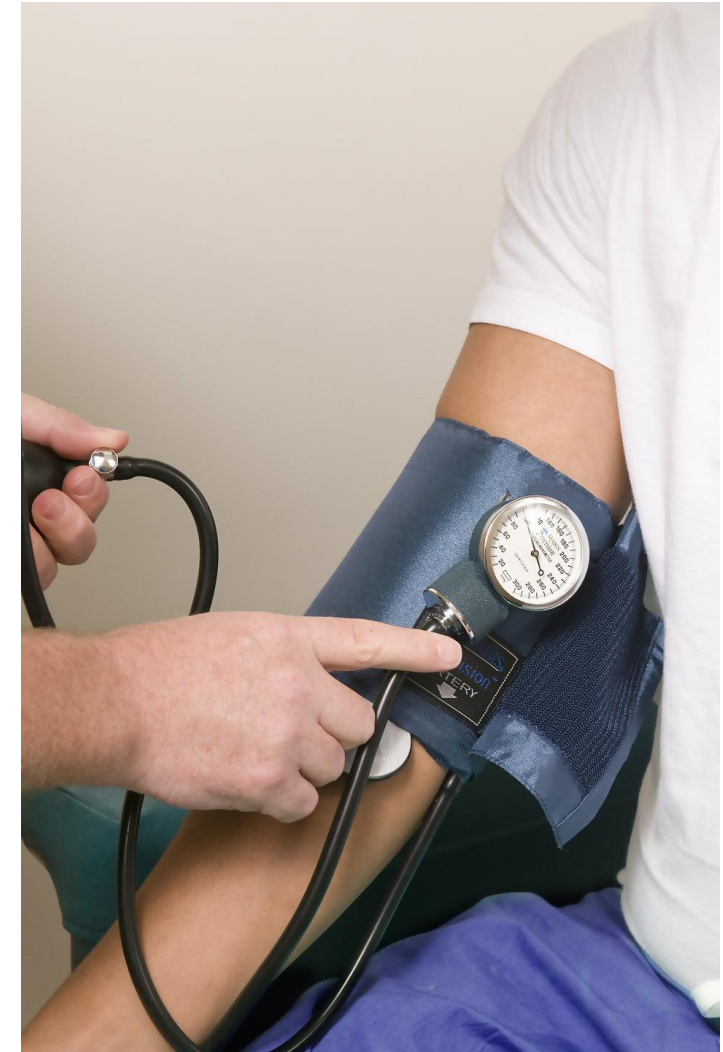
- Inhibit **5-HT and NE reuptake** by neurons
- Take 4-8 weeks to have effects
- Used in many psychiatric disorders
 - Depression
 - Generalized anxiety disorder
 - Social anxiety disorder
 - Panic disorder
 - PTSD
 - Obsessive-compulsive disorder
- Fibromyalgia (duloxetine)
- Diabetic neuropathy (venlafaxine)

Venlafaxine
Desvenlafaxine
Duloxetine
Milnacipran
Levomilnacipran

SNRIs

Serotonin-norepinephrine reuptake inhibitors

- Similar side effects to SSRIs
- **May increase blood pressure**
 - Norepinephrine effects
- Sexual dysfunction
 - Highest rate: venlafaxine



Public Domain

Bupropion

- Blocks reuptake of NE and dopamine
- Increases presynaptic release of catecholamines
- No effects on serotonin
- Used in **depression** and **smoking cessation**
- May *improve* sexual dysfunction of SSRIs
- Toxicity related to stimulant effects
 - Anxiety
 - Insomnia
- **Lowers seizure threshold**



Pixabay/Public Domain

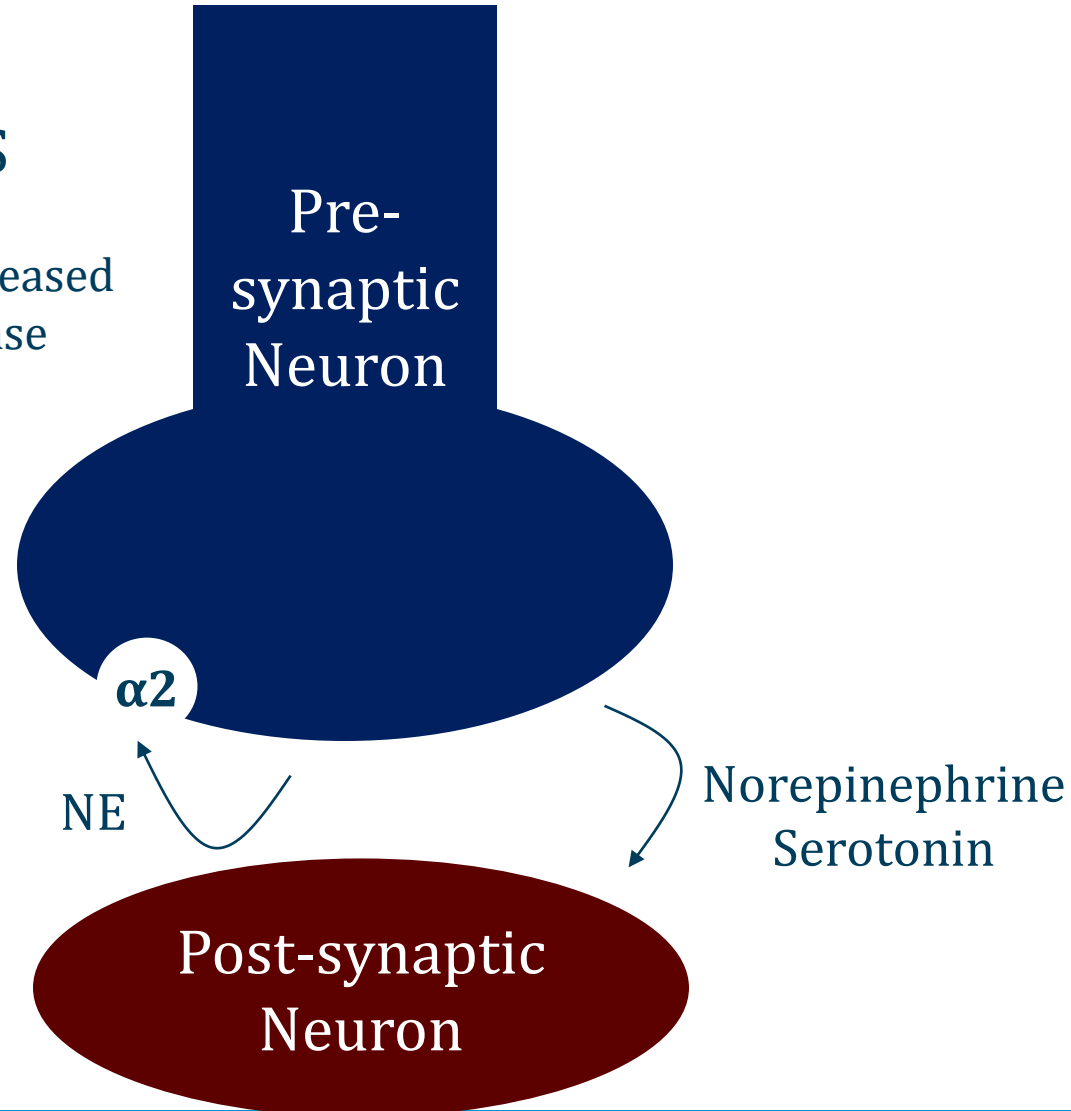
Mirtazapine

- Blocks presynaptic **alpha-2 receptors**
 - More norepinephrine and serotonin release
- Blocks postsynaptic serotonin **5-HT2 and 5-HT3**
 - More 5-HT1 activity
- Anti-histamine side effects
 - **Sedation**
 - Dry mouth
 - Increased appetite
 - Weight gain



Alpha 2 Receptors

α_2 receptors in CNS
Presynaptic receptor
Feedback to nerve when NE released
Activation leads to \downarrow NE release



Trazadone and Nefazodone

- Weak serotonin reuptake inhibitors
- Affects serotonin 5-HT_{2A} and 5-HT_{2C} receptors
 - Low doses: serotonin antagonist
 - High doses: serotonin agonist
- Trazadone
 - Main clinic use is **insomnia** (sedating)
- Nefazodone
 - May cause liver failure
 - Must monitor AST/ALT

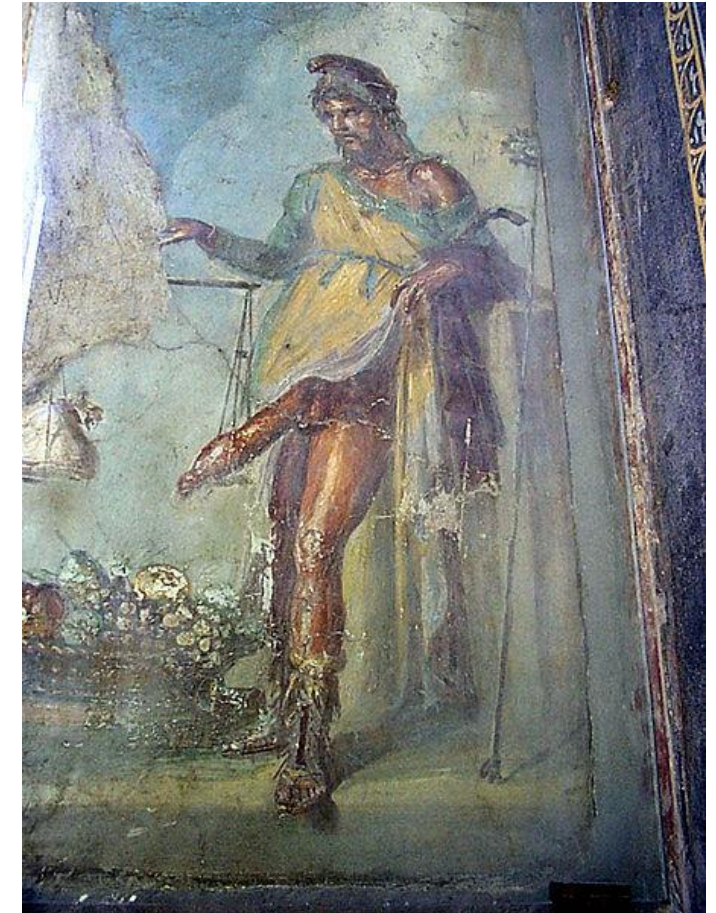


Public Domain

Priapism

- Persistent erection
- Causes compartment syndrome
- Hypoxia and acidosis in cavernous tissue
- Rare, dangerous adverse effect of **trazadone**
- Usually within 1 month of starting treatment
- Urgent urology evaluation
- Treatment: intracavernosal vasoconstrictor injection
 - Contracts cavernous smooth muscle allowing venous outflow
 - Epinephrine
 - Phenylephrine

Priapus
Greek Fertility God



Public Domain

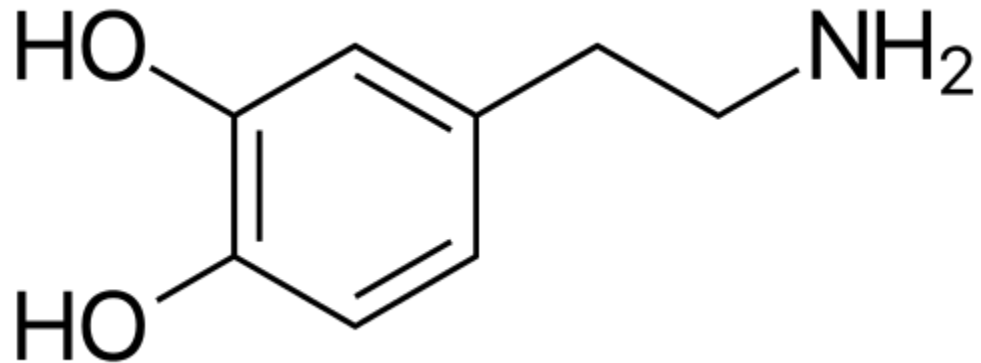
Antipsychotics

Jason Ryan, MD, MPH



Dopamine

- 1950s: **chlorpromazine** found to improve psychosis
- Also found to block CNS **dopamine** receptors
- Dopamine hypothesis



Antipsychotics

First Generation or Typical

- Haloperidol
- Chlorpromazine
- Trifluoperazine
- Fluphenazine
- Thioridazine
- Pimozide
- Primary antipsychotic effect: **D2 receptor blockade**

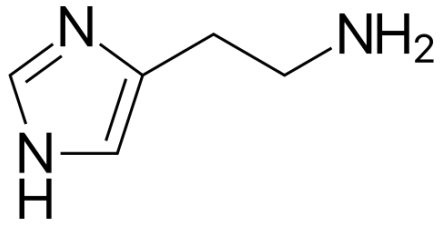
Parkinson's Disease

- Motor dysfunction
- Tremors, rigidity
- Associated with ↓ **CNS dopamine activity**

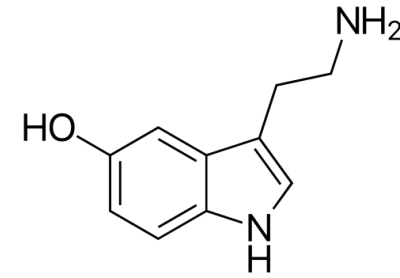


Wikipedia/Public Domain

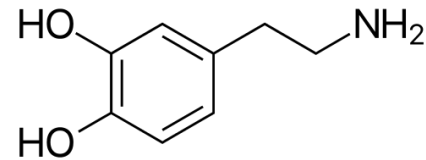
Neurotransmitters



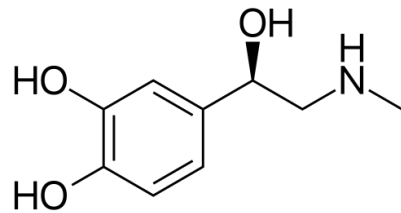
Histamine



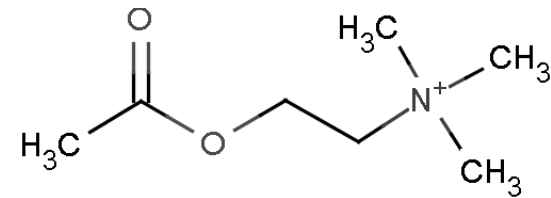
Serotonin
5-HT



Dopamine



Epinephrine



Acetylcholine
(Muscarinic)

Antipsychotics

First Generation or Typical

- Dopamine blockade
- Serotonin blockade
- Histamine blockade
- Acetylcholine (muscarinic) blockade
- Epinephrine (alpha-1) blockade

Chlorpromazine: $\alpha 1 = 5HT > D2$

Haloperidol: $D2 > \alpha 1 > 5HT > H1$

Antipsychotics

First Generation or Typical

- Dopamine blockade
 - Parkinsonian effects (extrapyramidal)
 - Hyperprolactinemia
 - Gynecomastia
 - Galactorrhea
 - Amenorrhea
 - **Anti-emetic** (Prochlorperazine/Chlorpromazine)



Antipsychotics

First Generation or Typical

- ACh muscarinic receptor blockade
 - Dry mouth
 - Constipation
 - Urinary retention
 - Tachycardia
 - Sexual dysfunction
- $\alpha 1$ receptor blockade
 - Hypotension
- Histamine receptor blockade
 - Sedation
 - Weight gain

Xerostomia
(Dry Mouth)



Wikipedia/Public Domain

Pyramidal vs. Extrapyrarmidal

- Pyramidal system
 - Corticospinal tract
 - Run in pyramids of medulla
 - Damage → weakness
- Extrapyrarmidal system
 - Basal ganglia nuclei and associated tracts
 - Modulation of movement
 - Damage → movement disorders



Wikipedia/Public Domain

EPS

Extrapyramidal Symptoms

- Response to dopamine receptor blockade
- **Movement** side effects
- Dystonia
- Akathisia
- Bradykinesia
- Tardive dyskinesia

Dystonia

Extrapyramidal Symptoms

- Acute side effect
- Occurs within hours/days
- Involuntary contraction of muscles
- Spasms, stiffness
- Treatments:
 - **Benztropine (anticholinergic)**
 - **Diphenhydramine (antihistamine)**
 - Improves dystonia

Writer's Cramp



Akathisia

Extrapyramidal Symptoms

- Occurs within days
- Most common EPS adverse effect
- Restlessness, urge to move
- Sometimes misdiagnosed as worsening agitation
- Treatments:
 - Lower dose
 - Benzodiazepines
 - Propranolol

Bradykinesia

Extrapyramidal Symptoms

- Occurs weeks after starting drug
- “Drug-induced Parkinsonism”
- Slow movements (Parkinson-like)
- Treatment: **benztropine**
 - Second line: amantadine



Tardive Dyskinesia

Extrapyramidal Symptoms

- Occurs months or years after starting drug
- **Choreoathetosis**
 - Chorea: irregular migrating contractions
 - Athetosis: twisting and writhing
 - Mouth, tongue, face, limbs
- Smacking lips, grimacing
- **Often irreversible**
 - Stopping drug doesn't help
- One FDA-approved drug: valbenazine
 - Inhibits VMAT2
 - Depletes dopamine storage in presynaptic vesicles

Antipsychotics

First Generation or Typical

- **High potency agents**
 - Haloperidol, fluphenazine, pimozide
- Lower dose required to achieve effect
- Example: haloperidol 1mg
- Little effect on histamine and muscarinic receptors
 - Less sedation (histamine) or dry mouth (muscarinic)
- **Extrapyramidal side effects**

Chlorpromazine: $\alpha 1 = 5HT > D2$

Haloperidol: $D2 > \alpha 1 > 5HT > H1$

Antipsychotics

First Generation or Typical

- **Low potency agents**
 - Thioridazine, chlorpromazine
 - Example: Thioridazine 50-100mg
- Less extrapyramidal side effects
- **More non-neurologic side effects**
 - Sedating (“sedatives”)
 - Dry mouth

Chlorpromazine: $\alpha 1 = 5HT > D2$

Haloperidol: $D2 > \alpha 1 > 5HT > H1$

Antipsychotics

First Generation or Typical

Low Potency
Thioridazine
Chlorpromazine

High Potency
Haloperidol
Trifluoperazine
Fluphenazine

Non-EPS Effects
Sedation
Dry mouth

EPS Effects
Movement symptoms



NMS

Neuroleptic Malignant Syndrome

- Rare, dangerous reaction to neuroleptics
- Usually high-potency first-generation drugs
 - Haloperidol, fluphenazine
- Usually 7-10 days after treatment started
- **Fever and rigid muscles**
- Mental status changes (encephalopathy)
- Elevated creatine kinase (muscle damage)
- Myoglobinuria → acute renal failure (rhabdomyolysis)

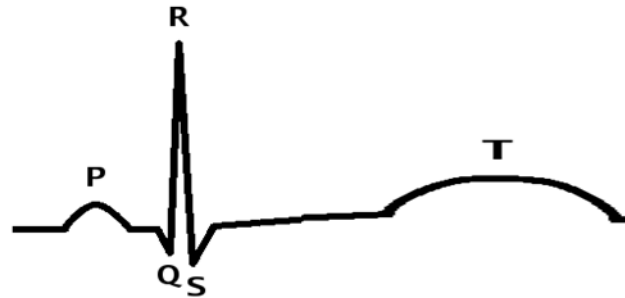
NMS

Treatment

- Dantrolene (muscle relaxant)
- Bromocriptine (dopamine agonist)
- Similar to malignant hyperthermia
 - Reaction to halothane, succinylcholine
 - Same treatment: dantrolene (muscle relaxant)

QT interval

- May block cardiac potassium channels
- Prolongs QT interval
- Strongest association with IV haloperidol



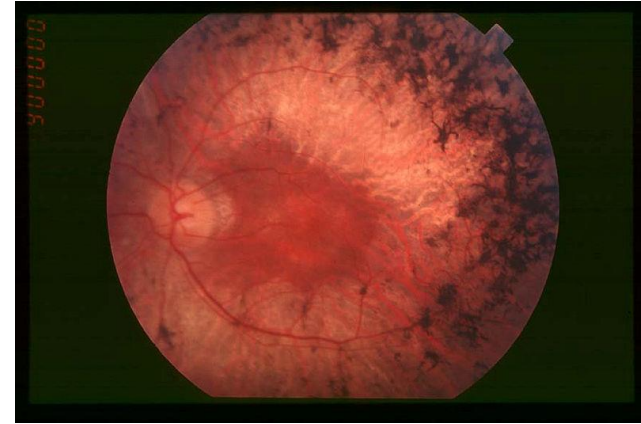
Prolonged QT



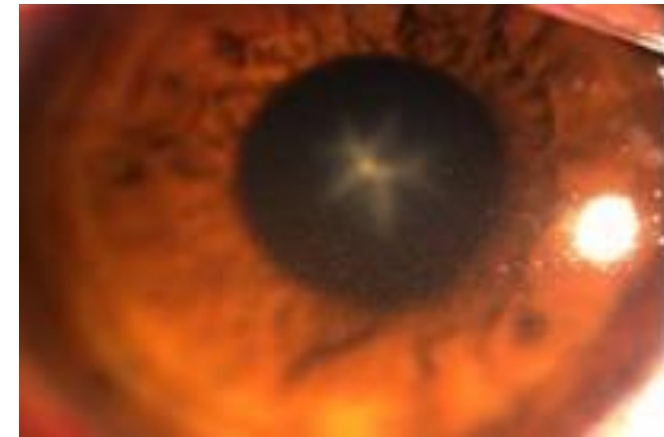
Torsade de Pointes

Thioridazine and Chlorpromazine

- **Retinal deposits**
 - Advanced cases resemble retinitis pigmentosa
 - May cause “browning” of vision
 - Uses lower doses to avoid this complication
 - More common with thioridazine (higher doses)
- **Corneal deposits**
 - May accelerate aging of lens
 - Possibly associated with cataracts



Christian Hamel



Sushil et al.. Opth Res 4(4) 108-111

Chlorpromazine

- **Skin effects**
 - Occurs in sun-exposed areas
 - Photosensitivity
 - Skin pigmentation (blue-gray)
- **Cholestatic jaundice**
 - Occurs in 1 to 2 percent of patients



International journal of dermatology 2016

[Chlorpromazine-induced severe skin pigmentation and corneal opacities in a patient with schizophrenia.](#)

Ana María Molina-Ruiz, Águeda Pulpillo, R. M. Molina-Ruiz, Teresa Sagrario, Luis Requena

Antipsychotics

First Generation or Typical

- **Common modern uses**
 - Acute agitation/confusion: haloperidol
 - Nausea/vomiting: prochlorperazine, chlorpromazine
- Adverse effects
 - Dystonic reactions
 - Qt prolongation

Antipsychotics

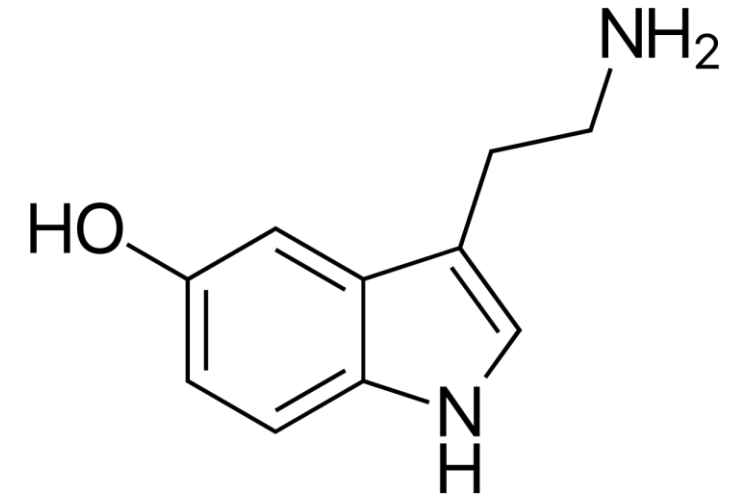
Second Generation or Atypical

- Clozapine
- Olanzapine
- Quetiapine ← Pines
Lowest EPS risk
Quetiapine is quiet
- Asenapine
- Iloperidone
- Paliperidone
- Risperidone ← Dones
Highest EPS risk
Especially high doses
Risperidone = highest risk
- Lurasidone
- Ziprasidone
- **Defining feature: Less EPS adverse effects**

Serotonin

5-hydroxytryptamine (5 HT)

- LSD (lysergic acid diethylamide)
 - 5-HT agonist
 - Produces hallucinations via **5-HT_{2A} activity**
- ↓ **5-HT_{2A}** activity seen with many atypicals
 - As or more effective 5-HT blockade versus dopamine



Serotonin

Clozapine: $\alpha 1 > 5HT > D2$
Olanzapine: $5HT > H1 > D2 > \alpha 1$

Metabolic Syndrome

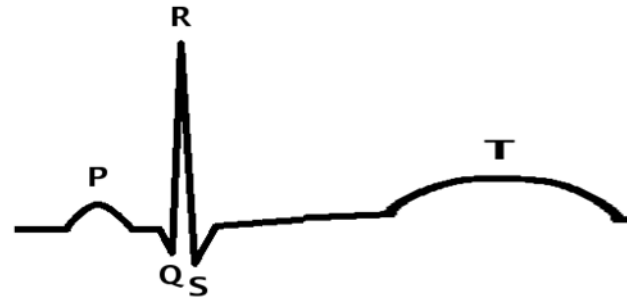
- May occur with any antipsychotic
- Common with “pines” – especially **clozapine** and **olanzapine**
- Weight gain
- Hyperglycemia
- Hyperlipidemia



Tibor Végh

QT interval

- Prolongation also can occur with atypical drugs
- More risk with “dones”
- Highest risk: **ziprasidone**



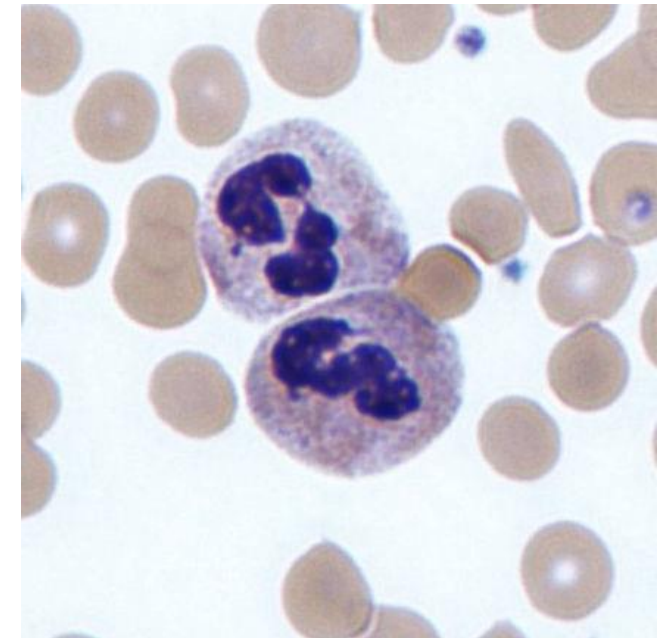
Prolonged QT



Torsade de Pointes

Clozapine

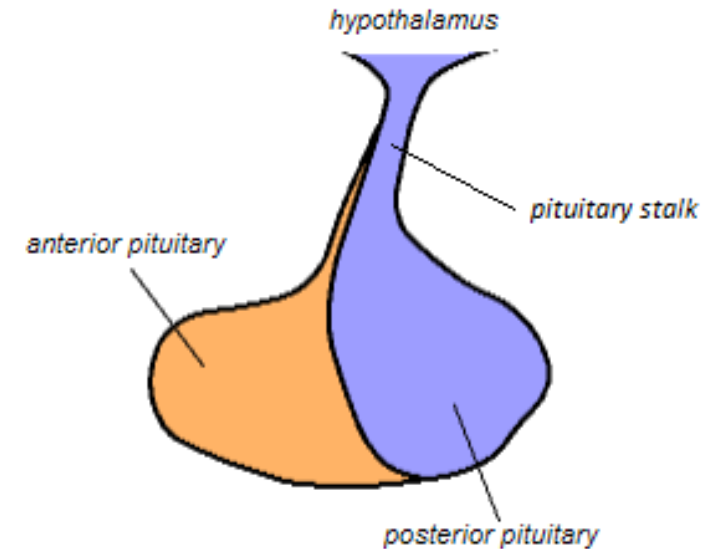
- Highly effective but not first line due to adverse effects
 - Used in refractory cases
- May cause **agranulocytosis** (1-2% of patients)
- Must monitor WBCs during therapy
 - Weekly at start
 - Every few weeks to monthly thereafter
 - Stop if neutrophil counts < 1500
- Reversible when drug stopped
- May also cause **seizures** (2-5% of patients)
 - Dose related
- Rarely associated with myocarditis



Dr Graham Beards

Hyperprolactinemia

- Antipsychotics: most common drug-induced cause
- Dopamine blockade → ↑ prolactin
 - Gynecomastia in men
 - Galactorrhea
 - Amenorrhea in women
- Highest rates:
 - Haloperidol
 - Fluphenazine
 - **Risperidone**
 - **Paliperidone**



Pituitary Gland

Aripiprazole

- **D2 partial agonist**
 - Some blockade, some agonist effects
- Hyperprolactinemia very rare
- Less weight gain, sedation
- Most common side effect: akathisia
- Associated with **loss of impulse control**
 - Pathologic gambling
 - Binge eating
 - Shopping sprees



Flickr/Public Domain

Atypical Antipsychotics

Drug	Key Adverse Effects
Olanzapine and “pines”	Metabolic syndrome
Ziprasidone and “dones”	Highest risk of QT prolongation
Risperidone and “dones”	Highest risk of EPS
Clozapine	Agranulocytosis
Quetiapine	Lowest risk of EPS (Quetiapine is quiet) Use in patients with movement disorders (Parkinson’s)
Aripiprazole	Loss of impulse control