# PATHOPHYSIOLOGY OF PSYCHIATRIC DISRODERS

| Disorder | Etiology and Epidemiology | Pathophysiology *and* Presentation | DSM-IV DIAGNOSIS *and* DIFFERENTIAL | Treatment |
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| **DEPRESSION** | | | | |
| **MAJOR DEPRESSIVE DISORDER (MDD)** | Leading cause of DALYs worldwide<br>Lifetime prevalence: 17%<br>2:1 F:M predominance<br><br>MDD is RF for CAD<br>MI is RF for MDD<br>MDD + MI is RF for mortality<br><br>Co-morbind with anxiety disorders, medical conditions, and substance abuse disorders<br><br>Heritability: 31 – 42%<br>*5-HTTPR, BDNF, COMT*<br><br>**RF** for depression:<br>Childhood maltreatment, stressors, negative cognitive style<br><br>**Natural History**<br>60% rate of recurrence after first MDE<br>Increasing risk with subsequent MDEs<br>Earlier episodes correlate with stressors | **PATHOPHYSIOLOGY**<br>Hypoactivity of PFC<br>Hyperactivation of hippocampus and amygdala<br>Dysfunctional monoamine metabolism<br>HPA axis dysregulation<br>Loss of negative feedback from cortisol<br>Increased CSF CRH<br><br>**PRESENTATION**<br>Mood: dysphoric, anhedonic<br>Symptoms: weight change, fatigue, psychomotor agitation, sleep disturbance<br>Behavior: no eye contact, stooping, lack of facial expression<br>Speech: latent, monotonous, slow, soft<br>Cognition: bradyphrenia, indecisiveness, loss of concentration<br><br>**MDD + Melancholic Features**<br>Diurnal variation<br>Very low mood<br>Anorexia and weigth loss<br>Refractory to psychotherapy<br>Tx with medications and ECT<br><br>**Atypical Depression**<br>Increased appetite and weight gain | Occurrence of > 1 Major Depressive Episode (MDE)<br><br>A: Require > 5 of following for majority of days over 2 wks. Must include (1) or (2)<br>1. Depressed mood<br>2. Anhedonia<br>3. Significant weight change<br>4. Sleep disturbance (insomnia or hypersomnia)<br>5. Psychomotor agitation<br>6. Fatigue<br>7. Feelings of worthlessness or inappropriate guilt<br>8. Loss of concentration; indecisiveness<br>9. Passive and active SI<br>B: Not Mixed Episode<br>C: Fx impaired<br>D: R/O medical and substance<br>E: R/O Bereavement<br><br>**Medical Differential**<br>Endocrine: hypothyroidism, Addison's, Cushing's<br>Neurologic: PD, AD, MS, Epilepsy<br>Nutritional: B12 and folate deficiency<br>Neoplastic: tumor in frontal lobes<br>Vascular: CVD, strokes in L frontal lobe<br>Infectious: neruo-HIV, neruosyphilis | Moderate – Severe MDD:<br>Combination of medications + psychotherapy<br><br>Severe and Psychotic MDD:<br>ECT (most effective)<br><br>**Somatic Treatment**<br>*Pharmacologic*<br>SSRIs<br>SNRIs<br>Atypical<br>Tricyclic<br><br>60 – 70% response rate<br><br>*Tx co-morbid disorders*<br>BZs: insomnia, anxiety<br>Antipsychotics<br>Thyroid hormone<br>Lithium<br>Stimulants<br><br>*Neuromodulation*<br>ECT (highest response rate, rapid onset) |

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| | 5 – 10%:evolve into bipolar disoprder<br>More likely with earlier onset of MDD | Hypersomnia<br>Leaden paralysis (profound fatigue)<br>Mood reactivity<br>Responsive to MAOIs, SSRIs, and psychotherapy<br><br>**Psychotic Depression**<br>20% of severe depression<br>Auditory hallucinations<br>Delusions (religious, somatic)<br>Requires hospitalization<br><br>**Seasonal Affective Disorder**<br>Fatigue<br>Hypersomnia<br>Increased appetive and weigth gain<br>Tx with phototherapy<br>RF: high latitude, female, young<br><br>**Post-Partum Depression**<br>MDE occurring < 1 mo. after delivery<br>May be associated with psychotic features<br>RF: prior episode, Hx of MDD<br><br>**Dysthymic Disorder**<br>Long-term (> 2 yrs) but less severe<br>May have concurrent MDD | **Substance Differential**<br>Sedatives and hypnotics<br>Antihypertensives (propranolol)<br>Steroids (prednisone)<br>ABx (IFN)<br>EtOH<br>Stimulant withdrawal: cocaine, amphetamines | Vagal-nerve stimulation (VNS)<br>Transcranial Magnetic Stimulation (rTMS)<br><br>**Psychotherapy**<br><br>*CBT*: identify and rate moods, modify negative cognition. Behavior changes<br>8 – 12 hourly sessions<br><br>*IPT*: ID interpersonal aspects (loss, conflict, life changes)<br>12- 16 hourly sessions<br><br>*Psychodynamic*: long-term therapy.<br>Tx chornic MDD, co-morbid personality disorder |
| **SUICIDAL IDEATION** | 3 – 4:1 M:F completed suicide<br>F > M prevalence of suicide attempts<br>RR = 5 for M > 85 yrs<br><br>2nd leading cause of death 15 – 24 yrs<br>Most occur in males 30 – 55 yrs | **PATHOPHYSIOLOGY**<br>Depletion of serotonin within ventral PFC<br>Polymoprhism in tryptophan hydroxylase | **ASSESSMENT OF SUICIDE RISK**<br>Prior attempt<br>Intensity of commitment<br>Stable mental status<br>Support within environment<br>Treatment alliance<br>Presenting SI: plan, current attitude, behaviors<br>Recent SI: time spent ruminating, plans, attempts<br>Past SI: number of attempts, most severe, most recent | **Prevention**:<br><br>Lithium + atypical antipsychotic (**clozapine**)<br><br>Dialectical Behavioral Therapy<br><br>Antidepressants for MDD (equivocal) |

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| | **RFs** for suicide<br>Leading RF: previous attempt<br>Male (completion), Female (attempts)<br>Ethnicity<br>Age: peak incidence at 10 – 24 yrs and >65 yrs<br>Males: Single marital status<br>Family history<br>History of Axis I disorder<br>Bipolar > MDD > multiple substance abuse<br>Medical illness<br>HIV, Huntington's, cancer, TBI, seizures, cord injury<br>Stressors<br>Loss, lack of social support, natural disaster, economic depression<br>Seasonality<br><br>Most completions: MDD | | | Restrict access to lethal means<br><br>Convene support system<br><br>Hospitalization (if risk is high) |
| **ANXIETY** | | | | |
| **GENERALIZED ANXIETY DISORDERD (GAD)** | Prevalence: 4 – 7%<br>F > M<br><br>Environmental factors predominate<br><br>Male relatives of index case: increase risk of EtOH abuse | **PATHOPHYSIOLOGY**<br>NE, GABA, 5-HT dysregulation within the frontal lobe and limbic cortex<br><br>**PRESENTATION** | A: Excessive anxiety occurring on majority of days > 6 mos. Pertains to multiple activities.<br>B: Difficult to control.<br>C: Require > 3 of the following for majority of days > 6 mos:<br>1. Restlessness<br>2. Easily fatigued<br>3. Loss of concentration<br>4. Irritability<br>5. Muscle tension | **DOC: SSRIs**<br>BZs for immediate anxiolytic effect<br>AND during intuition of therapy |

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| | **Medical co-morbidity**<br>Usually present for evaluation of symptoms<br><br>**Psychiatric co-morbidity**<br>Most frequent co-existence with another psychiatric illness<br>RF for MDD and substance abuse | | 6. Sleep disturbances<br>D: Not confined to Axis I disorder<br>E. Fx impairment<br>F: R/O medical, substance, other disorders<br><br>**Medical Differential**<br>Endocrine: hyperthyroidism, hyperparathyroidism, pheochromocytoma<br>Metabolci: hypoglycemia<br>CV: cardiac arrhythmias, mitral valve prolapsed, pulmonary embolus, MI<br><br>**Substance Differential**<br>Symptoms must occur during use or within 1 mo. of cessation<br><br>Caffeine intoxication, stimulant (amphetamine, cocaine) abuse, **EtOH withdrawal**, **sedative/hypnotic withdrawal**<br>Albuterol, steroids, thyroid hormone, antidepressants (Buproprion), decongestants (pseudoephedrine), caffeine supplements<br><br>**Psychiatric Differential**<br>Panic Disoder, Phobias, OCD, MDD, Adjustment Disorder + Anxiety, Hypochondriasis, Somatization Disorder, Personality Disorder | *CBT*: cognitive modification + simple exercises (breathing, muscle relaxation, imagery) |
| **PANIC DISORDER** | Prevalence is 2 – 3% in females<br>0.5 – 1.5% in males<br><br>First attack usually presents in the ED<br><br>30 – 40% remission<br>50% stable without major impairment<br>10 – 20% significant symptoms | **PATHOPHYSIOLOGY**<br>Some proposed mechanisms:<br>Increased CNS catecholamines<br>Lesion of LC<br>CO2 hypersensitivity<br>Error in lactate metabolism<br>Dysfunction of GABA neurotransmission<br>Imaging: abnormalities in hypothalamus, cerebral vasoconstriction | DIAGNOSIS OF PANIC ATTACK<br>Require ≥ 4 of the following. Acute onset and maximal within 10min.<br>(Palipations, tachycardia, diaphoreses, shaking, dyspnea, sensation of choking, chest pain, GI distress, dizziness, derealization/depersonalization, fear of loss of control, fear of dying, paresthesias, chills and flares) | **Medication + Therapy**<br>DOC: SSRIs<br>May use BZs for actue attacks and prophylaxis (not recommended)<br><br>CBT: patient education, distraction, breathing, exposure desensitization (may be exposed to |

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| | Hereditary factors predominate (45% concordance)<br><br>**Medical co-morbidity**<br>Peptic ulcer disease<br>Hypertension<br>Increased mortality<br><br>**Psychiatric co-morbidity**<br>91% have other disorders<br>MDD<br>EtOH abuse (self-medication)<br>Other anxiety disorders<br>Increased suicide risk | **PRESENTATION**<br>Require **recurrent** *Panic Attacks* + > 1 mo. of fallout symptoms<br>(anxiety about repeat attacks, behavioral change, anxiety about implications) | DIAGNOSIS OF PANIC DISORDER<br>A: Require both<br>Recurrent *Panic Attacks*<br>≥ 1 attack followed by > 1 mo. of:<br>Persistence concern about future attacks<br>Concern about implications<br>Significant behavioral chang<br>B: Absence or presence of agoraphobia (must be specified)<br>C: R/O medical condition and substance<br>D: R/O other disorder (e.g. Social Phobia)<br><br>**Medical Differential**<br>Equivalent to differential of GAD<br><br>**Substance Differential**<br>Equivalent to differential of GAD | feared stimulus or panic symptom) |
| **OBSESSIVE-COMPULSIVE DISORDER (OCD)** | Prevalence: 2 - %<br>Equal gender prevalence<br>Earlier onset in men<br><br>**RFS**: TBI, temporal lobe epilepsy, HD. Tourette's<br><br>Significant improvement:<br>20 – 30%<br>Moderate improvement:<br>40 – 50%<br>No improvement or worsening:<br>20 – 40%<br><br>Negative **RFs**: yielding, onset during childhood, exotic compulsions, hospitalization, mo-morbid MDD or PD | **PATHOPHYSIOLOGY**<br>Dysfunctional serotonin signaling<br>Increased metabolism in caudate and PFC<br>Increased motor programming and planning<br><br>**PRESENTATION**<br>Obsessions: recurrent and persistent thoughts. These are intrusive and result in significant anxiety.<br>Compulsions: Repetitive behaviors or mental acts in response to obsessions. These may transiently alleviate the anxiety associated with obsessions.<br><br>Require only obsessions or compulsions for Dx.<br><br>Typically ego-dystonic. | A: Require either Obsessions or Compulsions<br>OBSESSIONS<br>1. Recurrent, persistent, and intrusive thoughts resulting in anxiety<br>2. Thoughts are not excessive worries<br>3. Attempts to ignore, suppress, or neutralize thoughts<br>4. Recognition that thoughts are product of own mind<br>COMPULSIONS<br>1. Repetitive behaviors or mental acts<br>2. Behaviors are intended to reduce anxiety OR to prevent dreaded event<br>B: Insight is preserved. Recognition that obsessions are unreasonable.<br>NOT is peds!<br>C: Require > 1 hr per day, significant interference with daily function | **SSRIs**<br>Require longer duration of therapy at higher dose<br><br>If refractory: antipsychotic, psychosurgery (cingulotomy)<br><br>**Psychotherapy**<br>CBT: exposure and response prevention<br><br>Family therapy |

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| | Positive **RFs:** social and occupational adjustment, precipitating event (pregnancy), episodic course | | D: Not due to other Axis I disorder<br>E: R/O substance and medical illness<br><br>Specify level of insight. | |
| **SPECIFIC PHOBIA**<br><br>**SOCIAL PHOBIA**<br>(SOCIAL ANXIETY DISORDER) | **Specific Phobia**<br>Leading mental illness in women<br>Second leading illness in men | **Specific Phobia**<br>Fear of object or situation<br><br>**Social Phobia**<br>Fear of situation which may result in embarrassment<br><br>BOTH result in avoidance and anxiety upon exposure | | **CBT:** gradual exposure |
| **BIPOLARITY** | | | | |
| **BIPOLAR DISORDER I**<br>(MANIC DEPRESSION) | Data for BP I and II<br><br>Lifetime prevalence (U.S): 4%<br>3:2 F:M predominance for all BP<br>1:1 for BP II<br><br>Median age of onset: 25 yrs<br><br>Onset > 50 yrs is RARE (most likely medical or substance)<br><br>No ethnic variation<br><br>**Genetic Factors**<br>Heritability is 73 – 93% for all BP disorder<br><br>**Co-morbidities** | MANIA may be triggered by sleep deprivation or jetlag<br>Changes in sleep may be an early indication of impending Manic Episode<br><br>**PATHOPHYSIOLOGY**<br>Imaging: enlarged ventricles, white matter lesions (frontal lobe predominance), decreased limbic gray matter, increased anterior cingulated gyrus metabolism, decreased PFC metabolism<br>Low NAA levels<br>HPA dysfunction: elevated cortisol, loss of central negative feedback<br>Acute phase reactants: IL-6, IL-8, TNF<br><br>**PRESENTATION of MANIA**<br>(Usually presents with MDE before Mania)<br>Mood: elevated, euphoric, expansive | DIAGNOSIS OF BIPOLAR I DISORDER<br>≥ 1 Manic Episode<br>OR<br>≥ 1 Mixed Episode<br>MDE is NOT required for diagnosis<br><br>A: > 1 wk of mood elevation, expansiveness, or irritability<br>B: Require ≥ 3 of the following:<br>1. Grandiosity<br>2. Decreased sleep<br>3. Pressured speech, effusiveness<br>4. Subjective experience of racing thoughts (flight of ideas)<br>5. Distractibility<br>6. Increased goal-directed activity<br>7. Excessive indulgence in riskly pleasurable activities (spending, gambling)<br>C: R/O Mixed Episode | **Acute Mania**<br>Lithium + Antiepileptics (valproate, carbamezapine) + Atypical Antipsychotic (olanzapine, aripiprazole, quetiapine)<br><br>Adjuvant DZ<br><br>Hospitalization<br><br>**MDE**<br>Antidepressant + Lithium or other mood-stabilizer (Atypical Antipsychotic or Antiepileptic) |

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| | Substance abuse (60%)<br>Anxiety Disoders (50%)<br>MDD<br>SI | (indiscriminate interaction), irritability<br>Affect: labile (shifting within minutes to seconds)<br>Thought content: uncritical confidence, grandiosity, delusion, grandious delusions<br>Cognition: concreteness<br>Symptoms: decreased sleep<br>Though process: racing thoughts, disorganized (flight of ideas)<br>Behavior: increased goal-directed activity, impulsivity<br>Speech: loud, rapid, pressured<br>Insight: typically poor<br>Judgement: typically poor<br><br>Results in serious consequences (e.g. job loss)<br><br>**Rapid Cycling**<br>≥ 4 mood episodes per year (MDE or Manic)<br>Associated with younger age at onset<br>Higher risk of suicide | D: Fx impairment, hospitalization<br>E: R/O medical illness and substance | Psychotherapy<br>ECT: use if refractory or severe<br><br>**Maintenance**<br>DOC: Lithium + Antiepileptic (lamotrigine)<br><br>IPT + Social Rhythm: entraining routines to prevent provocation of mania<br><br>Tx co-morbid Substance-Abuse Disorder |
| **BIPOLAR DISORDER II** | | **PATHOPHYSIOLOGY**<br>Findings equivalent to BP I<br><br>**PRESENTATION of BIPOLAR II**<br>Hypomanic episodes are typically characterized by irritable mood<br>MDEs are typically more severe | DIAGNOSIS of BIPOLAR II<br>≥ 1 Hypomanic Episode<br>≥ 1 MDE<br>No Hx of Manic Episode<br>No Hx of Mixed Episode<br><br>DIAGNOSIS of HYPOMANIC EPISODES<br>A: ≥ 4 d. of mood elevation, expansiveness, or irritability<br>B: Equivalent to the DSM-IV in BP I<br>C: A significant change in Fx<br>D: Change in mood and Fx are appreciated by others | |

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| | | | E: NO IMPAIRMENT<br>F: R/O medical illness and substance | |
| **MIXED EPISODE** | | **Simultaneous** Mania *and* MDE<br><br>This is a very volatile state<br>There is a high risk of impulsive suicide | Meet DSM-IV Dx for Manic Episode + MDE (for ≥ 1 wk) | |
| **STRESS DISORDERS** | | | | |
| **POST-TRAUMATIC STRESS DISORDER (PTSD)** | Lifetime prevalence: 8%<br>Highest incidence in veterans<br><br>2:1 F:M predominance<br><br>< 20% of pts with traumatic experience develop PTSD<br><br>**RFs**<br>Severity of stressor<br>Type of stressor<br>Individual vulnerability<br>Female gender<br>Hx of prior trauma<br>Family Hx<br>Hx of MDD<br>Lack of support after trauma<br>BZ<br>EtoH<br><br>Typically develops in young adults | **PATHOPHYSIOLOGY**<br>Hyperactivity of adrenergic signaling<br>HPA axis dysfunction: low plasma cortisol, low ACTH response to CRF, enhanced dexamethasone suppression<br><br>**PRESENTATION**<br>**Trauma Exposure + Re-experiencing + Avoidance + Hyperarousal**<br><br>Re-experiencing symptoms: flashbacks, dreams, recollections<br>Avoidance: emotional detachment, isolation<br>Hyperarousal: insomnia, irritability, hypervigilance, startle response | A: Exposure to trauma<br>B: Re-experiencing<br>C: Avoidance<br>(includes amnesia, anhedonia, detachment, restricted affect, sense of foreshortened future)<br>D: Hyperarousal (require ≥ 2 items):<br>(includes insomnia, irritability, loss of concentration, hypervigilance, and exaggerated startle response)<br>E: Symptoms > 1 mo.<br>F: Fx impairment | **DOC:** SSRIs (sertraline, paroxitine)<br>Prazosin (α1-antagonist)<br>Reduces dreams<br><br>CI: BZs<br><br>CBT: gradual exposure + stress reduction techniques<br><br>Tx co-mrobid conditions<br>Substance abuse, mood disorders, anxiety disorder |
| **ACTUE STRESS DISORDER (ASD)** | **RF** for development of PTSD | **PRESENTATION**<br>Symptoms occur immediately after trauma<br>Limited ≤ 1 mo. | A: equivalent to PTSD<br>B: Require ≥ 3 of these symptoms during or immediately after event<br>(includes numbing, reduced awareness, | |

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| | | | derealization, depersonalization, dissociative amnesia)<br>C: Re-experiencing<br>D: Avoidance of stimuli<br>E: Anxiety and hyperarousal<br>F: Fx impairment<br>G: ≤ 4 wks<br>H: R/O medical illness, Brief Psychotic Disorder, exacerbation of Axis I or II Disorder | |
| **DEMENTIA and DELERIUM** | | | | |
| **DELERIUM** | Prevalence<br>25%: hospitalized with cancer<br>60%: nursing home and > 75 yrs<br>80%: with terminal illness<br><br>**RFs**<br>Age<br>CVD, Neurodegenerative Disease<br>Chronic Medical Illness<br>Surgery<br>Unfamiliar environment<br>Psychotropic medications<br>Malnutrition<br><br>**Etiologies**<br>Toxic: S/H, anticholinergics, opioids, steroids, EtOH and S/H withdrawal<br>Metabolic: Na+, Ca2+, glucose hypoxemia, hypercapnia, uremia (acute renal failure), hepatic | **PATHOPHYSIOLOGY**<br>Underlying medial illness → dysregulation of RAS → altered consciousness<br><br>**Complications:** pneumonia, decubiti<br><br>**PRESENTATION**<br>There are three MAIN FEATURES of DELERIUM<br>1. Fluctuation in symptoms<br>2. Impaired attention: distraction, perseveration, disorganized thought<br>3. Altered LOC: somnolence, agitation<br><br>Disorientation, disordered sleep cycle, hallucinations (visual), memory deficits, emotional disturbance | DSM DIAGNOSIS of DELERIUM<br>A: Altered LOC<br>B: Altered cognition OR perceptual disturbance (r/o progression of dementia)<br>C: Acute onset and fluctuating tempo<br>D: Evidence of underlying medical illness<br><br>CONFUSION ASSESSMENT METHOD (CAM)<br>1. Acute change in mental status + fluctuation<br>2. Impaired attention<br>3. Disorganized thought OR altered LOC | **Tx underlying dz**<br><br>May use antipsychotics<br><br>CI: BZ EXCEPT in delirium tremens |

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| | encephalopathy<br>Infectious: UTI in elederly, pneumonia, meningitis, encephalitis, sepsis, CNS abscess<br><br>TBI (SDH), stroke, post-ictal state<br>Cardiac arrhythmia, mycocardial ischemia<br>Pain, constipation, dehydration, malnutrition, sensory deprivation, new environment<br><br>15% mortality within 1 mo.<br>25% mortality within 6 mo. | | | |
| **DEMENTIA in ALZHEIMER'S DISEASE** | Prevalence<br>> 65 yrs : 6%<br>> 85 yrs: 20%<br>> 95 yrs: 45%<br><br>50% of dementia<br><br>Peak incidence between 75 – 85<br><br>Mean survival is 6 – 12 yrs<br><br>**RFs**<br>Age (strongest correlation)<br>ApoE4 allele<br>FHx of AD<br>Prior TBI<br>Late-life MDD<br>CV RFs: HTN, dyslipidemia, atrial fibrillation, smoking<br>EtOH (no intake or excess) | **PATHOPHYSIOLOGY of AD**<br>Mutations in APP result in aberrant proteolysis by secretin → generation of β-amyloid<br>Formation of neuritic plaques<br>Perivascular deposition of amyloid<br>Neurofibrillary tangles (tau protein and microtubules)<br>Degeneration of hippocampus and MTL<br><br>**PRESENTATION of AD**<br>Prior to dementia: mild cognitive impairment (MCI)<br>Converts to dementia at 12% per year<br>Affects STM → progressive loss of LTM<br>Other cognitive deficits: language, visuospatial, executive function<br><br>Progressive loss of IADL and ADL<br><br>MDD, anxiety, irritable mood, apathy, insomnia, paranoid delusions, hallucinations (visual), aggression | A: Require BOTH memory deficits and ≥ 1 cognitive deficits<br>1. Aphasia<br>2. Apraxia<br>3. Agnosia<br>4. Disturbance of execute function<br>B: All deficits cause signficiant Fx impairment.<br>C: Gradual onset with insidious and progressive decline.<br>D: R/O other CNS pathology, systemic illness, and substance<br>E. R/0 delirium<br>F: R/0 other Axis I disorder<br><br>**Neurologic Differential of Dementia**<br>Huntington's Disease<br>CJD, Neurosyphilis, Neuro-HIV | **Pharmacologic**<br>Donepezil<br>Galantamine<br>Rivastigmine<br>Memantine<br><br>Tx AD, vascular dementia, and DLB<br><br>Not effective for FTD<br><br>Omega-3 FAs<br><br>**Behavioral Therapy**<br>Distraction, counseling family members |

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| | | **Mixed Dementia**<br>(Second leading form of dementia)<br>AD + vascular dementia<br>AD + DLB | Wernicke-Korsakoff Syndrome<br>TBI<br>CNS neoplasm<br><br>**Reversible Dementia**<br>MDD (pseudodementia)<br>Hypothyroidism<br>B12 deficiency<br>Normal Pressure Hydrocephalus (NPH)<br>Subdural Hemorrhage (SDH) | **SSRIs** + **Atypical Antipsychotics**<br>Used with dangerous Behavior or if not responsive to behavioral therapy |
| **VASCULAR DEMENTIA** | **Dementia secondary to cerebrovascular disease**<br><br>Peak incidence between 65 – 75 yrs (due to mortality from CAD)<br><br>**RFs**<br>(These are equivalent to resik factors for CAD)<br>Dyslipidemia<br>Hypertension<br>(Obesity) | **PATHOPHYSIOLOGY**<br>Cognitive deficits associated with stroke and cortical involvement<br>Temporal: language deficits<br>Frontal: apathy, disinhibition, personality change<br>Focal deficits on neurologic exam<br><br>**PRESENTATION**<br>Stepwise clinical course: sudden changes in cognition due to recurrent infarction<br><br>May be concurrent with AD | | |
| **LEWY BODY DEMENTIA** | | **Parkinson's Disease Dementia (PDD)**<br>Predominance of Parkinsonism<br>Onset of dementia > 1 yr after motor involvement<br>Diffuse subcortical distribution of Lewy Bodies<br><br>**Dementia with Lewy Bodies (DLB)**<br>The main findings:<br>1. Fluctuating symptoms<br>2. Visual hallucinations<br>3. Cognitice deficits<br>4. Less severe Parkinsonian symptoms<br>Cortical distribution of Lewy Bodies | | |

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| **FRONTOTEMPORAL DEMENTIA** | **Actually refers to a collection of syndromes**<br><br>Peak incidence between 50 – 65<br><br>May have FH of early-onset dementia | **PATHOPHYSIOLOGY**<br>Tau inclusion bodies (neurofibrillary tangles)<br>Lobar degeneration of frontal and temporal lobes<br><br>**PRESENTATION**<br>Behavioral disturbance (disinhibition, apathy)<br>Aphasia (with temporal lobe involvement)<br><br>Rapid decline with average survival of 5 yrs after Dx | Must distinguish from MDD and Mania<br>FTD is not responsive to standard therapies | Dementia Medications have **no efficacy** in FTD |
| **SCHIZOPHRENIA and PSYCHOSIS** | | | | |
| **SCHIZOPHRENIA** | Mean onset (males): 21 yrs<br>Majority of onset: 15 – 25 yrs<br>Mean onset (females): 27 yrs<br>Majority of onset: 25 – 35 yrs<br><br>20 – 40% suicide attempt rate<br>**RF:** male gender, MDD, substance abuse, isolation, unemployment<br>75 – 90% smoke tobacco<br>30 – 35% substance abuse<br>80% with medical co-morbidities<br><br>**Genetics**<br>SNPs in neuregulin-1, dysbindin, COMT, BDNF<br><br>**RFs:**<br>Development: intrauterine injury, maternal influenza, maternal starvation, fetal injury in second trimester<br>Psychosocial: low SES, family with highly expressed emotion | **PATHOPHYSIOLOGY**<br>Reduced total tissue volume<br>Selective reduction in temporal lobe (superior temporal gyrus) and thalamus<br>Enlarged ventricles<br>Decreased frontal lobe metabolism<br><br>Increased DA activity in MCL pathway<br>Increased 5-HT activity<br>Increased glutamate signaling<br><br>**Cognitive Dysmetria**<br>Hypofrontality → disinhibiton of VTA cells → increased DA flux through MCL → further suppression of PFC<br><br>**Neurodevelopmental**<br>Heterotopy of hippocampal and PFC neurons (cytoarchitectural disturbance)<br><br>**PRESENTATION**<br>**Positive Symptoms**<br>*Hallucinations*<br>Mainly auditory<br>Command, First-Rank | **First-Rank Symptoms**<br>Audible thoughts<br>Conversing voices<br>Somatic passivity experience<br>Though withdrawal<br>Thought broadcasting<br>Delusions<br>Bleuler's Cognitive and **Negative Symptoms**<br>Associational disturbance<br>Affective disturbance<br>Autism (difficulty communicating)<br>Ambivalence<br><br>A: Require ≥ 2 of the following for majority of 1 mo.<br>1. Delusions<br>2. Hallucinations<br>3. Disorganized speech<br>4. Disorganized or catatonic behavior<br>5. Negative symptoms: affective blunting, alogia, avolition<br>(Require only one item if first rank | PRODROME: may be usueful to Tx with antipsychotics<br><br>ACUTE: atypical antipsychotics<br>Metabolic ARs<br>If refractory to Tx: use clozapine and track CBCs<br><br>RESIDUAL:<br>**Psychosocial Rehabilitation** |

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| | **NATURAL HISTORY**<br>PRODROME: social withdrawal, anhedonia, deterioration in hygiene, angry outbursts<br>May be confused with Mood Disorder or Substance Abuse Disorder<br><br>ACTIVE PHASE: psychosis developing over weeks – mos.<br><br>RESIDUAL PHASE: Highly variable<br>**RF for poor prognosis**: lower pre-morbid Fx, male, earlier onset, negative symptoms, cognitive symptoms, structural abnormality, long prodrome, absence of Mood episodes, obsessions and compulsions, neurologic soft signs, industrialized nations | Visual<br>Tactile, olfactory are RARE<br>Suspect medical illness or substance<br>*Delusions*<br>Persecutory<br>Ideas of reference<br>First-Rank: broadcasting, withdrawal, passivity<br><br>Exotic if not plausible<br><br>**Negative Symptoms**<br>Result in most morbidity of Schizophrenia<br>*Affective Blunting*<br>Restriction of affect<br>*Alogia*<br>Diminished thought (reduced speech, lack of content)<br>*Avolition*<br>Unable to initiate and complete goal-directed activities<br>**Cognitive Symptoms**<br>Diordered thought<br>Loosened associations<br>Illogical processes<br>Incomprehensible speech<br>Poor hygiene, inappropriate dressing, impaired ADLs<br>Inattention<br>Ambivalence<br><br>**Anosognosi**a<br>Loss of insight; common in acute psychosis<br>**Anhedonia**<br><br>**Neurologic Soft Signs**<br>Distinguish from EPS due to therapy<br>L and R discrimination | hallucinations or exotic delusions)<br>B: Fx impairement<br>C: Prodrome, Active, or Residual symptoms for > 6 mos. (May have negative or attenuated symptoms)<br>D: R/O Schizoaffective disorder and Mood disorder with psychosis<br>E: R/O substance and medical illness<br>F: Require > 1 mo. of hallucinations and delusions if concurrent Autism or other disorder<br><br>**Medical Differential**<br>Neurologic: temporal lobe epilepsy, neurodegenerative (HD, Wilson's)<br>Infection: neurosyphilis<br>Nutritional: B1 deficiency<br>Autoimmune: SLE<br>Toxic: Heavy Metals<br>Development: 22q11 deletion (VCF)<br><br>**Substance Differential**<br>Stimulants, Hallucinogens, L-DOPA and DA receptor agonists, anticholinergics<br>EtOH, BZ withdrawal | **Community Treatment**<br><br>**Family Psychoeducation**<br><br>**CBT** |

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| | | Gait ataxia<br>Incoordination<br><br>**SUBTYPES**<br>**Paranoid:** typically persecutory delusions, related auditory hallucinations, fewer negative symptoms, later onset<br>Associated with better prgnosis<br>**Disorganized**: Prominent negative symptoms, affect is blunted or not congruent to mood<br>Associated with poor prognosis<br>**Catatonic**<br>Motoric immobility<br>Waxy Flexibility<br>Akathesia<br>Mutism<br>Posturing, stereotyped movements | | |
| **SCHIZOAFFECTIVE DISORDER** | Schizophrenia + Mood Disorder<br><br>Prognosis is more favorable than isolated schizophrenia BUT worse than isolated mood disorder | Must be distinguished from Mood Disorders with Psychotic Features | A: Require item A of DSM-IV on Schizophrenia + MDE, Manic Episode, OR Mixed Episode<br>B: require delusions or hallucinations ≥ 2 wks WITHOUT Mood disturbance<br>C: Require Mood symptoms > 2 wks during active and residual phases<br>D: R/O medical illness and substance | |
| **DELUSIONAL DISORDER** | F > M prevalence<br>Onset during mid and late life | **PRESENTATION**<br>Non-exotic delusions<br>Hallucinations are not prominent<br>Absence of negative and cognitive symptoms | A: non-exotic delusions > 1 mo.<br>B: Exclude item A from DSM-IV on Schizophrenia<br>C: No significant Fx impairment<br>D: Relatively minor concurrence of Mood episodes | |

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| | | | E: R/O medical illness and substance | |
| **BREIF PSYCHOTIC DISORDER** | | **PRESENTATION**<br>< 1 mo. duration<br>Delusions, hallucinations, disorganized thought and behavior | | |
| **SCHIZOPHENIFORM DISORDER** | | **PRESENTATION**<br>1 mo. – 6 mos. duration<br>Items A, D, E from DSM-IV on Schizophrenia | At > 6 mo: convert to Dx schizophrenia | |
| **PEDIATRIC NEUROPSYCHIATRIC DISRODERS** | | | | |
| **ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)** | Symptoms present < 3 yrs<br>Dx when symptoms manifest in school (typically > 5 yrs)<br><br>**RFs:** genetic, prenatal tobacco exposure<br><br>**Natural History**<br>Hyperactivity symptoms remit before distraction symptoms<br><br>**RFs** for non-remission:<br>FHx of ADHD, negative events, comorbid disorders (CD, MDD, anxiety)<br><br>Rare remission < 12 yrs<br><br>Typically, remission occurs between 12 – 20 yrs<br><br>Progression to adult ADHD: 15 – 20%<br><br>ADHD is **RF for**: anxiety disorder, tic disorder, MDD, enuresis, | **PATHOPHYSIOLOGY**<br>Some subtle structural differences:<br>Reduced total brain volume, reduced gray matter<br>Thinning of frontal, temporal, parietal, and visual association cortices<br>Undeveloped PFC<br>Increased white matter volume<br><br>**PRESENTATION**<br>Excessive hyperactivity, impulsivity, or attention relative to expected developmental level<br>Psychomotor agitation<br>Emotional lability<br>Short attention duration<br>Failure in work completion<br>Poor organization<br>Aggression or defiance<br>Easily distracted | A: Require ≥ 6 INATTENTION items or HYPERACTIVE items<br>Must be maladaptive and incongruent to developmental level<br>Inattention: difficulty listening, poor organization, distracted, etc.<br>Hyperactive : excessive motor activity, effusiveness, blurting, interruption, etc<br><br>B: Require presence of symptoms < 7 yrs<br>C: Require symptoms in ≥ 2 environments<br><br>D: Fx impairment<br><br>E: R/O Pervasive Developmental Disorder, Schizophrenia, other Psychotic Disorder<br><br>**Psychiatric Differential**<br>Normal variation in development<br>Anxiety Disorders<br>Primary MDD<br>Manic Episode<br>Learning Disorders<br>CD | **Stimulants**<br>Methylphenidate<br>Dextroamphetamine<br><br>Screen: congenital heart disease, cardiac RFs<br><br>**Non-stimulants**<br>Atomoxetine<br><br>Buproprion, SNRIs, clonidine, tricyclics<br><br>**Psychosocial Interventions**<br>Structured environnment, family intervention |

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| | other behavioral disorder, substance abuse (if co-morbid CD) | | OPD<br><br>**Medical Differential**<br>Sleep disorder<br>Hyperthyroidism<br>Lead Toxicity<br>Malnutrition | |
| **PERSONALITY DISORDERS (Axis II)** | | | | |
| **Medical Differential**<br>Neoplastic: tumor in frontal lobe<br>Mechanical: TBI<br>Infectious: neuro-HIV, neurosyphilis, herpes encephalitis<br>Endocrine: hyperthyroidism<br>Autoimmune: CNS lupus<br>Neurologic: TLE, degenerative diseases (AD, HD)<br><br>**Treatment**<br>DIELECTICAL BEHAVIORAL THERAPY: validation, mindfulness, emotional regulation, distress tolerance, interpersonal effectiveness<br><br>BPD: antipsychotics, anticonvulsants, antidepressants<br>CI: BZs due to disinhibition and tendancy for abuse<br><br>ASPD: Lithium, anticonvulsancts, antipsychotics | | | | |
| **PARANOID PD** | **GROUP A**<br>Odd and Eccentric<br><br>**Genetics**<br>Associated with FHx of schizophrenia | Pervasive distrust of others<br>Similar to Delusional Disorder with paranoia<br><br>Typically not detected due to avoidance of health care | | Prevalence: 0.5 – 2.5% |
| **SCHIZOID PD** | | Pervasive social detachment<br>Voluntary social isolation<br>Limited affect | | |
| **SCHIZOTYPAL PD** | | Ideas of reference<br>Odd beliefs<br>Unusual perceptions: illusions, hallucinations | | Prevalence: 3% |

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| | | Odd though, speech, and behavior<br>Paranoia<br>Restricted affect<br>Social anxiety<br><br>Thus: similar to schizophrenia without meeting DSM-IV requirements | | |
| **ANTISOCIAL PD** | **GROUP B**<br>Dramatic and Emotional<br><br>**Genetics**<br>Strong heritability of Antisocial PD and Borderline PD<br><br>**BPD**: most have childhood Hx of abuse | Disregard to rights of others<br>Lack of empathy<br>Malicious childhood behaviors<br>Typcially Dx with CD<br><br>**Co-morbidity**: substance abuse, mood disorders, anxiety disorders, ADHD, pathological gambling<br><br>High rates of criminal activity<br>Increased rates of suicide and accidents | A: Pervasive violation of rights of others. Onset before 15 yrs. Require ≥ 3 of:<br>1. Noncomformity to social norms<br>2. Deceit<br>3. Impulsivity<br>4. Irritability and aggression<br>5. Recklessness<br>6. Irresponsibility<br>7. Lack of remorse<br>B: Age ≥ 18 yrs<br>C: Onset of CD ≤ 15 yrs<br>D: R/P schizophrenia and Manic Episode | Prevalence: 3% in males and 1% in females<br><br>Chronic course: 12% remission over 30 yrs |
| **BORDERLINE PD** | | A severe mood and behavior disturbance<br><br>Unstable interpersonal relationships<br>Distorted self-perception<br>Impulsive behavior (including self-harm)<br><br>Co-morbidity: mood disorders, PTSD, anxiety disorders, eating disorders, substnaceabuse<br><br>10% suicide completion rate<br><br>Symptoms are chronic<br>However, the diagnosis may not be maintained > 10 yrs | Pervasive instability in interpersonal relationships, self-perception, and affect. Impulsivity. Require ≥ 5 of:<br>1. Efforts to avoid abandonment (may be fictitious)<br>2. Unstable relationships with alternating idealizaiotn and devaluation<br>3. Identity disturbance<br>4. Impulsivity (in ≥ 2 persistent behaviors)<br>5. Recurrent SI or self-mutilation<br>6. Unstable affect<br>7. Empty mood<br>8. Poorly controlled anger<br>9. Transient paranoid delusion or dissociation | Prevalence: 2% with 3:1 predominance of F:M |

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| **HISTRIONIC PD** | | Excessive emotional display<br>Excessive desire for attention<br><br>Theatricality (behavior and dress)<br>Labile emotions | | Prevalence: 2% |
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| **AVOIDANT PD** | **GROUP C**<br>Anxious and Fearful | Social inhibiton<br>Subjective sense of inadequacy<br>Hypersensitivity to criticism<br><br>Isolation due to fear of social embarrassment | | |
| **DEPENDANT PD** | | Submissive and clinging behavior<br>Fear of separation | | |
| **OBSESSIVE-COMOULSIVE PD** | | Ego-syntonic perfectionist traits<br>May actually be adaptive in some professions<br>Insight is not preserved | | |
| **DISORDERS of EATING** | | | | |
| **ANOREXIA NERVOSA** | Psychiatric disorder with highest mortality (10%)<br>Starvation, electrolyte disturbance, suicide<br>Prevalence (females): 1%<br>10:1 predominance F:M<br><br>**RF:** industrialized nation, occupation (ballet, modeling, wrestling), female gender<br><br>Typical onset: 14 – 18 yrs<br><br>**Co-morbidities:**<br>MDD (65%)<br>Social Phobia, OCD<br><br>**RF** for poor outcome:<br>Long duration of AN, older age | **PATHOPHJYSIOLOGY**<br>Decreased NE transmission, increased 5-HT<br>HPA activation<br>Suppressed thryroid function<br>Elevated endogenous opioids<br>Societal modeling: typically results in dieting<br><br>**PRESENTATION**<br>Suspect AN in postmenarcheal females with acute onset amenorrhea<br>Associated with perfectionism traits<br>Weight maintained at < 75% of IBW<br>Fear of weight gain<br>Disturbed perception of body weight and habitus<br>Extreme dieting, elaborate exercise routines, binge and purge behavior<br><br>**Restricting Type:** no binging and purging.<br>**Binge and Purge Type:** vomiting, laxatives, diuretics, | A: Refuse to maintain weight within normal limits. Weight ≤ 85% of IBW due to weight loss, or lack of gain.<br><br>B: Intense fear of weight gain despite underweight.<br><br>C: Disturbed perception of weight and habitus. (Poor insight)<br><br>D: Amenorrhea in postmenacheal females. | Hospitalization may be required:<br>Re-feeding, stabilize metabolic state<br><br>**CBT**: monitor intake, binging and purging, ID emotions<br><br>**Maudsley Method**: familial intervention. Parents monitor and enforce intake.<br>Not effective with older patients (thus, |

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| | at onset, Hx of psychiatric hospitalizations, poor premorbid adjustment, co-morbid personality disorder<br><br>Typically severely underweight | enemas<br><br>**Some Complications:** dehydration, hypothermia, bradycardia, hyptotension, electrolyte disturbance, arrhythmias, hypogonadism (males; due to depletion of testosterone), impaired cognition, depressed mood | | focus on early intervention)<br><br>**Fluoxetine**<br>Approved for BN<br>Not approved for AN, but may be effective |
| **BULEMIA NERVOSA** | Typically less severe clinical course than AN<br><br>Typically NML weight | **PRESENTATION**<br>Recurrent binge eating followed by COMPENSATORY behavior (purging or restriction)<br>Subjective disgust and guilt after binging episodes<br><br>**Purging Type:** vomiting, laxatives, diuretics, enemas<br>**Non-purging Type:** fasting, excessive exercise, NO purging behaviors<br><br>**Some complications:** hypocalcemia, hypokalemia, metabolic alkalosis, ECG abnormalities, fatty degeneration of liver, malnutrition, enlargement of parotid gland, dental caries, esophageal lesions. | A: Require recurrent episodes of binge eating<br>1. Eating excessive amounts within 2 hrs<br>2. Subjective sense of lack of control<br>B: Recurrent compensatory behavior<br>Vomiting, laxatives, diuretics, enemas<br>Fasting, exercise<br>C: Binging and purging occurs over ≥ 3 mos. and ~ 2/wk<br>D: Weight and habitus are misperceived and an inappropriate influence on self-perception<br>E: Not occurring during AN episodes | CI: tricyclics, buproprion<br><br>Antipsychotics: if delusions are severe<br>However, may exacerbate cardiac arrhythmias<br><br>Other drugs used in BN Tx:<br>Naltrexone: opioid antagonist<br><br>Ondasteron: 5-HT3 antagonist |
| **SUBSTANCE ABUSE DISORDERS** | | | | |
| **SUBSTANCE INTOXICATION** | Symptoms are determined by the primary neurologic effect of the substance | **Alcohol**: sedation, severe incoordination, dysarthria, apnea, poor judgment<br>50 mg/dL: slight impairment in cognition, coordination<br>80 mg/dL: impaired driving<br>200 – 300 mg/dL: severe impairment<br>400 – 600 mg/dL: coma, death<br><br>**Opioids**: euphoria progressing to somnolence, respiratory depression, apnea, miosis<br><br>**Stimulants**: anxiety, psychosis, seizures, MI, cerebral ischemia | Airway protection<br>Assess for trauma<br>Assess mental status (triage)<br>Full plasma and urine toxicology screen<br><br>**Alcohol:** metabolized at 1 standard drink/hr → 20 – 30 mg/dL cleared per hr if BAL > 100 mg/dL<br>No pharmacologic therapy for intoxication<br><br>**Opioids**: naloxone | |

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| | | **Hallucinogens**: psychosis with impulsive behavior | | |
| **SUBSTANCE DEPENDENCE** | Symptoms determined by opponent process<br><br>Most relapse occurs within 1 yr of cessation | **Alcohol** and **BZs:** increased Glutamate transmission (not counteracted by GABA)<br>Anxiety, agitation, psychosis, seizures, insomnia, psychomotor agitation, headache, tachycardia, HTN, diaphoresis<br>This is a volatile condition<br>**Some guidelines for screening**<br>Excessive drinking:<br>M < 65 yrs: : ≥ 14 per wk or > 4 during each occasion<br>F < 65 yrs: ≥ 7 per wk or > 3 during each occasion<br>These standards are modified with age<br><br>**Opioids**<br>NVD, craving, rinorrhea, lacrimation, myalgia, mydriasis<br>Dehydration<br><br>**Stimulants**: increased GABA transmission<br>Sedation, avolition, abulia, overeating, depression<br>This is a relatively benign but aversive condition<br><br>Excitation is more dangerous than sedation | **Alcohol:** require 72 – 96 hrs for resolution<br>DT may continue for > 10 d.<br><br>**Heroin:** withdrawal is complete within 7 d.<br><br>**Methadone:** requires several wks.<br><br>**Stimulants:** cocaine withdrawal resolves more rapidly than methamphetamine<br><br>DSM-IV DIAGNOSIS<br>Maladaptive pattern of substance use.<br>Require ≥ 3 over 12 mos.<br>1. Tolerance: increased dose for same effect, decreased effect with constant dose<br>2. Withdrawal: characteristic withdrawal syndrome, substance use to avoid withdrawal symptoms<br>3. Use in larger amounts or longer periods than intended<br>4. Persistent desire or unsuccessful efforts to reduce substance use | **TREATMENTOF WITHDRAWAL**<br><br>**Alcohol:** BZ taper, thiaminem Mg2+<br>Reassess with CIWA<br>Anticonvuslants<br><br>**Bz:** long-acting BZ taper, anticonvuslants<br><br>**Opioids**: buprenoprhine, methadone, clonidine<br><br>**Stimulants**: supportive<br><br>**PSYCHOSOCIAL TREATMENT**<br><br>Motivational Enhancement Therapy: similar to TIBS<br><br>12-step program (AA)<br><br>**Relapse Prevention** and **CBT**:<br>Avoidance of stimuli, environmental changes, management of negative affective states (e.g. anhedonia and stress following EtOH abstinence) |

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| | | | 5. Devotion of excessive time or energy towards obtaining and using substance<br>6. Reduction in important activities due to substance euse<br>7. Use despite recognition of physical or psychological injury | **ALL**: selection of positive replacements<br><br>**TREATMENT OF ABUSE and DEPENDENCE**<br><br>**Naltrexone**; blocks the reward stimulus (endogenous opioids) associated with EtOH use<br><br>**Acomprosate**: decreases glutamate transmission to reduce opponent process. Prevent relapse due to negative affect.<br><br>**Disulfram**: Inhibits aldehyde DH → increased aldehyde with EtOH ingestion → aversive state |
| **SUBSTANCE ABUSE (ADDICTION)** | | The diagnosis is based on adverse consequences of substance use<br><br>If patient has had prior episode of Substance Dependence, we cannot make the diagnosis of abuse | DSM-IV DIAGNOSIS<br>A: Require ≥ 1 occurring over 12 mos.<br>1. Recurrent failure to meet obligations (occupational, school, etc)<br>2. Recurrent use in hazardous situations<br>3. Recurrent legal consequences<br>4. Continued use despite recurrent social and interpersonal harm<br>B: R/O Substance Dependence | |