Update on Depression and Anxiety

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Learning Objectives

- To have a clear picture of how to diagnose Major Depressive Disorder in medically ill patients
- To review first- and second-line treatments for Major Depression
- To distinguish pathological anxiety from normal worry
- To review short- and long-term treatments for common anxiety disorders.

Outline

- Major Depression
  - Why treat?
  - Epidemiology
  - How diagnose
- Anxiety Disorders
  - The nature of Anxiety Disorders
  - Diagnosis
- Treatment of Depressive and Anxiety Disorders

A model for mental distress in the medically ill:

Figure 1: Propensity for mental illness

$$\frac{\text{Stress}}{\text{Resilience}} = \text{Propensity for illness}$$

Depressive Disorders

DSM 5 Nosology

- Major depressive disorder (MDD)
- Persistent depressive disorder
  - Includes “chronic depression” and “dysthymia”
- Premenstrual dysphoric disorder
- Disruptive mood dysregulation disorder

Major Depression is Prevalent and Morbid

Annual incidence is 9.5% of adult US population

Prevalence rates in primary care ≥ 10%

Lifetime prevalence of 12% in men & 20% in women

Leading cause of workplace absenteeism, diminished productivity, and increased use of health care resources

Major Depression is Prevalent and Morbid

- The leading cause of disability worldwide
- Associated with decreased quality of life and suicide
- Associated with increased mortality across all age groups

Depression under-diagnosed and under-treated in Primary Care

Only ~50% of depressed patients are recognized by Primary Care Providers

When PCPs alerted to the diagnosis, often does not change treatment

PCPs frequently under-dose antidepressant medications

Many patients discontinue medications within the first 3 months

Depression under-diagnosed and under-treated in Primary Care

Recognition and treatment of depression in primary care hampered by clinician and patient factors.

We have a say about the clinician factors…

Therefore...

Clinicians need to distinguish between appropriate distress and Major Depression

Should know the basic treatments for mild-to-moderate depressive disorders

…And be comfortable in initiating and maintaining treatment

Mrs. S

- A 57yo married woman with metastatic liver cancer.
- History of COPD and spinal stenosis (wheelchair bound).
- History of major depressive disorder and alcohol dependence (in remission for 10 years).
- Presents with depressed mood and worsened amotivation 6 weeks after learning that her cancer is progressing despite treatment.
- Current psychiatric medications include:
  - Bupropion XL 150mg Daily & Clonazepam 0.5mg Twice Daily
- What would be the LEAST appropriate next step?

Case of Mrs. S: Next Steps

A. Offer support
B. Refer to psychotherapy
C. Increase the bupropion dose
D. Stop the clonazepam
E. Start an SSRI (e.g. sertraline)

Depression: A word and a syndrome

A term used to describe clinical signs and symptoms ranging from:

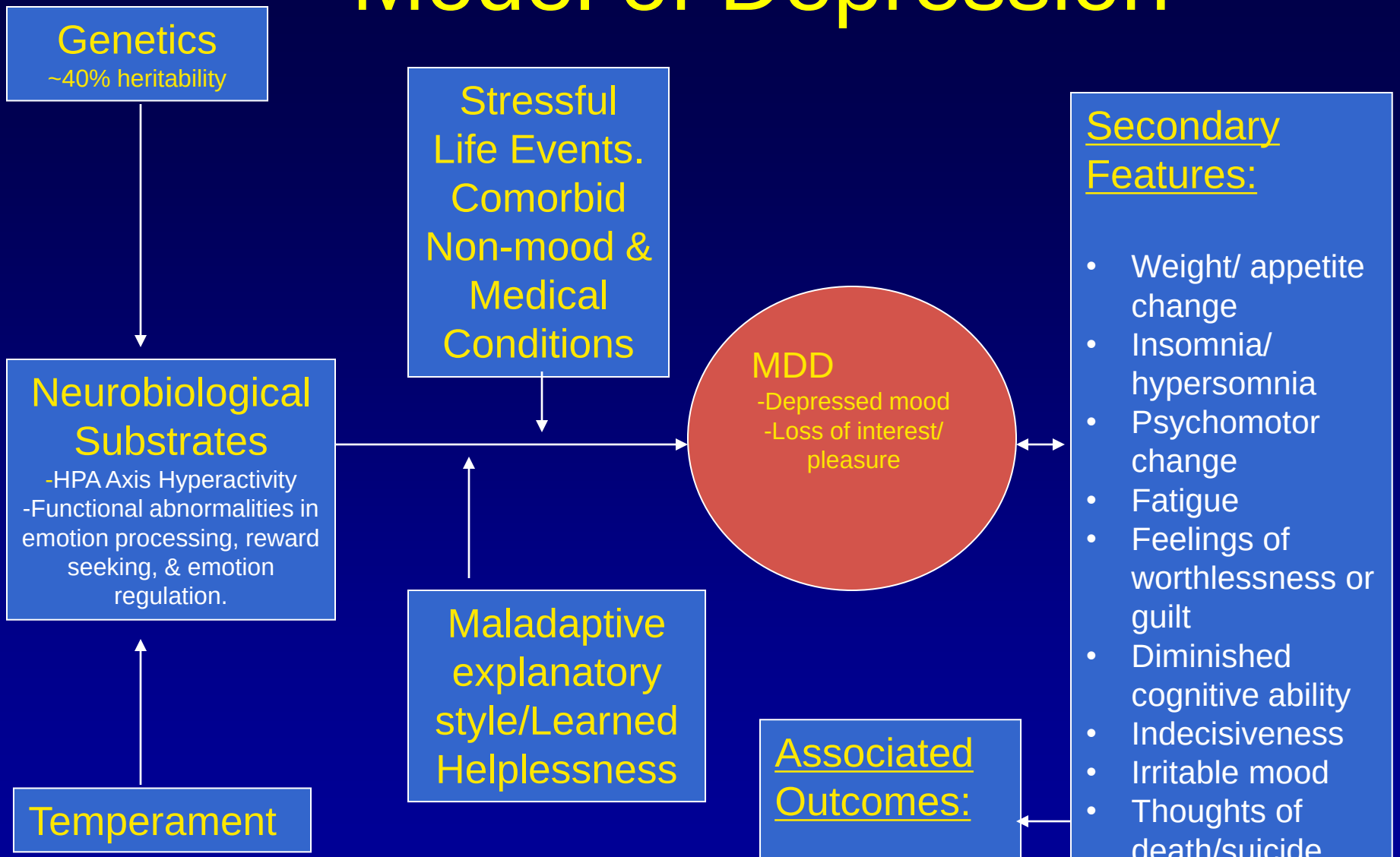
1. Transient feelings of discouragement, disappointment, sadness, grief, existential despair, or despondency (Depression) to…
2. A discrete episode of low mood and neurovegetative symptoms (Major Depressive Episode) to…
3. A relapsing, remitting syndrome (Major Depressive Disorder)

DSM 5 Criteria for Major Depression(s):

Dx requires 4 or more of symptoms below **along with:**
depressed mood or anhedonia for > 2 weeks

- Sleep disturbance (increased or decreased)
- Interests (diminished)
- Guilt (or preoccupation of thought)
- Energy (decreased)
- Concentration (decreased)
- Appetite disturbance (increased or decreased)
- Psychomotor (agitation or retardation)
- Suicidal thoughts (or thoughts of death)

Model of Depression



Slide adapted from Rosanna Scott, LICSW

Some Risk Factors For Depression

Personal or family history of substance abuse, depression, or bipolar Illness

Being female: depression is twice as likely to occur in women

Having any significant chronic illness

Some specific illnesses (e.g. pancreatic cancer, Parkinson's Disease, HIV, etc.)

Having specific personality styles (e.g., attention-seeking, controlling, perfectionistic)

Depression in the Medically Ill

Physical symptoms of medical illness **overlap** with neurovegetative symptoms of depression

Psychological stressors include:

- Loss of self-esteem
- Loss of a sense of control

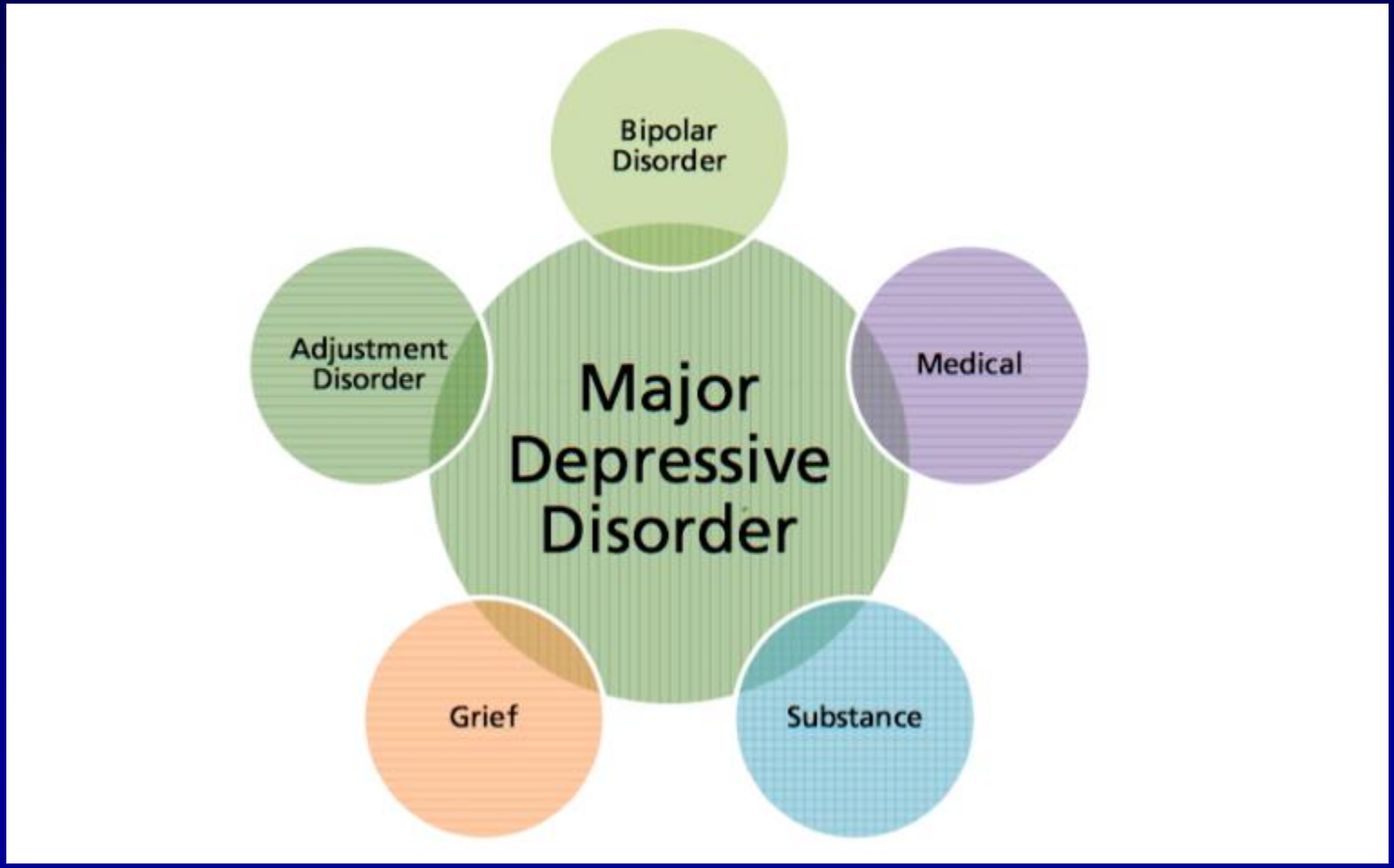
Physical stressors include:

- The illness (e.g. HIV)
- Its sequelae (e.g. paraneoplastic syndromes), or
- Its treatment (e.g. corticosteroids).

The "ABCs of Depression" in the Medically Ill: Affect, Behavior, and Cognition

- *Affective symptoms*
  - Depressed mood
  - ***Lack of pleasure (Anhedonia)***
  - Crying
  - Irritability
  - Hopelessness
  - Worthlessness
  - Guilt
- *Behavioral symptoms*
  - Apathy
  - ***Noncompliance***
  - Social withdrawal
  - Psychomotor retardation
- *Cognitive symptoms*
  - Decreased concentration
  - ***Suicidal ideation***
  - Pseudodementia
  - Intractable pain
  - Excessive somatic preoccupation

Major Depressive Disorder Differential Diagnosis



Slide adapted from Wayne Bentham, MD

MDD: Differential Diagnosis

- Bipolar Depression
  - ALWAYS screen for history of mania/hypomania before diagnosing MDD
- Substance use disorders
  - Both active use and withdrawal can mimic MDD
- Grief
- Adjustment Disorder
  - Maladaptive response to stress
  - Missing neurovegetative symptoms

MDD: Differential Diagnosis

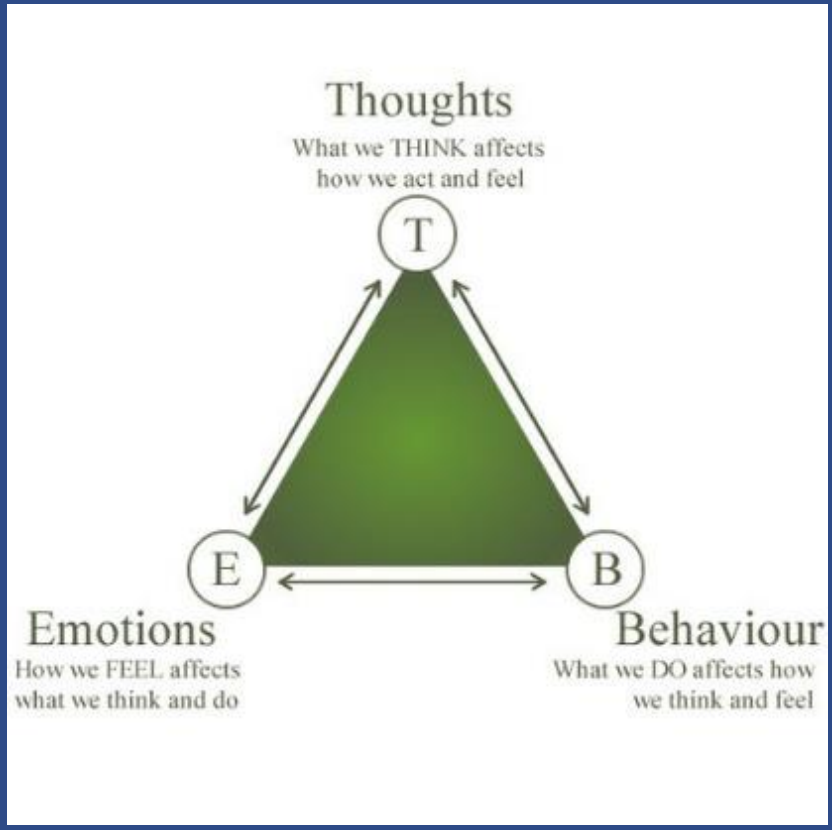
Medical Conditions

- Endocrine (e.g., thyroid)
- Neurologic (e.g., multiple sclerosis, CVA, brain tumor, Parkinson's, Alzheimer's/other dementia, Huntington's, seizure d/o)
- Neoplastic (e.g., pancreas)
- TBI
- Autoimmune (e.g., neuropsychiatric systemic lupus erythematosus / NPSLE)
- Hematologic (e.g., acute intermittent porphyria / AIP)
- Nutritional (e.g., B12)
- Infectious (e.g., HIV, Syphilis)
- Medication-induced (e.g., corticosteroids, interferon)

Anxiety Disorders

Anxiety: Definition

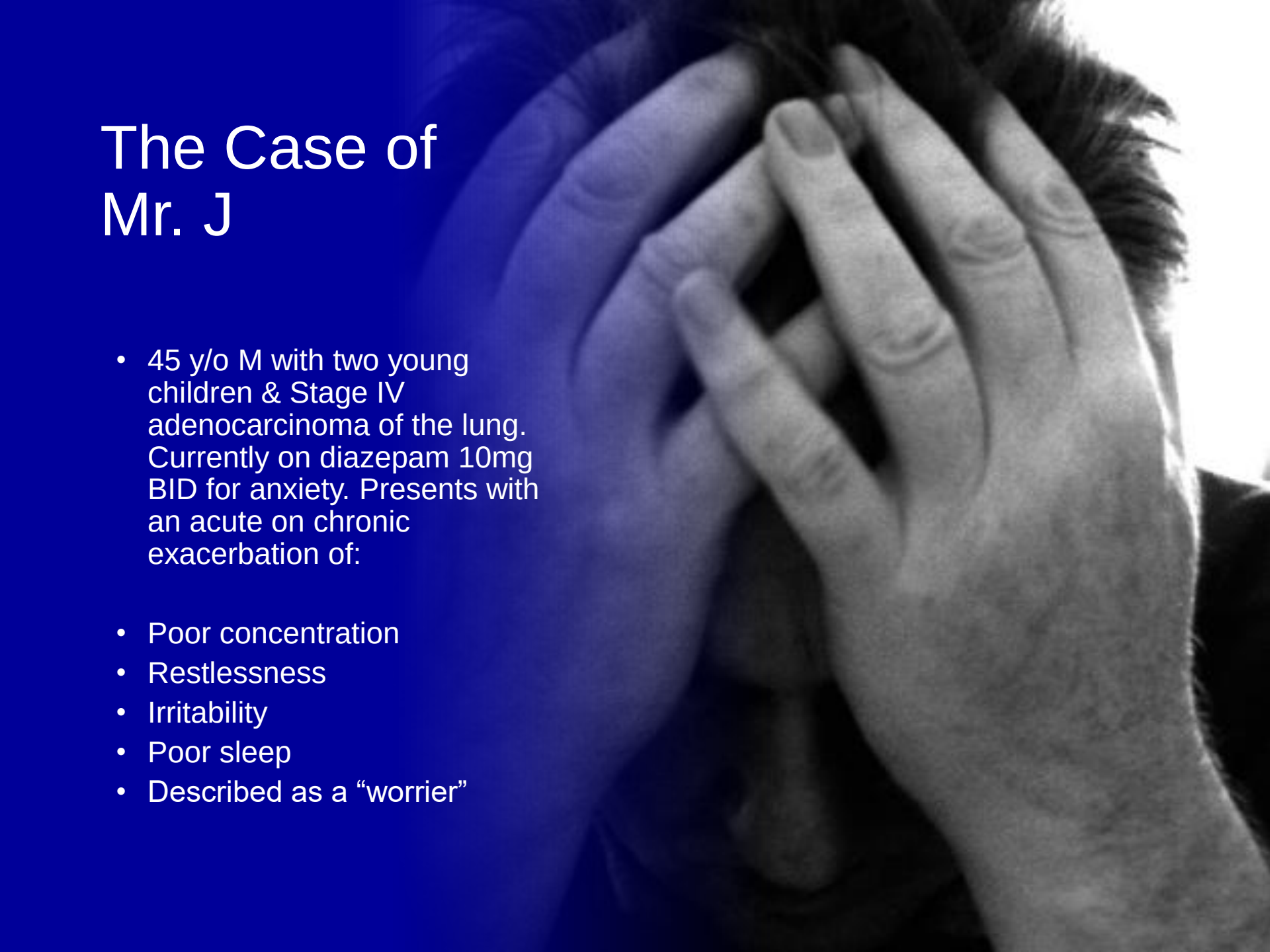
A sense of dread and foreboding with a variety of autonomic (primarily sympathetic) symptoms



Anxiety Symptoms

- Sympathetic:
  - Diaphoresis, dizziness, dyspnea, dry mouth, headache, hyperventilation, muscle tension, nausea, palpitations, shortness of breath, tachycardia, tremulousness, urinary frequency, vomiting
- Cognitive:
  - Recurrent, unpleasant thoughts about illness along with fears of death, disfigurement
  - Overgeneralization and catastrophizing cognitive styles
- Behavioral:
  - Perceive environment as hostile and therefore want to flee/avoid treatment or are non-adherent

The Case of Mr. J



- 45 y/o M with two young children & Stage IV adenocarcinoma of the lung. Currently on diazepam 10mg BID for anxiety. Presents with an acute on chronic exacerbation of:

- Poor concentration
- Restlessness
- Irritability
- Poor sleep
- Described as a “worrier”

The Case of Mr. J: Next Steps?

A. Start SSRI
B. Stop diazepam
C. Refer to psychotherapy
D. Both A and B
E. This is a normal reaction – no changes

Anxiety Disorders Highly Prevalent

Annually: 18.1 % of American adults

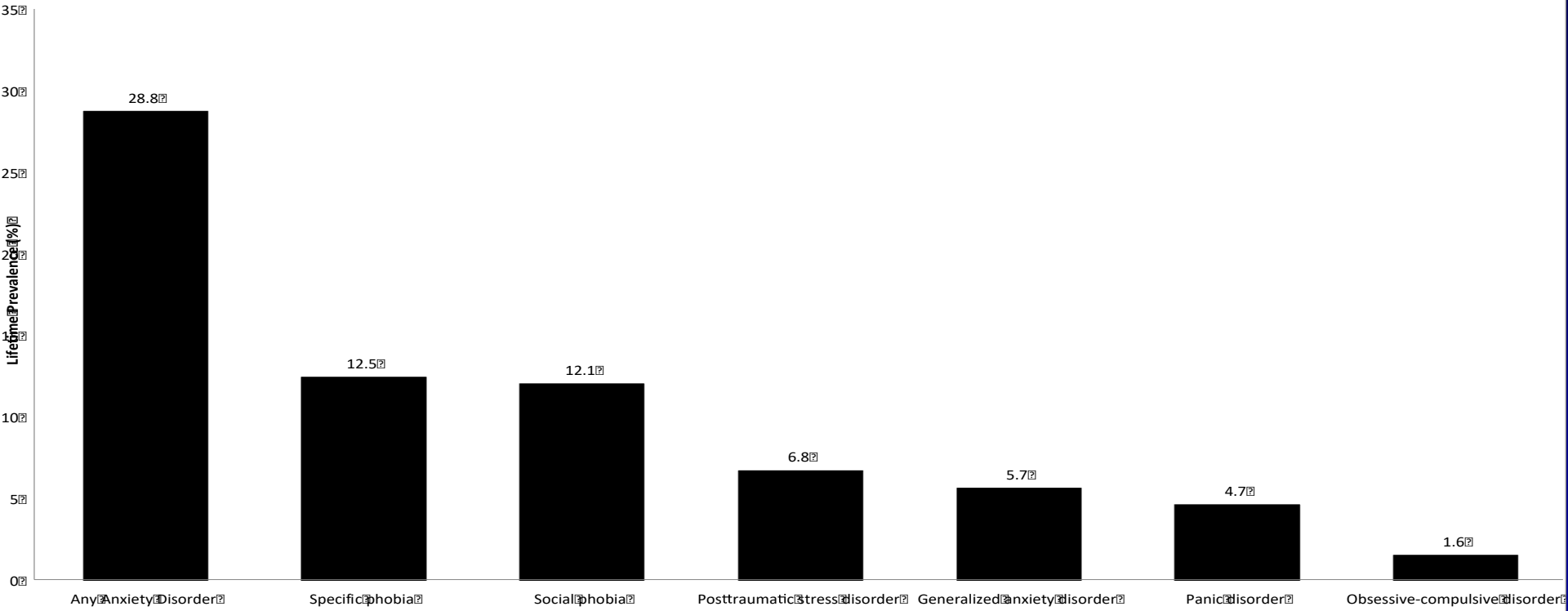
Lifetime: 28.8% of American adults

Frequently co-occur with depressive disorders or substance abuse

Majority of people with one anxiety disorder also have another anxiety disorder

About 75% of people diagnosed with an anxiety disorder will have their first episode by age 21.5

Prevalence Of Anxiety Disorders
National Comorbidity Survey Replication



Anxiety: Differential Diagnosis

Medical etiologies (including delirium)

Normative Anxiety

Anxiety Disorders

Existential & Psychodynamic Distress

Anxiety: Medical Etiologies

Metabolic: Hypoxia, hyponatremia, hypoglycemia, hyperkalemia

Withdrawal: Benzos, opioids, alcohol

Cardiovascular: CHF, CAD, a-fib, hypovolemia

Endocrine: Thyroid dysfunction, hypo/hypercalcemia

Respiratory: COPD, asthma, PE, pulmonary edema

Neurologic: Akathisia, encephalopathy, partial complex sz

Medications: Stimulants, corticosteroids, beta-adrenergic agonists, etc.

Normative vs. Pathologic Anxiety

- Normal anxiety is adaptive.
  - Inborn response to threat *or* to the absence of people or objects that signify safety
  - Can result in cognitive (worry) and somatic (racing heart, sweating, shaking, freezing, etc.) symptoms.
- Pathologic anxiety is anxiety that is excessive and leads to **impaired function.**

Anxiety Disorders in DSM 5

Social anxiety disorder:

- Excessive and unreasonable fear of social situations.
- A fear of being watched/judged by others.
- “A stare is a threat.”

Panic disorder:

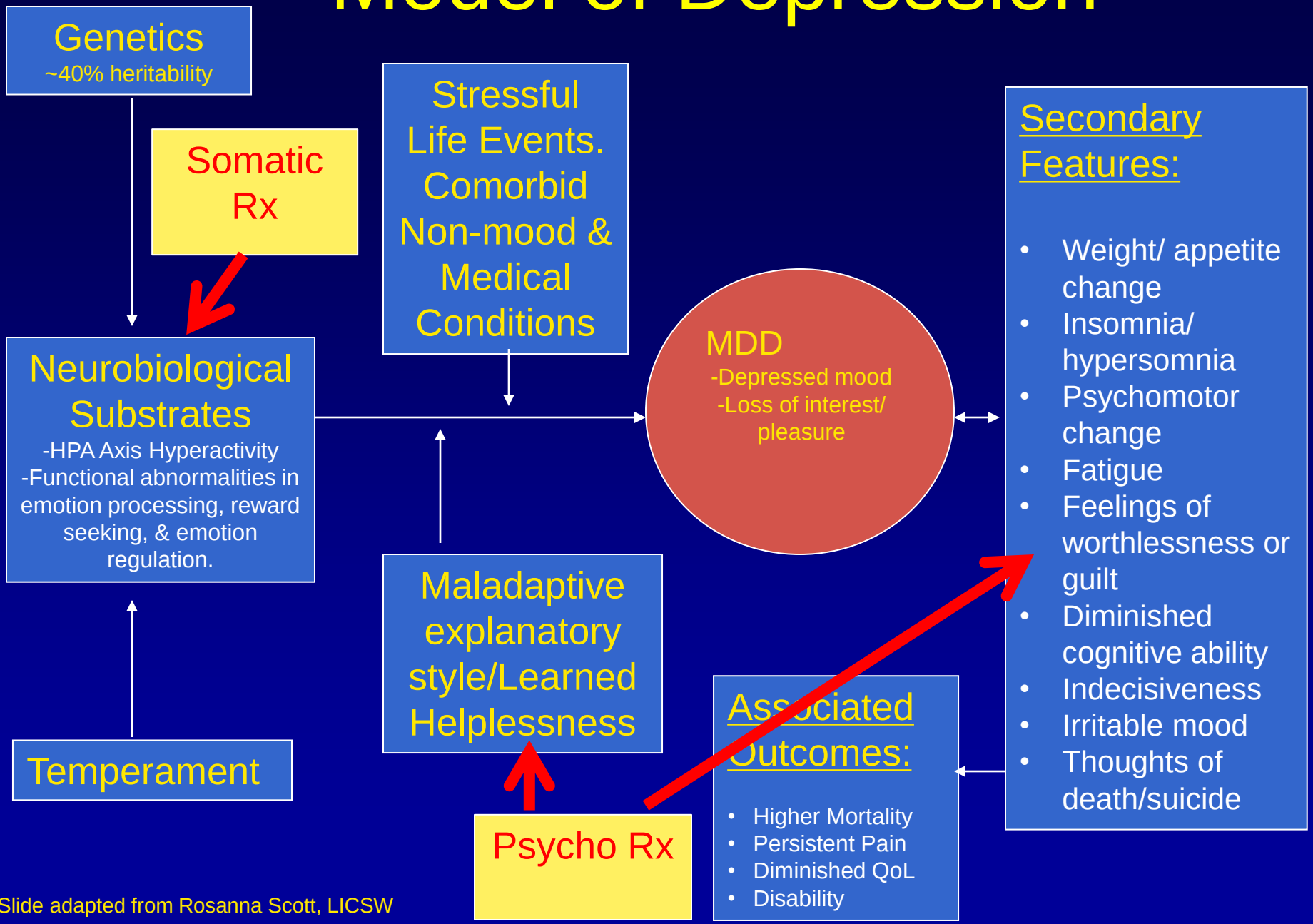
- Recurrent panic attacks *and* maladaptive behavior changes in attempt to avoid future panic attacks

Generalized anxiety disorder:

- Excessive / unrealistic anxiety for 6+ months about two or more aspects of life.
- Accompanied by physical symptoms (e.g. palpitations, dyspnea, dizziness.)

Treatment of Depression

Model of Depression



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Treatment of Depression

- Psychotherapy (Which flavor?)
- Pharmacotherapy
  - SSRIs
  - SNRIs (esp. with pain syndromes)
  - Atypical antidepressants
  - Tricyclic antidepressants (esp. with pain)
  - Additional adjuvant medications
- Interventional therapies
- New Models of Care

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Well-absorbed from the GI tract
- Metabolized in the liver
- Half-life:
  - sertraline, paroxetine, fluvoxamine: 1 day
  - escitalopram: 1.5 days
  - fluoxetine: 2-3 days
- Consider drug-drug interactions
  - E.g. Fluoxetine and Paroxetine inhibit CYP2D6
- Pick one and get to know it well!

SSRI Side Effects

- Tremor
- Irritability
- Anorexia/Increased appetite
- GI distress
- Insomnia
- Anorgasmia
- Rarely – SIADH, bradycardia, syncope
- Potentially fatal serotonin syndrome in combination with Monoamine Oxidase Inhibitors

Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)

- Common SNRIs: Duloxetine, Venlafaxine
- Combine features of both TCAs and SSRIs
- Have a role in the treatment of neuropathic pain
- Have similar side effect profile as SSRIs
  - Occasional cardiac effects (e.g. hypertension)
  - Can have significant withdrawal syndromes.
- Fewer drug-drug interactions than SSRIs

Tricyclic Antidepressants (TCAs):

- Common TCAs:
  - Tertiary - Amitriptyline, Imipramine
  - Secondary – Nortriptyline, Desipramine
- Useful in the treatment of certain pain syndromes
- Burdensome side effects:
  - Orthostatic hypotension
  - Anticholinergic effects
  - Conduction system effects

Atypical Antidepressants and their side effects

- Bupropion
  - Activating – avoid in anxiety
  - Small risk of lowering seizure threshold
- Mirtazapine
  - Serotonin and histamine agonist
  - Mild weight gain and sedation
- Trazodone
  - Used as a hypnotic agent
  - Causes significant orthostasis at higher
  - Associated with priapism (avoid in Sickle Cell Dz)

Additional Adjuvant Medications

- Psychostimulants
  - Often used to treat medically-ill and/or geriatric patients with depression
- Atypical anti-psychotics
  - E.g. Aripiprazole, risperidone, olanzapine
- Low dose lithium

Interventional Treatments

- Electro-convulsive Therapy
  - Most effective treatment for major depression
  - 80-90% remission rate
  - 50-80% relapse rate (6mos out)
  - SEs: musculoskeletal, headache, *cognitive*
- Others:
  - Transcranial Magnetic Stimulation
  - Light Boxes (Seasonal Affective Disorder)
- Severe Cases:
  - vagal nerve stimulation (VNS)
  - deep brain stimulation (DBS)

Transcranial Magnetic Stimulation

Transcranial Magnetic Stimulation

- Non-invasive method of brain stimulation
  - Targets specific neural circuits
- Magnetic fields induce electric currents in the cerebral cortex, thereby depolarizing neurons.
- TMS is an efficacious treatment for treatment-resistant major depression.
- Role in treatment algorithm of MDD being worked out

New Antidepressant Medications

Ketamine/Esketamine – For Refractory Depression

- NMDA receptor antagonist
- Transiently alleviates treatment refractory depression
- Rapid response in at least 50% of patients (within 40-120 minutes)
- Effect dissipates by day 10-14
- Side effects: large dissociative and psychotomimetic effects post infusion, hemodynamic effects, blurred vision, dizziness, nausea, vomiting

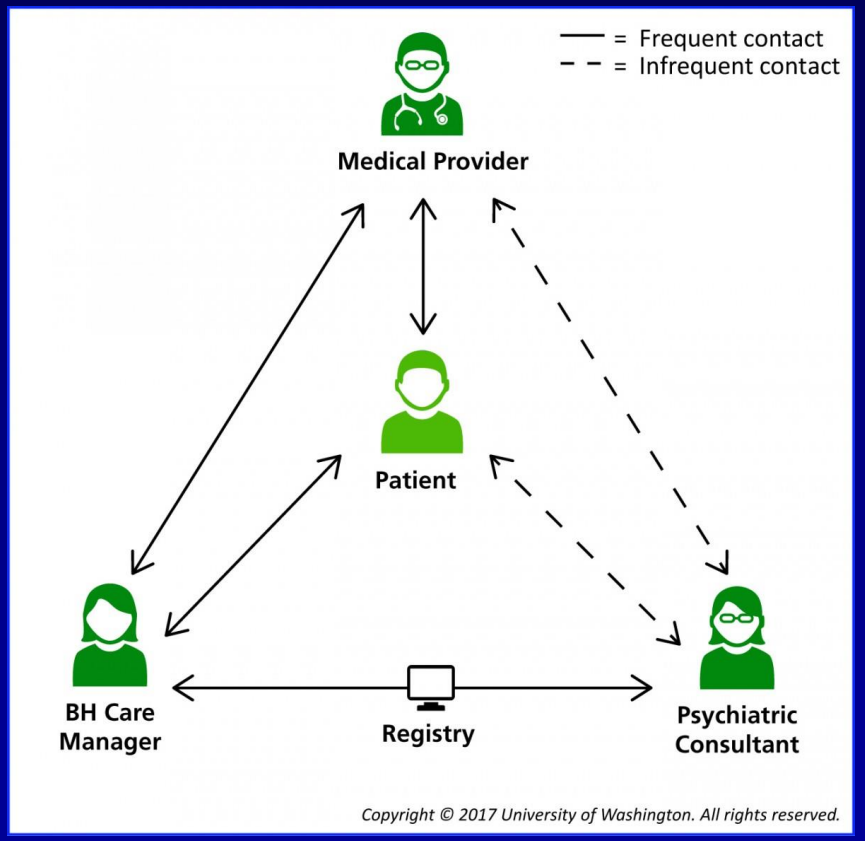
Refer for formal psychotherapy

- Cognitive Behavioral Therapy
- Interpersonal Psychotherapy
- Psychodynamic Therapy
- Existential Psychotherapy
- Group therapy

World of Integrated Care

Collaborative Care Model

- Measurement-based care: Screening and outcomes
- Systematic case registry and review
- Ensures consistent, persistent treatment
- Focus on treating to target/remission



Treatment of Anxiety

(The patient's job is to be anxious, yours is not to be.)

Ideal Treatment:

- Combination of Psychotherapy AND Pharmacologic treatment
- The choice of which modality or both modalities made in conversation with patient
  - E.g. Start drug treatment for patient too anxious for psychotherapy or unwilling to do homework

Anxiety: Optimal Treatments

- Psychopharmacology
  - Short-Term Relief
  - Long-term Treatment
- Non-Pharmacological Aids
  - Environmental Factors
  - Psychosocial Interventions
  - Cognitive Behavioral Therapy

Psychopharmacology for Anxiety

- Short-Acting Relief
  - Benzodiazepines
    - Standing doses better than PRN
    - Longer-acting drugs over shorter acting drugs (e.g. Avoid alprazolam)
  - Other adjuvant agents
    - E.g. hydroxazine, gabapentin, quetiapine

Psychopharmacology for Anxiety

- Long-term Treatment:
  - Use doses higher than for treating depression
    - SSRIs
    - SNRIs (esp. with pain syndromes)
    - Tricyclic antidepressants (esp. with pain)
    - Atypical antidepressants
    - Buspirone

Conclusions

- Be prepared to make the diagnosis of mood and anxiety disorder
- Treat depression and anxiety when you encounter it
  - Do not assume it is an appropriate reaction to a stressful situation
- Consider combination therapy
  - Pharmacotherapy and psychotherapy
- Consider psychiatric consultation

Questions?