Mood Disorders:
Part 1

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Mood Disorders

- Group of clinical conditions involving loss of control over mood states: depression, elation, irritability, etc.
- Specific constellation of signs and symptoms during a specific time period.
- Changes in energy level, concentration, cognitive abilities, activity level and disturbances in appetite, sleep and sex.

Mood Disorders

- “Unipolar” Depressive Disorders:
  - Major Depressive Disorder, Dysthymia
- Bipolar Disorders:
  - Bipolar I Disorder, Bipolar II Disorder, Cyclothymia
- Four types of Mood Episodes: major depressive episode, manic episode, mixed episode, and hypomanic episode.

Mood Disorders And Primary Care

- 1 in 4 patients in primary care setting has a psychiatric illness
- 10% of pts in primary care and 15% of inpatients on medicine services have Major Depressive disorder.
- Symptoms often physical: fatigue, aches, sleep problems, weight change

Mood Disorders and Primary Care

- Enormous burden to society because of:
  - high health care utilization
  - enormous disability
  - loss of work productivity, including absenteeism
  - indirect or direct worsening of medical illnesses, (cardiovascular, diabetes, etc.)

Mood Disorders and Primary Care

- W.H.O.: Depression: 5th leading cause of disability in all age groups throughout the entire world.
- 50% Americans with a psychiatric illness receive no treatment.
- Of those treated: 50% by their primary care doctor.
- 50% treated for depression in primary care still depressed after 1 year.
- Approx. 90% of pts seeking psychological help first go to their primary care physician.
- In primary care: pattern of under diagnosis and under treatment of mood and other psychiatric illnesses.
High Mortality, Mainly From Suicide

- 15% of people with mood disorders complete suicide.
- 10 to 15% of patients hospitalized for depression will eventually complete suicide.
- Among completed suicides in general: 45 to 70% suffered from a mood disorder.
- Yet, mood disorders are among the most treatment responsive illnesses in all of medicine.

Mood Disorders Throughout History

- Concept of depression as a disorder in ancient texts: ancient Egypt, Old Testament, etc.
- Many great figures in history and art through the millennia have suffered from severe depression: Abraham Lincoln, Winston Churchill, Alexander the Great, Plato, Ernest Hemmingway, William Styron, etc.

Depressive Disorders

- Major Depressive Disorder
- Dysthymia
- Depressive Disorder Not Otherwise Specified
- Substance Induced Mood Disorder, (with depressive features)
- Mood Disorder due to a General Medical Condition, (with depressive features, or with major depressive like episode)

Epidemiology of Major Depression

- Lifetime prevalence: 15%, (5 to 12% in men, and 10 to 25% in women).
- More common in women than men, with a 2 to 1 ratio: (differences in hormones, psychosocial stressors, and “learned helplessness”).
- Mean age: 40 yrs old; 50% in ages 20 to 40, but can occur at any age. Mean age of onset is decreasing.
- Unmarried persons more susceptible.
- No difference in prevalence among different socioeconomic, racial or cultural backgrounds.

Etiology of Major Depressive Disorder

- Mood disorders run in families: due to genetic and environmental factors.
  - Environmental: role modeling, learned behavior, environmental (such as loss)
  - Genetic: 50% have 1st degree relatives with depression
  - Identical twin concordance: 50%, sibling and fraternal twin concordance: 15%

Neurobiology of Depressive Disorders

- Four main areas of abnormality: neurotransmitters, brain structure, neurophysiology, and neuroendocrine function.
- Neurotransmitters: dysregulation of norepinephrine, serotonin, and dopamine causes depression.
- 1st clue: 1950s, Isoniazid, TB drug with monoamine oxidase inhibitor properties alleviated depression.
- Monoamine oxidase: an intracellular enzyme that breaks down the biogenic amines norepinephrine, serotonin, epinephrine, dopamine and tyramine.
Neurotransmitters and Depression: Acute and Delayed Effects

- Acute effects: neurotransmitters, stored in synaptic vesicles, released by nerve impulse, pumped back into cells by presynaptic neuronal pumps. Many antidepressants work by blocking either norepinephrine or serotonin (or both) reuptake.
- Delayed effects: post-synaptic receptor mediated events leading to signaling and second messenger systems.

Neurotransmitters and Depressive Disorders: Norepinephrine

- Reserpine: depletes catecholamines norepinephrine, dopamine and epinephrine) and causes depression.
- Desipramine: tricyclic, an almost pure norepinephrine reuptake inhibitor, is an effective antidepressant.
- Norepinephrine pathways originate in Locus Ceruleus.
- Increased norepinephrine causes down-regulation of B-adrenergic receptors.
- Integration of multiple intracellular signals: changes in G protein, cyclic-AMP or protein kinase and induction of gene transcriptions (regulation of specific gene expression).
- Decreased norepinephrine associated with depression, increased norepinephrine associated with mania.

Other Neurotransmitters and Depression

- Serotonin: decreased serotonin in CSF and brains of depressed pts, and those who completed suicide from depression.
- Selective Serotonin Reuptake inhibitors effective in treatment of depression, (fluoxetine: Prozac, sertraline: Zoloft) etc.
- Dopamine: reduced in depression, increased in mania. Bupropion (Wellbutrin), an effective antidepressant which enhances dopamine.
- Other neurotransmitters: GABA, vasopressin, opiates, glutamate (NMDA receptor).

Neuroendocrine and Neurophysiologic Factors in Depression

- Neuroendocrine:
  1. HPA axis: 50% of depressed pts have increased cortisol, Cushing’s dx assoc. with depression.
  2. Hypothyroidism assoc. w/ depression, hyperthyroidism w/ mania. T3 used to augment antidepressants.
- Structural: Left-sided lesions: depression (left pre-frontal cortex key role), Right-sided lesions: mania.
- Neurophysiology: Decreased delta sleep, decreased REM latency, increased REM density.

Psychosocial Factors In Depression

- Depressive episode 5-6 times more likely within 6 months of a major stressor or loss.
- “Kindling theory”: stressful life events and the illness episodes themselves sensitize neurotransmitter systems to develop further episodes with less or no stressors.
- Stressful events induce release of cortisol.
- Loss of parent before age 11: life event most associated with depression as an adult.
- Lack of social support contributes to depression.

Psychological Factors in Depression

- Traits associated with depression: introversion (causing lack of social supports), dependent, obsessive (perfectionistic), and hysterical traits.
- “Learned helpless”: lack of or inability to experience positive reinforcement.
- Psychoanalytic: loss– anger turned inward.
Diagnosing Major Depressive Disorder

- Cannot make diagnosis until symptoms occur for at least 2 weeks; average depressive episode lasts 6 to 9 months
- After one episode, 50% will have another; after 2, 70%; after 3, 90%.
- Must ask about suicidal thoughts and plan.
- Risk factors for suicide: age > 40, alcohol or drug use, history of attempts, living alone, having a plan, anxiety component.

DSM-IV-TR Diagnostic Criterion

- Five or more of the following symptoms, present during the same 2 week period: at least one is either (1) depressed mood or (2) loss of interest or pleasure.
  1. Depressed mood most of the day, nearly every day.
  2. Markedly diminished interest or pleasure in all or almost all, activities most of the day, nearly every day.

DSM-IV-TR Criterion For Major Depression

1. Depressed mood most of the day, nearly every day.
2. Markedly diminished interest or pleasure in all or almost all, activities most of the day, nearly every day.
3. Significant weight loss when not dieting or weight gain.
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day.
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day.

DSM-IV-TR Criterion For Major Depressive Disorder

9. Recurrent thoughts of death, recurrent suicidal ideation without a plan or suicide attempt or a specific plan for committing suicide.
   - Not a mixed episode.
   - Cause significant distress or impairment.
   - Symptoms not from medical illness or a substance.
   - Symptoms accounted for by bereavement (last more than 2 months after loss, or cause impairment, feeling worthless, suicidal).

Other Descriptors Of Major Depression

- With psychotic features (mood congruent or mood incongruent).
- Melancholic type: severe anhedonia, early morning awakening, weight loss, profound feelings of guilt.
- Atypical type: overeating, oversleeping, leaden paralysis of extremities, extreme sensitivity to rejection.
- Catatonic type: motoric immobility (catalepsy), excessive, purposefully activity, extreme negativism, posturing and grimacing.
- Postpartum type: occurs within 4 months of birth.
- With Seasonal pattern: regular, temporal relationship of onset of a mood episode and a particular time of year, occurring during at least 2 different years.

SIG=ECAPS

- SIG=ECAPS: The prescription (SIG) for depression is Energy Capsules.
- S: Sleep disturbance, I: decrease Interest or pleasure, G: feelings of Guilt, E: poor Energy, C= poor Concentration or memory, A: Appetite disturbance, P: psychomotor agitation or retardation, and S: Suicidal ideation.
Differential Diagnosis

Drugs and Medications

- Drugs: benzodiazepines, opiates, cocaine, amphetamines, marijuana, alcohol.
- Medications: Cardiac: clonidine, hydralazine, propranolol, digitalis.
- Neurological: levodopa, baclofen, phenytoin.
- Pain: ibuprofen, opiates
- Antibiotics, antifungals: ampicillin, tetracycline, sulfonamides, metronidazole
- Steroids and hormones: corticosteroids, prednisone, oral contraceptives.

Differential Diagnosis

Medical Conditions

- Endocrine: Cushing’s disease, hypothyroidism, post-partum and menses related.
- Infections: AIDS, mononucleosis, pneumonia
- Inflammatory: rheumatoid arthritis, lupus
- In diagnosing Major Depressive dx. concommitant with a medical dx: count ALL symptoms, including the physical ones, (which could be accounted for in both illnesses), in the diagnosis of Major Depressive Disorder. Use an “inclusive” approach.

Differential Diagnosis

Psychiatric

- Dysthymia
- Schizophrenia
- Bipolar I, Bipolar II
- Anxiety Disorders, especially Obsessive-Compulsive Disorder.
- Personality disorders, especially Borderline, Narcissistic, and Dependent Personality Disorders.

Dysthymia

- Main features:
  1. chronic, low-grade depression lasting for at least 2 years
  2. gradual, insidious onset, often beginning in childhood and adolescence
  3. with a persistent or intermittent course
- Double depression: patient with dysthymia develops a Major Depressive episode.

Dysthymia: Etiology And Epidemiology

- Etiology: Biological, genetic, and psychosocial factors, similar or same as Major Depressive disorder.
- Genetic: family members: have Bipolar, Dysthymia or Major Depressive disorder.
- Biological: decreased REM latency, increased REM density, disturbance of adrenal and thyroid axes.
- Psychosocial: trauma, loss, social isolation, “learned helplessness.”
- Epidemiology: 5 to 6% of population, women greater than men, almost 2 to 1.

Dysthymia: DSM-IV-TR Criterion

- Depressed mood for most of the day, nearly every day, for at least 2 years.
- Presence, while depressed, of 2 or more of the following symptoms:
  1. poor appetite or overeating
  2. insomnia or hypersomnia
  3. low energy or fatigue
  4. low self-esteem
  5. poor concentration or difficulty making decisions
  6. feelings of hopelessness
Dysthymia: DSM-IV-TR Criterion

- No Major Depressive episode has occurred during the 1st 2 yrs, or if there was, full remission for at least 2 years.
- Symptoms not from another psychiatric illness, substances or medications, or a medical disorder.
- Symptoms cause a lot of distress or problems functioning.

Treatment of The Unipolar Depression

- Standard of care: an antidepressant and psychotherapy.
- You MUST refer these patients: patients with Bipolar Disorder, suicidal thoughts or history of suicide attempts, psychosis, or a concomitant personality disorder.
- You MUST refer after 2 adequate trials (high enough dose, long enough period of time) are ineffective.

Treatment of Depression

- You must hospitalize patients who are suicidal, psychotic, severely debilitated, unable to care for selves.
- Medications: First-line drugs: the SSRIs, (fluoxetine, sertraline, paroxetine, fluoxamine, citalopram, escitalopram).
- Dual acting antidepressants: bupropion (dopamine and norepinephrine), and venlafaxine, mirtazapine and duloxetine (norepinephrine and serotonin).
- Last-line (only for resistant depressions treated by a psychiatrist): tricyclics, MAO inhibitors.

Treatment of Unipolar Depressive Disorders

- In general, all antidepressants are equally efficacious; 65 to 70% of patients improve markedly.
- The class of medication effective for a biological family member will probably be effective for your patient.
- Start low, wait 4 to 6 weeks at therapeutic dose before switching.
- Remind the patient to take the antidepressant every day for 6-12 mos., or longer for dysthymia, and for life after 3 episodes of recurrent Major Depressive Disorder.
- Monitor the patient frequently, for mood and suicidality, especially at first and especially after discontinuation of the antidepressant.
- Augmenting strategies: add an antidepressant from a different class, lithium, T3, and Ritalin.

Treatment of Depression

- ECT for severe depression, very suicidal patients, those who do not respond to 2 or 3 adequate trials of an antidepressant, and pregnancy.
- Cognitive-Behavioral therapy: monitor and correct negative, distorted thought patterns.
- Interpersonal psychotherapy: improves current interpersonal problems.
- Psychodynamic psychotherapy: promotes personality change through an understanding past events, conflicts.
- Generally, the combination of psychotherapy and medication is more effective than either alone.