

# Substance and Medication Induced Mood Disorders



**KELLY GODECKE, MD  
PSYCHIATRY DEPARTMENT  
UNIVERSITY OF UTAH**

# Substance Induced Depressive Disorder



- A.** A prominent and persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities.
- B.** There is evidence from the history, physical examination, or laboratory findings of:
  - The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to a substance.
  - The involved substance is capable of producing the symptoms of Criterion A.
- The disturbance is not better explained by a depressive disorder.

# Substances Implicated in Causing Depression



- Alcohol
- Alpha-2-adrenergic agonists
- Amphotericin
- Anabolic steroids
- Beta-blockers
- Bismuth
- Carbamazepine
- Cis-retinoic acid
- Corticosteroids
- Cyclosporin
- Digitalis
- H-2 blockers
- Levodopa
- Theophylline
- Metoclopramide
- Metronidazole
- Nifedipine
- Phenytoin
- Psychostimulants
- Reserpine
- Sedative-hypnotics
- Thiazide diuretics

# Substances Implicated in Causing Depression



- **Barbiturate and Topiramate**

- These two medications are anti-epileptics that work on the GABA neurotransmitters system and may produce fatigue, sedation, impaired cognition, and depression.
- 4-7% of patients develop depressive symptoms.

- **Flunarizine**

- A calcium-channel antagonist used for acute and prophylactic treatment of migraine headaches, has been associated with depression.
- 8% of patients develop depressive symptoms.

# Substances Implicated in Causing Depression



- **Digoxin**

- Neuropsychiatric symptoms at both toxic and therapeutic levels.
- 5% of patients develop “mental disturbances” per package label.
- Digoxin toxicity can masquerade as depression.

- **Carbonic Anhydrase Inhibitors**

- Nearly 50% of patient had a mild syndrome of fatigue, malaise, anorexia, and depression that was associated with acidosis.

# Substances Implicated in Causing Depression



- **Interferon-alpha**
  - 58% of patients develop significant depressive symptoms.
- **Carmustine**
  - 16% of patients developed depression in Phase II trials (vs 10% treated with placebo).
- **Busulfan**
  - 23% of patients developed depression.
- **L-Asparaginase**
  - 31% developed CNS abnormalities (most commonly, moderate to severe depression associated with personality disturbances).

# Substances Implicated in Causing Depression



- **Clonidine**

- Central alpha-adrenergic agonist associated with a number of neuropsychiatric effects; fatigue and sedation are the most common effects, with sedation occurring in 33% of patients.
- 1-2% of patients develop depressive symptoms.

- **Amiodarone**

- Indirect depressive symptoms via thyroid abnormalities due to high iodine content.
- 15% of patients develop thyroid abnormalities.

# Substances **NOT** Implicated in Causing Depression



- **Accutane**
  - No association with depression.
- **HMG-CoA reductase inhibitors**
  - Have not been associated with increased rates of depression or suicide despite evidence that low cholesterol levels have been correlated with depression, one study noted a 4- to 7- fold increase risk of severe depression in men with chronically low cholesterol levels.
- **Beta-Blockers**
  - 2002 meta-analysis of 15 trials found that beta-blockers were not associated with a significant increase in reports of depressive symptoms.
- **Calcium-channel Blockers**
  - Associated with fatigue but have not been associated with depression.

# Treatment of Substance Induced Depressive Disorder



- **Eliminate instigating agent.**
- **If ongoing symptoms, treat with antidepressant agent.**

# Substance and Medication Induced Bipolar Disorder



- A.** A prominent and persistent disturbance in mood that predominates in the clinical picture and is characterized by elevated, expansive, or irritable mood, with or without depressed mood, or markedly diminished interest or pleasure in all, or almost all, activities.
- B.** There is evidence from the history, physical examination, or laboratory findings of:
  - The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to a substance.
  - The involved substance is capable of producing the symptoms of Criterion A.
- The disturbance is not better explained by a bipolar disorder that is not substance-induced.

# Substances Implicated in Causing Bipolar Disorder

## Definitive

- Levodopa
- Corticosteroids
- Anabolic-androgenic steroids

## Probable

- Thyroxine
- Iproniazid
- Isoniazide
- Sympathomimetic drugs
- Chloroquine
- Baclofen
- Alprazolam
- Captopril
- Amphetamine
- Phencyclidine



## **Anti-depressant Induced Bipolar Disorder**

# Adverse Drug Event verses Indicator for Bipolar Diathesis

- Risk factors that correlate with polarity switching:
  - ✦ Early age of onset of affective illness
  - ✦ Bipolar family history
  - ✦ Severity of initial depression

# Treatment of Substance Induced Bipolar Disorder



- **Eliminate instigating agent.**
- **If ongoing symptoms:**
  - Atypical antipsychotic (Olanzapine)
  - Benzodiazepines
- **Standard mood stabilizers may warrant introduction based on the severity, duration, and clinical characteristics of a switch event.**

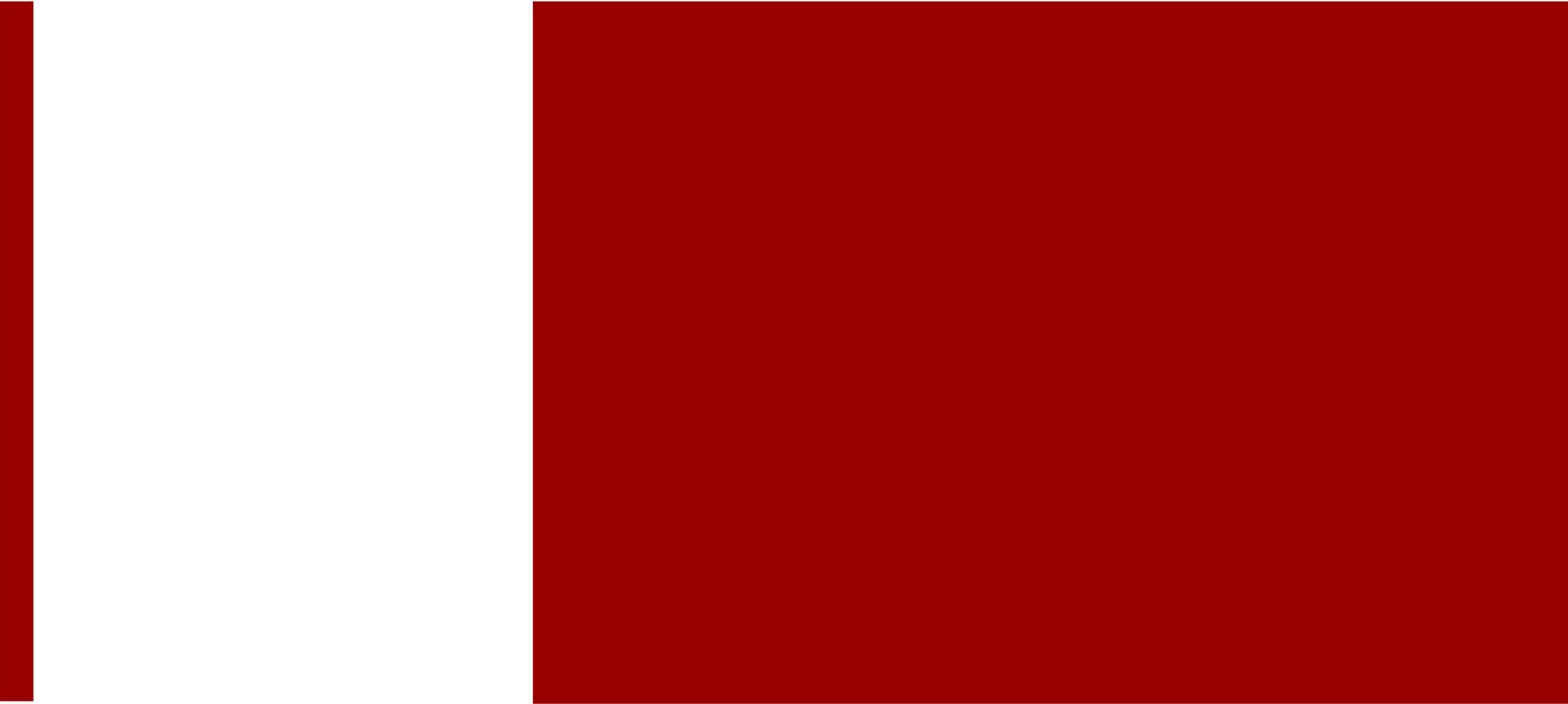
# Corticosteroids



- Two large meta-analyses reported corticosteroid-induced psychiatric "reactions" ranging from 6% (for severe reactions, including psychosis, in addition to mania and depression) to 23% for moderate reactions. Euphoria and hypomania were the most common psychiatric symptoms reported during short courses of steroids; during long-term treatment, depressive symptoms were the most common.

# Questions?



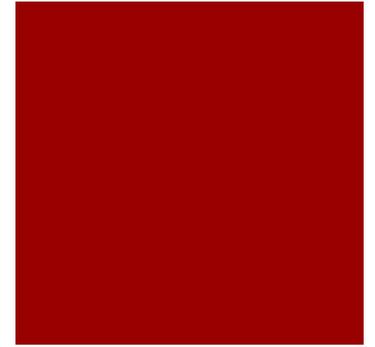


# Depression Secondary to Medical Illness

Sarah Mallowney, MD PGY3  
Psychiatry Resident  
University of Utah

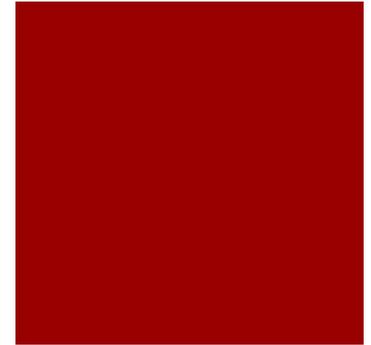
# Objectives

- Diagnosis
- Differential diagnosis
- Laboratory / Imaging Evaluation
- Common medical conditions observed with depressive symptoms
- Case discussion



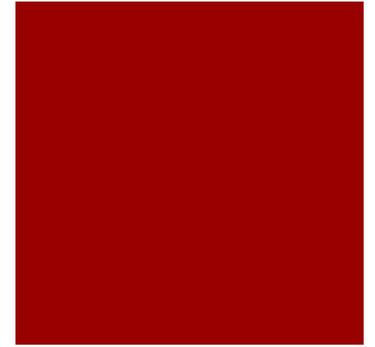
# DSM 5 Diagnosis

- Depressive Disorder due to Another Medical Condition
  - A prominent and persistent period of depressed mood or markedly diminished interest or pleasure in all, or almost all, activities that predominates in the clinical picture.
  - There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct pathophysiological consequence of another medical condition.
  - The disturbance does not occur exclusively during the course of a delirium.
  - The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

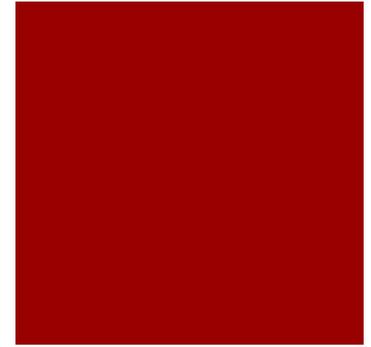


# DSM 5 Diagnosis

- Specifiers
  - With depressive features
  - With major depressive-like episode
  - With mixed features

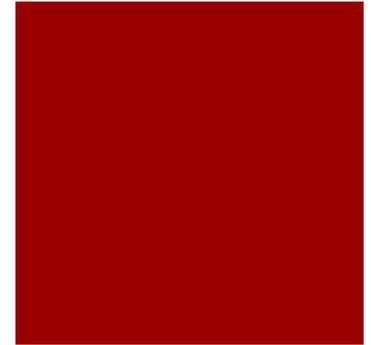


# How can we know that depression is related to a medical condition?



- Presence of a general medical condition
- Pathophysiologically possible to cause depression
  - Evidence suggestive of relationship is helpful
- Temporal association between onset, exacerbation, or remission of the medical condition and the mood disorder
- Atypical features
  - Ex. No history of mood disorder prior to onset of medical disorder

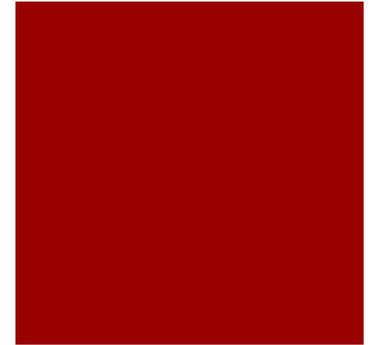
# Adjustment Disorder with Depressed Mood



- **DSM 5:**
- Low mood, tearfulness, or feelings of hopelessness that occur in response to an identifiable stressor within three months of onset of the stressor
- Symptoms are clinically significant by at least one of the following
- The syndrome does not meet criteria for another psychiatric disorder
- The syndrome does not represent an exacerbation of a preexisting psychiatric disorder
- The syndrome does not represent bereavement.
- After the stressor and its consequences have ended, the syndrome resolves within six months.

# Diagnostic Evaluation

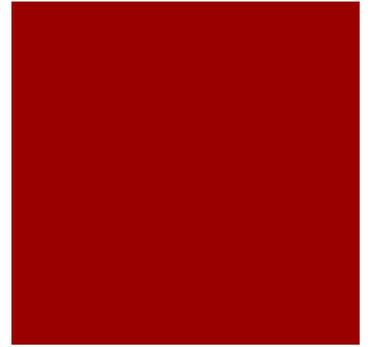
- Physical exam
- Lab evaluation recommended for:
  - Severe depression
  - Medical concerns based on history or exam
  - Treatment resistant depression
  - New onset depression
- Lab tests:
  - CBC
  - CMP
  - TSH
  - Urine toxicology
  - B-HCG
    - B12
    - Folate
    - ECG
- Neuroimaging
  - Concerns for structural abnormalities
  - Elderly patients
  - No prior history of mood disorder



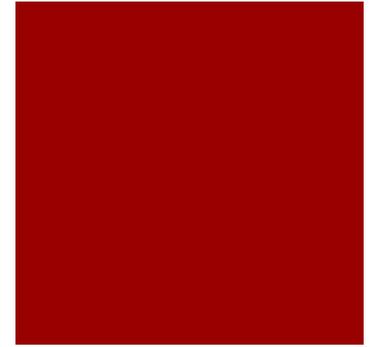
# Medical conditions commonly associated with mood disorders

- Endocrine disorders
  - Thyroid disorders
  - Hyperparathyroidism
  - Cushing Disease
  - Addison Disease
  - Hypopituitarism
  - Adrenal insufficiency
  - Hypercortisolism
  - Low testosterone
  - Pregnancy- Postpartum Period
  - Premenstrual period
- Obstructive sleep apnea
- Heart failure
- Severe anemia
- Neurologic Disorders
  - Stroke
  - Normal pressure hydrocephalus
  - Cerebral tumors
  - Subdural hematoma
  - Traumatic Brain Injury
- Infectious Diseases
  - Tuberculosis
  - Epstein-Barr infection
  - HIV
  - Pneumonia
  - Tertiary Syphilis
  - Encephalitis/Postencephalitic states
- Chronic Inflammatory Conditions
  - Lupus
- Vitamin deficiencies
  - B12
  - Vitamin D
- Malignancies
  - Breast, lung, pancreatic cancers
  - Brain cancers
  - Carcinomatosis
- Neurodegenerative and Demyelinating Diseases
  - Alzheimer Disease
  - Multiple Sclerosis
  - Parkinson's Disease
  - Huntington Disease
- Metabolic
  - Hyponatremia
  - Hypokalemia
  - Uremia
  - Porphyria
  - Wilson Disease

# Case Discussion



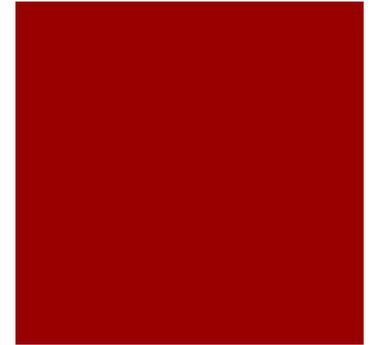
# Case Discussion



- Psychiatric manifestations of primary and secondary brain tumors:
  - Mood disturbances
  - Personality changes
  - Memory impairment
  - Low energy
  - Fatigue
  - Hypersomnolence
  - Loss of interest in everyday activities
  - Abulia

# Summary

- Any new onset medical condition can cause stress that can lead to an adjustment disorder or depressive episode.
- The diagnosis of depression related to another medical condition can be made:
  - With presence of a general medical condition that is pathophysiologically related to depression.
  - Temporal association between onset, exacerbation, or remission of the medical condition and the mood disorder
  - Can be complicated as medications used to treat these medical conditions can also cause mood disorders (steroids).
- Medical history/ROS/Physical+neurological exam is always recommended in assessment of patients with depression.
- Lab evaluation recommended for severe depression, treatment resistant depression, and new onset depression (especially if unclear trigger). Neuroimaging recommended for patients with concern for structural abnormalities and to be considered for elderly patients or patients with new and sudden onset depression.



Questions?

