جامعة الملك سعود
King Saud University

MED437
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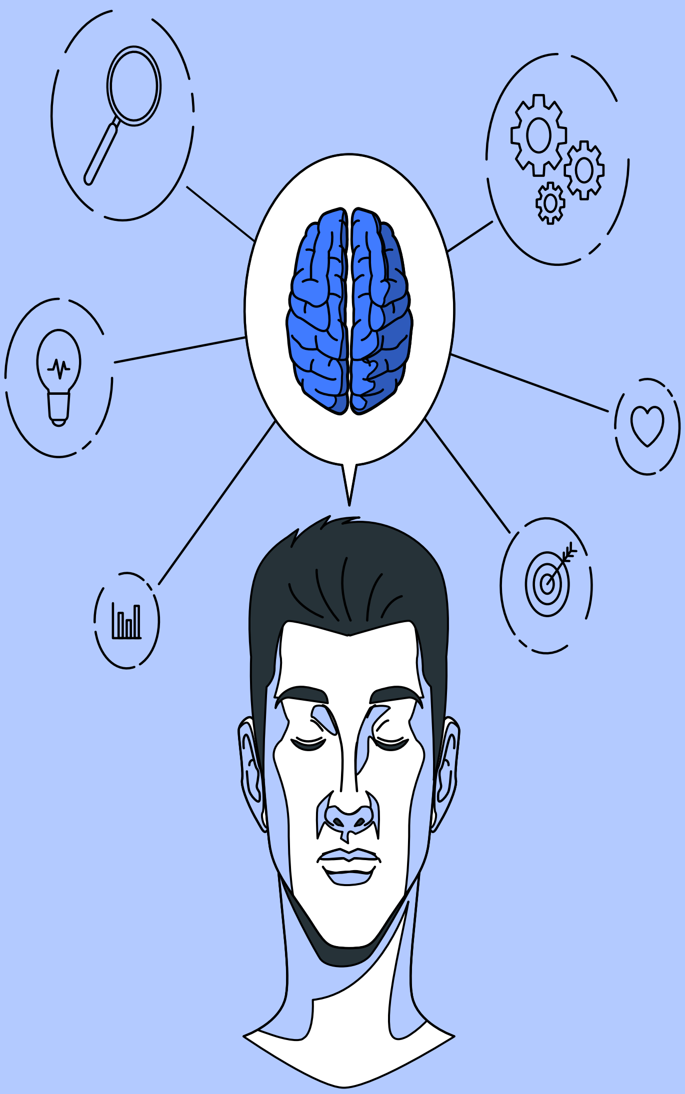

Bipolar Disorder

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Bipolar I vs. Bipolar II

Bipolar I	Bipolar II
• Manic episode ≥ 7 days. Only one episode is enough to say it is type I. • Significant functional impairment and/or hospitalization. • An initial episode of mania is considered diagnostic, even without a history of depression. They might have major depressive episodes but not necessary for the diagnosis.	• Never had a manic episode. • Hypomania ≥ 4 days. At least one episode. • No need for hospitalization. • Must have experienced one or more major depressive episodes with at least one hypomanic episode.

- If someone has MDD they can not have Bipolar Disorder.
- Major depressive episode could be part of major depressive disorder (MDD) or bipolar disorders (BAD). **However, MDD and BAD CAN NOT COEXSIST TOGTHER**.

Criteria for Manic Episode

A	• A distinct period of **abnormally and persistently elevated, expansive, or irritable mood** and **abnormally and persistently increased activity or energy**, lasting **at least 1 week** and present most of the day, nearly every day (or any duration if hospitalization is necessary). • Energy is assessed by sleeping hours. Pt. Usually sleeping for few hours (3-4h) and still have high energy.
B	Accompanied by at least 3 of the following (4 if mood is only irritable): • Inflated self-esteem (still not to the level of delusions)/grandiosity (Pt. Becomes delusional). • Decreased need for sleep. • More talkative than usual. • Flight of ideas. • Distractibility. • Increase in goal-directed activity/psychomotor. Pt. Wants to work on a lot of things. • agitation. • Excessive involvement in pleasurable but high risk activities. Like speeding, spending a lot of money or risky sexual activities.
C	Mood disturbance is **severe enough to impair functioning and/or requires psychiatric hospitalization and/or psychotic symptoms are present**. This is how we differentiate mania from hypomania. In hypomania there is no psychotic symptoms.
D	Symptoms not due to a substance or a general medical condition.

Criteria for Hypomanic Episode	
A	A distinct period of **abnormally and persistently elevated, expansive, or irritable mood** and **abnormally and persistently increased activity or energy**, lasting **at least 4 consecutive days** and present most of the day, nearly every day.
B	At least 3 of the same symptoms as manic episodes (4 if mood is irritable).
C	Mood disturbance is associated with a change in functioning that is uncharacteristic of the individual when non-symptomatic.
D	Mood changes are observable by others.
E	Mood disturbance is **not severe enough** to cause marked impairment in functioning, psychiatric **hospitalization is not needed, and psychotic symptoms are not present**.
F	Symptoms are not due to a substance or a general medical condition.

Criteria for Major depressive Episode	
A	At least 2 weeks of persistently sad mood and/or a lack of interest and pleasure.
B	At least 5 of the following present for at least 2 weeks: • Depressed mood. • Decreased interest. • Decreased/increased appetite, weight loss/gain. • Insomnia or hypersomnia. • Psychomotor agitation or retardation. • Fatigue or lack of energy. • Feelings of worthlessness or inappropriate guilt. • Diminished ability to think/concentrate and/or make decisions. • Thoughts of death, suicidal ideation, suicide plans, and/or suicide attempt.
C	Significant impairment in functioning.
D	Symptoms not due to a substance or a GMC.

Specifiers

“With Rapid Cycling” Specifier:

- At least 4 episodes of mood disturbance in the previous 12 months. Like in a Pt. who have had 4 episodes (2 major depressive episodes + 1 mania episode + 1 hypomania episode).
- Episodes must meet criteria for a manic, hypomanic, or major depressive episode.
- Episodes must be separated by either partial or full remission for at least 2 months or a switch to an episode of opposite polarity. That is how we differentiate it from untreated or partially treated bipolar.
- Characteristics of Rapid Cycling Patient:
  - Higher incidence in bipolar II subtype.
  - Higher incidence of suicide attempt.
  - Higher incidence in women.
  - Earlier age of onset.
  - Longer duration of illness.
  - Higher comorbidity and morbidity.

“With Psychotic Features” Specifier:

- Mood-congruent. Mania and grandiosity.
- Mood-incongruent. Mania and depressive thinking or guilt.

“With Peripartum Onset” Specifier:

- Mood symptoms occur during pregnancy or onset” within 4 weeks following delivery.

Other Specifiers:

- With melancholic features.
- With atypical features.
- With catatonia.

Clinical Presentation and Diagnosis

- Bipolar Disorder most **often starts with depressive episode** (70-75%). That is why we usually mistakenly diagnose them with MDD.
- 10% experience only manic episodes. Bipolar pt. Will experience depression more than mania and hypomania in their lifetime.
- Manic/hypomanic episodes have, in general, a rapid onset.
- Bipolar disorder is a **recurrent, episodic illness**.

Distinguishing BDI and BDII

- Many clinicians incorrectly assume that BDII is a milder form of BDI.
- However, **BDII is at least as disabling as BDI**.
- Epidemiologic, clinical, genetic, and neuroimaging studies emphasize that **BDI and BDII are distinct**.
- Compared with BDI, BDII experience:
    - More frequent and more protracted episodes of
    - depression.
    - More chronic course of illness.
    - More days depressed over lifetime.
    - Less likely to return to premorbid functioning between episodes.
    - High risk of suicide.
    - More rapid cycling.

Diagnosing Bipolar Disorder

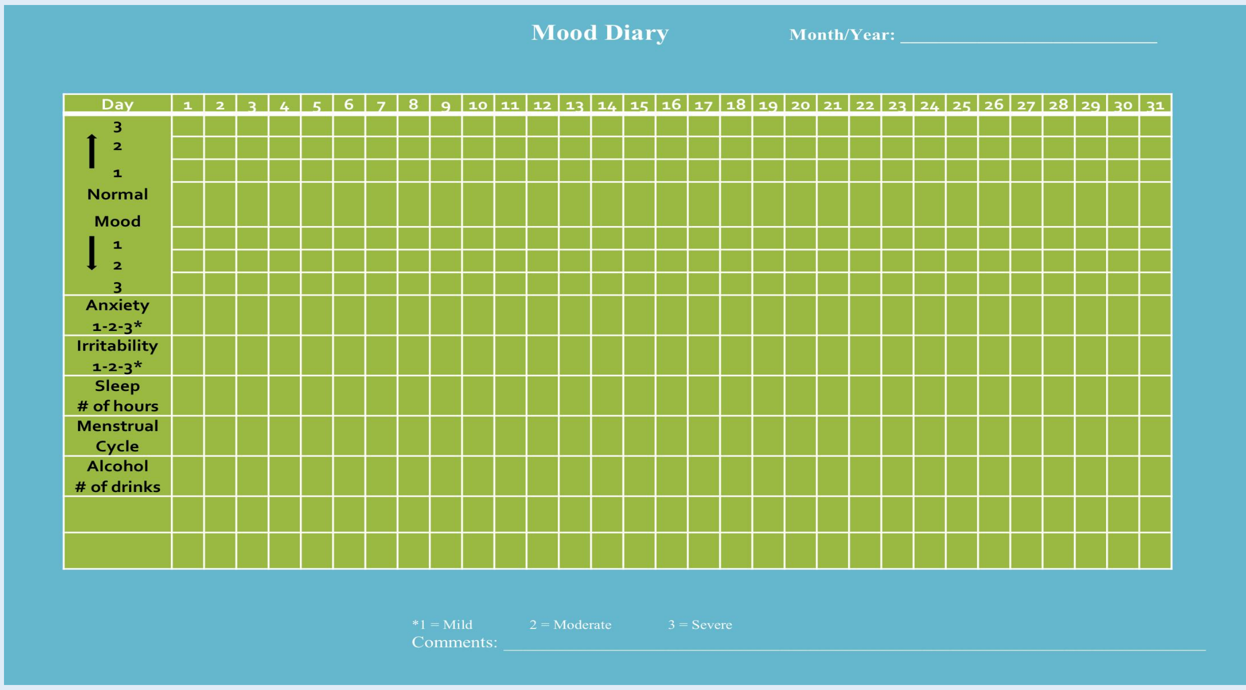
- Family history.
- Symptoms presentation.
- Establishing the premorbid mood baseline for a particular individual.
- Questionnaires:
    - Depression (several scales available).
    - Mood Disorders Questionnaire (screening tool).
    - Hypomania/mania (YMRS: Young Mania Rating Scale).
- Longitudinal evaluations.
- Prospective mood diaries.

Symptom presentation

Symptoms	Mania	Depression
Appearance	Colorful/strange makeup or dress style.	Disinterest in personal grooming or hygiene.
Mood	Prolonged euphoria, excessively optimistic, heightened irritability.	Feelings of sadness, suicidal ideation.
Speech	Talking fast and loudly,difficult to interrupt.	Slowed, monotonous, monosyllabic.
Activity	Risk-taking, impulsive, restlessness.	Difficulty initiating tasks, decreased psychomotor activity, diminished interest in hobbies.
Sleep	Decreased need for sleep.	Early morning waking with insomnia or Hypersomnia and daytime nappinG.
Cognition	Distractible, difficulties planning, reasoning and decision making.	Reduced ability to concentrate, problems with memory.
Self-Perception /Thinking	Exaggerated self-confidence, grandiose ideas.	Reduced self-esteem, feelings of worthlessness and guilt, pessimistic thoughts sense of hopelessness.

Mood Diary

- Useful in rapid cycling and bipolar II.



Epidemiology

Impact of Bipolar Disorder on Patients' Lives:
Results for patients developing bipolar disorder in their mid-20s.

- Life expectancy > Reduced by 9 years. Not because of bipolar but because of its comorbidities.
- Healthy life > Reduced by 12 years.
- Divorce/separation > Twice as common.

Predictors of Poor Long-Term Outcome

- Substance abuse.
- Rapid cycling.
- Psychosis.
- Poor compliance.
- Ongoing residual affective symptoms.

Bipolar Disorder and Suicide

- Bipolar II more at risk of suicide.
- Completed Suicide: 10 – 19% (15 times that of the general population).
- Suicide rates are even higher than depression

Differential Diagnoses

- Unipolar Depression (major depressive disorder).
- Substance Abuse (cocaine, amphetamine).
- Attention Deficit Hyperactivity Disorder (ADHD).
- Personality Disorders (borderline, narcissistic).
- Organic Mood Disorders.
- Schizoaffective Disorder.

BD vs. ADHD:

BD	ADHD
• Onset of clear-cut symptoms after age 8. Teens and older. • Onset with dysthymia or depression. • Episodicity. • Family history of mood disorders. • Variable or negative response to stimulants. • Response to mood stabilizers.	• Onset of clear-cut symptoms before age 7. • Onset of hyperactivity or disruptive behaviors. • Continuous. • Family history of disruptive disorders. • Response to stimulants • Variable or no response to mood stabilizers.

BD vs. Borderline personality disorder:

BD	BPD
• Biphasic mood dysregulation. • Mood symptoms meet threshold criteria for MDE. • Reasonable functioning during euthymic episode. • Family history of bipolar disorder.	• Mood dysregulation in the depressive spectrum. • Mood symptoms often do not reach threshold for MDE. • Dysfunction persists even in euthymic periods. • Family history of deprivation and abuse.

BD vs. Substance Abuse:

- For diagnostic clarity, longest possible period of abstinence is optimal (6 months – 1 year).
- **The onset of bipolar disorder usually precedes that of substance use disorder**. Then bipolar disorder could be considered a risk factor for the development of substance use disorder.

Medical Conditions and Medications Reported to Precipitate Manic Episodes

- Multiple sclerosis.
- Stroke.
- Tumor.
- Cushing syndrome.
- Hyperthyroidism.
- Corticosteroids.

Table 10–5. Selected causes of secondary mania

Neurological conditions	Medications and substances
Frontotemporal dementia	Alcohol
HIV encephalopathy	Amantadine
Huntington's disease	Amphetamines
Multiple sclerosis	Anabolic steroids
Psychomotor seizures	Antidepressants
Stroke (temporal, right hemispheric)	Cocaine
Traumatic brain injury	Corticosteroids/corticosteroid withdrawal
Tumors	Cyclobenzaprine
Viral encephalitis	Dextromethorphan
Wilson's disease	Dopamine agonists (levodopa, pramipexole)
Other systemic conditions	*Hypericum perforatum* (St. John's wort)
Carcinoid	Isoniazid
Cushing's syndrome	Methylphenidate and other stimulants
Hyperthyroidism	Modafinil
Niacin deficiency	Phencyclidine
Postoperative delirium	Procarbazine
Puerperal postpartum psychosis	Propafenone
Vitamin B_{12} deficiency	Sympathomimetic amines (e.g., ephedrine)
	Thyroid preparations
	Zidovudine

Medical Conditions and Medications Reported to Precipitate Depressive Episodes

- Secondary to Neurological Conditions:
  - Cerebrovascular disease.
  - Dementia.
  - Epilepsy.
  - Huntington's disease.
  - Multiple Sclerosis.
  - Parkinson's.
  - Postconcussional disorder.
  - Sleep apnea.
  - Stroke.
  - Subarachnoid hemorrhage.
- Secondary to Endocrine Disorders:
  - Addison's Disease.
  - Cushing's syndrome.
  - Hypopituitarism.
  - Hyperthyroidism.
- Secondary to Infections:
  - Encephalitis.
  - Epstein–Barr virus.
  - Hepatitis.
  - HIV.
  - Pneumonia.
  - Post-influenza.
  - Tertiary syphilis.
- Secondary to Medications:

Medications
Amphetamine withdrawal
Antihypertensives: methyldopa, clonidine, guanethidine, reserpine
Barbiturates
Benzodiazepines
Cocaine withdrawal
Corticosteroids
Opiates
Chemotherapeutic agents: vinblastine, vincristine, procarbazine, L-asparaginase, interferon alfa
Gonadotropin-releasing hormone agonists
Interleukin
Interferon alfa-2
Mefloquine
Metoclopramide
Progesterone-releasing implanted contraceptives

- Secondary to Other condition:
  - Alcoholism.
  - Anemia.
  - Heavy Metal poisoning.
  - Hypercalcemia.
  - Hypomagnesaemia.
  - Hypokalemia.
  - Systemic lupus erythematosus.

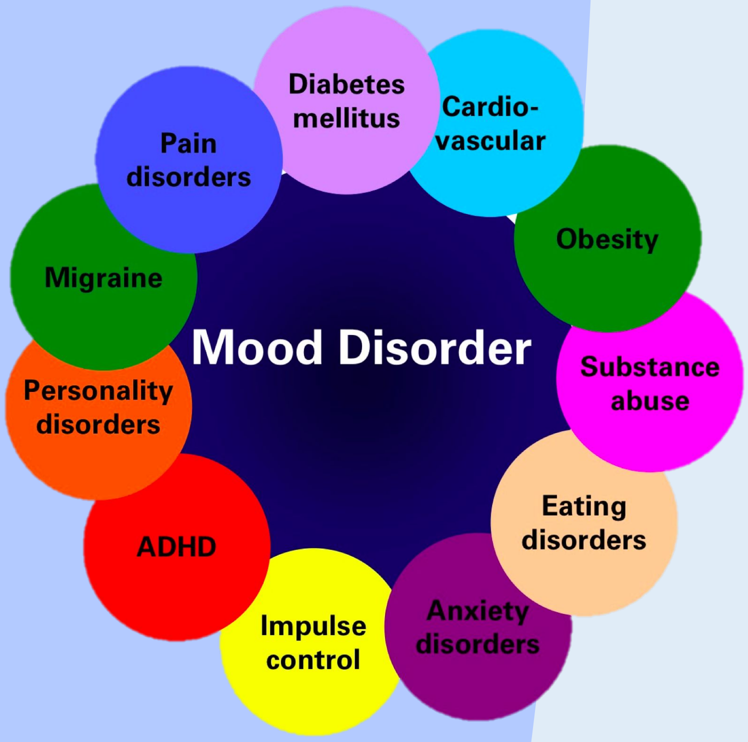
Comorbidities

Important

- Complicate the diagnosis and management of bipolar disorder. like in GAD + Bipolar. GAD first line of treatment is SSRI but you can't use it in this case because pt. Might get manic or hypomanic.
- Possible earlier age of onset.
- More sever disease course.
- Poorer treatment adherence.
- Greater risk of depressive and mixed episodes and suicidal behavior.
- Impaired psychosocial function.
- Decreased QoL.

Medical and Psychiatric Comorbidities:

- The prevalence of psychiatric/medical comorbidities in bipolar disorder is **high**.
- **Cardiometabolic disorders most common specific cause of premature mortality.**



Etiological Theories of Bipolar Disorder

- Neurotransmitter System Abnormalities: (Monoaminergic, Cholinergic, Glutamatergic, GABA–ergic, Glucocorticoid, Peptidergic).
- HPA axis Function: HPA abnormalities have been demonstrated in all phases of bipolar disorder.
- Neuroimaging and Neurophysiological Findings: Several areas in the brain are involved.
- Family Studies and Genetics: A family history of BD is one of the strongest and
- most consistent risk factors for the development of this condition.

Circadian Rhythms in Bipolar Disorder

- Changes in sleep, day time activity and energy levels are important in acute mania and depression.
- Changes in sleep-wake cycle and represent core features of BD with sleep abnormalities in about 90% during acute episodes.
- Even in euthymia, sleep abnormalities persist.
- Changes in sleep is highly predictive of impending mental illness presentations.
- Sleep disturbance is the most common prodrome of mania.

- Change in sleeping pattern is a very imp. symptom and usually appear first in pt.

Environmental Risk Factors

- **Life events** can influence both the onset and relapse of BD.
- **Childhood adversities** relate to earlier onset of the disorder and greater comorbidities.
- **Stress** precipitates episodes, but its role diminishes as the illness progresses. Any type of stress (relationships, work related, financia)
- **Complications during pregnancy or delivery.**

Treatment modalities

- **Medications**: these are mood stabilizers, when we talk about (mania or hypomania > high) and (depression > low)
  - Lithium.
  - Valproic acid.
  - Lamotrigine
  - Carbamazepine.
  - Certain antipsychotics.
  - Others.
- **Psychotherapy**: Long term treatment.
  - Psychoeducation.
  - CBT (cognitive behavioral therapy).
  - Family-focused therapy.
  - Interpersonal and social rhythm therapy.
  - Others.
- **Neurostimulation**: electroconvulsive therapy. Used for severe mania when other treatments fail.
- **Others**.

Medications

“Lithium”:

- More effective in **preventing high.** It is less effective but yet effective to prevent lows.
- Lithium **decreases risk of suicide attempts and completions.**
- Low therapeutic index. It might get to the toxic level.
- Dosing - Guided by Plasma Levels:
    - **Elderly - usually require lower doses.**
    - Needs dose adjustment in renal impairment.
    - Targeted lithium levels varies depending on the stage of illness, among other factors.
- **Onset of action: ~5-14 days.** That’s why when we use it we should combine it with another drug that will work faster.
- **100 % renal excretion.**
- **Require particular lab monitoring.**
- **Side effects** can be mild or sever:

Mild	Sever
• Fine Tremor (worse with high doses, caffeine, and neuroleptics). • Reversible agranulocytosis. • Rash. • Hair loss. • Cognitive Impairment. • Sedation. • Acne. • Nausea / vomiting / diarrhea / dry mouth. • Excessive thirst (polydipsia), polyuria. Diabetes insipidus • Weight gain (+3.8 kg over one year).	• Psoriasis Exacerbation. • **Hypothyroidism.** • Hyperparathyroidism. • ECG Changes. • Nephrogenic Diabetes Insipidus. • Chronic Renal Disease.

- ### Contraindications:
    - **Significant renal impairment.**
    - Severe dehydration or electrolyte imbalance.
    - Significant Cardiac Impairment.
    - Psoriasis - Relative Contraindication.

- ### Pregnancy and breastfeeding:
    - If used during the second and third trimester, the
    - serum lithium levels should be monitored closely
    - because of changes in blood volume during pregnancy.
    - Cross into breast milk and therefore, is generally discouraged during breastfeeding.

- Toxicity: Considered to be an emergency, pt. may die.
  - Symptoms:
    - Coarse tremor.
    - Drowsiness.
    - Lethargy.
    - Weakness.
    - Agitation.
    - Muscle fasciculation.
    - Ataxia.
    - Dysarthria.
    - Vomiting, Diarrhea.
    - Dizziness, Syncope.
    - Arrhythmias.
    - Polyuria, Polydipsia.
  - Management:
    - IV fluids ++.
    - Might need hemodialysis in certain situations.

"Valproic acid (VPA)":

- Commonly used.
- Useful in high (mania).
- Main mechanism of action: inhibit GABA transaminase.
- Can measure its level to guide the dose, among other considerations.
- Particular lab monitoring is required.
- **Metabolized in the liver.**
- **Require particular lab monitoring.**
- Onset of action is 3-7 days. Works faster than lithium.
- **Side effects** can be mild or sever:

Mild	Sever
• Tremor. • agranulocytosis and anemia. • Hair Thinning / Loss. • Sedation. • Benign Rash. • Nausea, Vomiting, Diarrhea. • Weight Gain. • Benign hepatic transaminase elevation.	• Osteoporosis/reduced bone density. • Thrombocytopenia. • Hyperammonemic encephalopathy. • Stevens-Johnson syndrome. • Polycystic ovary syndrome. Doctors avoid to use it with females. • Hepatotoxicity. • Acute pancreatitis. • Interaction with aspirin and warfarin. • HypoNa

VPA and Polycystic Ovary Syndrome	VPA and Stevens-Johnson Syndrome
• Signs and symptoms: ○ Hyperandrogenism (hirsutism, acne, alopecia). ○ Chronic Anovulation (oligomenorrhea or amenorrhea). ○ Polycystic ovaries on Ultrasonography. • Can lead to **infertility** and **metabolic syndrome**. • **Avoid valproate use in women under 18.**	• It is an emergency. • Stevens-Johnson Syndrome (<10%)/ • SJS/TEN Overlap Syndrome (10-30%)/ • Toxic Epidermal Necrolysis (>30%). • Prodromal flu-like **systemic symptoms.** • **Mucosal surfaces affected.** • Characteristic lesions with **target-like appearance.** - Last 3 points is how we differentiate it from benign rash.

- Contraindications:
  - Hepatic disease.
  - Be cautious of drug interactions.
  - In pregnancy: Valproate is associated with **neural tube defects, cardiac/limb malforms.**

"Lamotrigine":

- Useful in low only (depression).
- Does not interfere with GABA system. Mainly inhibit voltage sensitive sodium channel.
- Can measure its level to guide the dose, among other considerations.
- **No elevated LFT.**
- No major hematological side effects.
- **Weight Neutral.**
- **Cognitive side effects are unusual.**
- **Helpful in treating depressive symptoms (not effective for manic and hypomanic features).**

MCQ: pt came to ER with hypomania what NOT to give? Lamotrigine

- Side effects:
  - Sedation.
  - Nausea/vomiting/diarrhea.
  - Headache.
  - Others:
    - Benign rash.
    - Stevens-Johnson syndrome/SJS/TEN Overlap syndrome/Toxic epidermal necrolysis. Same as in VPA.
- Lamotrigine and benign rash:
  - 8.3% of patients.
  - Characteristics of benign rash:
    - Spotty.
    - Non-tender.
    - Itchy.
    - **No systemic features.**
    - **No lab abnormalities.**

“Carbamazepine (CMZ)”:

- **Absorption of carbamazepine is slow and unpredictable.**
- Several drug interactions.
- Several possible side effects.
- Dose may need to be increased after weeks or months because of **autoinduction**. It increases its own metabolism

Other Bipolar and related disorders

“Bipolar and Related Disorder Due to Another Medical Condition”:

A. A prominent and persistent period of abnormally elevated, expansive, or irritable mood and abnormally increased activity or energy that predominates in the clinical picture.
B. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct pathophysiological consequence of another medical condition.
C. The disturbance is not better explained by another mental disorder.
D. The disturbance does not occur exclusively during the course of a delirium.
E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning, or necessitates hospitalization to prevent harm to self or others, or there are psychotic features.

“Substance/ Medication- Induced Bipolar and Related 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 both (1) and (2):
    1. The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to a medication.
    2. The involved substance/medication is capable of producing the symptoms in Criterion A.
C. The disturbance is not better explained by a bipolar or related disorder that is not substance/medication-induced.
D. The disturbance does not occur exclusively during the course of a delirium.
E. The disturbance causes clinically significant distress or impairment.

“Other Specified Bipolar and Related Disorder”:

- This category applies to presentation in which symptoms characteristic of a bipolar and related disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but **do not meet the full criteria for any of the disorders in the bipolar and related disorders diagnostic class**. The other specified bipolar and related disorder category is used in **situations in which the clinician chooses to communicate the specific reason** that the presentation does not meet the criteria for any specific bipolar and related disorder.
- For example: Short-duration hypomanic episodes (2-3 days) and major depressive episodes.

“Unspecified Bipolar and Related Disorder”:

- This category applies to presentation in which symptoms characteristic of a bipolar and related disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but **do not meet the full criteria for any of the disorders in the bipolar and related disorders diagnostic class**. The unspecified bipolar and related disorder category is used in **situations in which the clinician chooses not to specify the read that the criteria are not met** for a specific bipolar and related disorder, and includes presentation in which there is insufficient information to make a more specific diagnosis (e.g., in emergency room settings).

Summary

- Bipolar Disorder types I and II are chronic, intermittent lifelong disorders, with strong tendencies for relapse and recurrence of major and minor affective episodes.
- Lifetime prevalence: 1-3%.
- **Healthy life and life expectancy**: reduced by about 10 years.
- **Bipolar II disorder is underdiagnosed** and represents the majority of bipolar patients.
- **Bipolar II as compared to Bipolar I** experience more depressive episodes, rapid cycling, and are at higher risk for suicide.
- **Depressive pole is predominant** in BD-I and BD-II.
- **Psychiatric and medical comorbidities** are common.
- Comorbidities complicate diagnosis, treatment, and outcome.
- Often associated with **cognitive deficits** (and poor functional outcome).
- **Completed suicide** is higher than in the general population, MDD and Schizophrenia.
- Several pharmacological and non-pharmacological treatments exist.

Ms. Amal is a 27-year-old single woman works as a teacher. She has a five-week history of low mood, chest tightness, poor appetite, disturbed sleep, excessive guilt feelings, and loss of interest in her social activities. Her father has a history of mood (affective) disorder.

Healthy people have a sense of control over their moods, and experience a wide continuum range of feelings with normal variations [usual sadness **< < <** - - - - - - - - - - - - - - - **-> > >** usual happiness **]**.
Patients with mood(affective) disorders have a loss of that sense of control over feelings , a subjective experience of great distress and abnormality in the range of mood (e.g. depression, euphoria) and result in impaired interpersonal, social, and occupational functioning. Anxiety disorders are not considered as part of mood disorders in the modern classification, they are classified in a separate category although anxiety is a variant of normal mood.

Depressive Disorders (DSM-5)

- Major Depressive Disorder, Single and Recurrent Episodes
- Persistent Depressive Disorder (dysthymic Disorder & chronic major depressive disorder)
- Disruptive Mood Dysregulation Disorder
- Premenstrual Dysphoric Disorder
- Substance/Medication-Induced Depressive Disorder
- Depressive Disorder Due to Another Medical Condition
- Other Specified Depressive Disorder
- Unspecified Depressive Disorder

Bipolar and Related Disorders (DSM-5)

- Bipolar I & II Disorders
- Cyclothymic Disorder
- Substance/Medication-Induced Bipolar and Related Disorder
- Bipolar and Related Disorder Due to Another Medical Condition

Mood/Affect?!
Affect/Mood?!
Confusing terms !!

Mood is the *sustained* and *pervasive* feeling tone that influences a person's behavior and perception of the world. It is *internally* experienced. Mood can be normal, depressed, or elevated.
Affect is the person's *present* transient emotional state. *It represents the external* expression of mood.

Subjective affect: one's verbal expression of

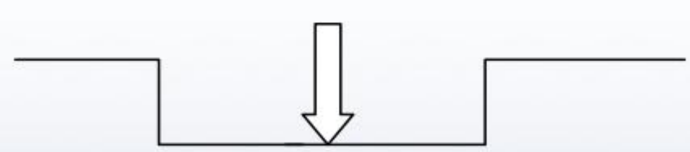
Objective affect: observer's evaluation of expression of affect, through nonverbal signs; facial expression, eye contact, tone of voice, posture & movements.

Episodes / Disorders! , These terms should not confuse me.

Episodes (discrete periods of abnormal mood; low, high, or mixed mood)

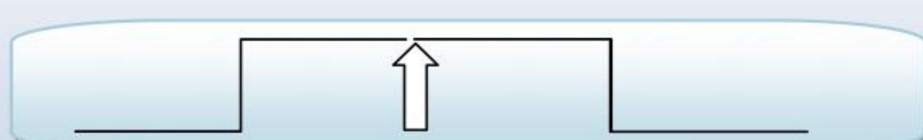
1.Major depressive episode (MDE):

≥ 2 weeks of low mood/loss of interest + other features



2.Manic episode:

≥ 1 week of elevated, expansive, or irritable mood + other features



3.Mixed episode:

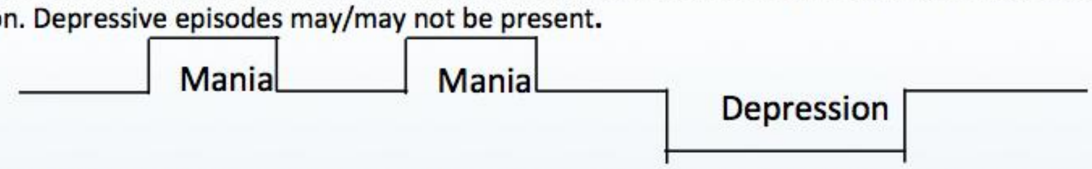
≥ 1 week of both depressed and manic mood + other features

4.Hypomanic episode:

≥ 4 days less severe elevated mood + other features

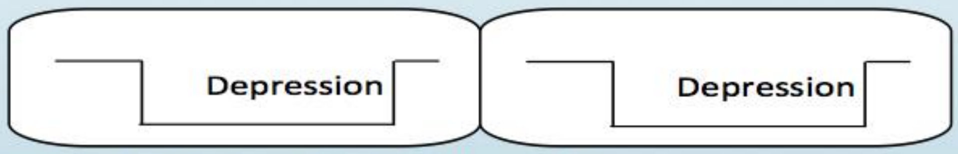
Disorders (longitudinal view / diagnostic term)

1.Bipolar I disorder: patient has met the criteria for a full manic or mixed episode, usually sufficiently severe to require hospitalization. Depressive episodes may/may not be present.



2.Bipolar II disorder: patient has at least one major depressive episode and at least one hypomanic episode, but ***NO*** manic episode.

3.Major depressive disorder (MDD): patient has major depressive episodes (MDEs) but no manic or hypomanic episodes.



4.Dysthymic disorder: ≥ 2 year-history of chronic less severe low mood.

5.Cyclothymic disorder: Less severe bipolar mood disorder with continuous mood swings; alternating periods of hypomania and moderate depression.

Majed, what is Ms. Amal's condition?

Well, Badr, I think she has **MDE**, which can be a presentation of **MDD, Bipolar I or Bipolar II disorders.**

Uhhaa ! this means MDE≠MDD. Okay, how one would proceed in such a case?

Take a detailed past psychiatric history especially **previous manic, mixed, or depressive episodes.**

This is very essential in such a case.

Why?

Not only to reach a proper **diagnosis** , but also to **treat her properly.** If she had previous manic or mixed episodes and you treat her with **antidepressants** without careful observation she may **swing into a manic or a mixed episode** with serious behavioral problems.

Major Depressive Episode (MDE)

A. ≥ 5 of the following symptoms have been present during the same **2-week period** and represent a change from previous functioning; at least one of the symptoms is either no.1 or no.2:

1. Low mood. 2. Loss of interest in pleasurable activities (anhedonia).
3. Appetite or body weight change (increased or decreased).
4.Insomnia or hypersomnia. **5**. Psychomotor agitation or retardation.
6. Fatigue or loss of energy. **7.** Feelings of worthlessness or excessive guilt.
8. Diminished concentration. **9.** Recurrent thoughts of death or suicide.

B. Significant distress or impairment in functioning.

C. The symptoms do not meet criteria for a mixed episode.

D. Not due to substance abuse , a medication or a medical condition(e.g., hypothyroidism).

Ms. Amal's sister reported that; Amal had a distinct period of irritable and euphoric mood 4 years ago for 5 weeks with tremendous energy, hyperactivity, and reduced sleep.

(نوبة الهوس) Manic Episode

A. A distinct **period** of abnormally and persistently elevated, expansive, or irritable mood, lasting at least **1 week.**

B. **B.** During the period of mood disturbance **≥ 3** of the following (4 if mood is irritable):

1. Inflated self-esteem or grandiosity. **2.** Decreased need for sleep.
3. Pressured speech. **4.** Racing thoughts or flight of ideas.
5. Distractibility (reduced concentration).
6. Increase in goal-directed activity (socially, at work, or sexually).
7. Excessive involvement in pleasurable activities that have a high potential for p
engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).
C. The symptoms do not meet criteria for a mixed episode.
D. Significant distress or impairment in functioning.
E. Not due to substance abuse, a medication or a general medical condition (e.g., hyperthyroidism).
Note: Manic-like episodes that are clearly caused by antidepressant treatment should not count toward a diagnosis of bipolar I disorder.

youtube.com/watch?v=zA-fqvC02oM

Psychotic features may occur in severe cases of mania:
A.Mood - congruent hallucinations; e.g. voices talking to the patient about his special powers. Occasionally visual hallucinations (e.g. seeing Angels).
B.Mood-congruent delusions; usually grandiose delusions (e.g. being a prophet, a prince ...), Patients with delusional disorder (grandiose type) have long-lasting grandiose delusions but no manic features; pressure of speech, racing thoughts, flight of ideas e.t.c. Some manic patients develop delusions of persecutions or of reference

Hypomanic vs. manic episode:

		Hypomanic episode	Manic episode
1	**Minimum Duration**	4 days	7 days
2	**Severity**	Not severe enough to cause marked impairment in social or occupational functioning	Causes severe impairment in social or occupational functioning.
3	**Features**	No psychotic features (hallucinations/delusions).	May have psychotic features.
4	**Diagnosis**	Bipolar II disorder	Bipolar I disorder
5	**Management**	Does not require hospitalization	Usually necessitates hospitalization to prevent harm to self or others.

Mixed Episode

≥ 1 week of both manic and depressive symptoms **occurring simultaneously** nearly every day (e.g. overactive overtalkative patient may have at the same time profound depressive thoughts including suicidal ideas) **>>> Bipolar I disorder**.

Alternating Affective Sates

Manic and depressive features **follow one another** in a sequence of rapid changes in a short time (e.g. a manic patient may be intensely depressed for few hours and then quickly becomes manic) **>>> Bipolar I disorder**.

Etiology of mood disorders?!

What neurotransmitters are involved in mood regulation?

Norepinephrine (NE), Serotonin (5HT), and Dopamine (DA) - for details see chapter 1, Basic Psychiatry. Remember, the etiology of mood disorders, like other psychiatric disorders, is **multifactorial;**
Bio - Psycho-Social

Genetic: one parent with bipolar I >25 % chance of mood disorder in child.
Two parents with bipolar I > 50 % chance of mood disorder in child. Concordance rates for monozygotic twins are approximately 75%, and rates for dizygotic twins are 5 to 25%. Some studies found some defects in chromosomes 5, 11 and X.

Neurochemical: disturbance in biogenic amines (norepinephrine, serotonin, and dopamine).

Psychosocial: psychosocial stresses may trigger manic or mixed episode in a vulnerable persons.

Manic-like episodes may be induced by;

A. Medications; e.g. steroids , antidepressants.
B. Medical diseases; e.g. Hyperthyroidism, SLE, Multiple sclerosis.
C. Substance abuse; e.g. stimulants.

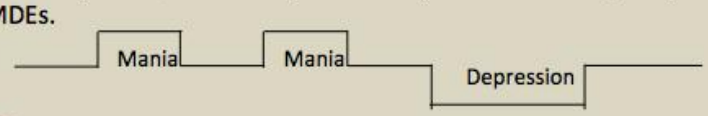
Bipolar I Disorder (It was known as **manic-depressive disorder).**
Patient has met the criteria for a full manic or mixed episode, usually sufficiently severe to require hospitalization. Depressive episodes may/may not be present (episodes of major depression are ***not*** required for the diagnosis). However, most patients with bipolar I disorder experience MDE and manic or mixed episodes (20% of patients experience only manic episodes).
Epidemiology: onset usually 18-30 years. Lifetime prevalence: 1% . ♂ = ♀.

Bipolar I Disorder, <u>Single</u> Manic Episode

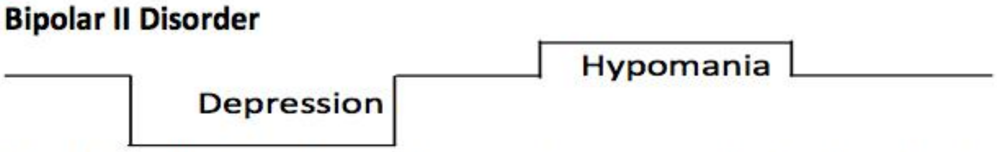
Patients who are having their first episode of bipolar I disorder MDE cannot be distinguished from patients with MDD. Thus, according to DSM-IV-TR, patients must be experiencing their ***first*** manic episode to meet the diagnostic criteria for bipolar I disorder *(*Bipolar I Disorder, ***Single*** Manic Episode).

Bipolar I Disorder, <u>Recurrent</u>

When there are other episodes (whether manic, mixed, or MDE) after the first manic episode, DSM-IV-TR specifies diagnostic criteria for ***recurrent*** bipolar I disorder. Recurrent bipolar I disorder is specified based on the symptoms of the most recent episode: bipolar I disorder, most recent episode manic; hypomanic; depressed; or mixed.
Manic episodes are considered distinct when they are separated by at least 2 months without significant symptoms of mania or hypomania. Between manic episodes, there may be interspersed normal (euthymic) mood or MDEs.



Bipolar II Disorder



Patient has at least one major depressive episode and at least one hypomanic episode, but ***no*** manic episode. If there has been a full manic or mixed episode even in the past, then the diagnosis is bipolar I disorder, **not** bipolar II. Features are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
Epidemiology; onset usually 18- 30 years. Lifetime prevalence: 0.5%. Slightly more common in **women**.

SEASONAL AFFECTIVE DISORDER
Recurrent major depressive episodes that come with shortened day light in winter and disappear during summer (may be followed by hypomania). Absence of clear-cut seasonally changing psychosocial variables. Characterized by atypical features of depression: hypersomnia, hyperphagia (carbohydrate craving), weight gain, increased fatigue. Related to abnormal melatonin metabolism. Treated with exposure to light (artificial light for 2 – 6 hours a day).
It may occur as part of bipolar I or II disorders.

Rapid Cycling Bipolar I or II Mood Disorders

≥ 4 alternating mood episodes (MDE, Manic, Hypomanic or Mixed) in the previous 12 months, separated by intervals of 2-3 days. It is usually more chronic than non-rapid cycling disorders.
Around 80 % are lithium-treatment failures. Carbamazepine and sodium valproate are usual agents of choice.

CYCLOTHYMIC DISORDER

Less severe bipolar mood disorder with continuous mood swings; alternating periods of hypomania and moderate depression. It is non-psychotic chronic disorder. It starts in late adolescence or early adulthood. The treatment is similar to that of bipolar mood disorder.

Mood disorders vs. Schizoaffective Disorder.

To differentiate mood disorder with psychotic features from schizoaffective disorder patient with schizoaffective disorder has either major depressive episode, manic episode, or mixed episode during which criteria for schizophrenia are also met. There should be delusions or hallucinations for at least two weeks in the absence of prominent mood symptoms. Schizoaffective disorder can be either depressive type or bipolar type.
Course and prognosis is between that of schizophrenia and of bipolar mood disorder.
Treatment includes hospitalization, antipsychotics, mood stabilizers (lithium is a good choice) and antidepressants when needed._ Symptoms not due to general medical condition or drugs.

Course and Prognosis of bipolar disorders

If left untreated, most manic episodes will resolve within 8 -12 weeks (rarely last longer than 24 weeks). The risk of recurrence is particularly high (50 %). About 80 % of manic patients eventually experience a full depressive episode. About 50 % will have multiple relapses with good interepisodic functioning. Chronic deterioration may occur in up to 30 % of bipolar patients. The prognosis is much better than schizophrenia, but there is a wide variation; some people having their lives repeatedly disturbed, whilst others experience only a single episode. Some individuals have years of normal functioning between episodes. Others have episodes in clusters. Some patients have rapidly cycling episodes. As the disorder progresses, the time between episodes often decreases. After about five episodes, however, the interepisodic interval often stabilizes at 6 - 9 months. Patients with bipolar I disorder have a poorer prognosis than do patients with major depressive disorder.

Treatment of Bipolar Mood Disorder

Short-term treatment (for acute manic or mixed episode):

Manic behavior can be damaging for the patient and others (e.g. loss of career, financial disaster, and sexual insult).
Hospitalization can provide a secure, protective environment. The initial task is to quieten the agitation that commonly occurs. This is usually accomplished with **antipsychotic medication**; typical (e.g. haloperidol 10 - 20 mg or chlorpromazine 400-800 mg) or atypical (e.g. olanzapine 10-20 mg, or risperidone 4-8 mg). They reduce psychotic symptoms and over-activity. Thus, they bring the acute symptoms of mania under control. Haloperidol is a potent antipsychotic, less sedative and causes less postural hypotension compared with chlorpromazine, which is sometimes the drug of choice in mania for its sedative property.
When the manic patient settles (usually within weeks), he can be treated as an outpatient with close observation and frequent assessment. Antipsychotics can then be reduced gradually and carefully.

Long-term treatment

Mood disorders often recur and have relapsing course, thus preventive (prophylactic) treatment is required.

Lithium has been found effective in preventing recurrence of manic-depressive episodes.

Carbamazepine appears to be as effective as lithium in the prophylaxis of bipolar mood disorder, and can be considered in patients who are intolerant of lithium or who respond poorly to lithium (e.g. rapid-cycling mood disorders).

Sodium valproate has been found effective in patients with refractory bipolar illness, even when there has been a poor response to lithium and carbamazepine. Combination of lithium with carbamazepine can be used, particularly in rapid-cycling disorders, and combination of lithium with sodium valproate has been shown to be effective in the treatment of resistant patients.

MOOD STABILIZERS

LITHIUM

Mechanism of action:
The exact mechanism is unknown, however it is thought that it stabilizes neuronal activities (decreases sensitivity of postsynaptic receptors and inhibits release of neurotransmitters). **Before starting lithium**, a note should be made of any other medications taken by the patient and a physical examination should be carried out. Prerequisite laboratory test: Renal functions and electrolytes / Thyroid functions/ ECG if cardiac disease is suspected. Pregnancy test (if indicated).

Contraindications: Renal or cardiac failure / Recent myocardial infarction / Chronic diarrhea sufficient to alter electrolytes. First trimester of pregnancy (fetal cardiac anomalies)

Lithium is not recommended in children.

Side effects:
- Fine tremor/ Gastric discomfort and diarrhea **/**Dry mouth, metallic taste /Fatigue **/**Weight gain
- Reversible hypothyroidism / Reversible nephrogenic diabetes insipidus (polyuria – polydepsia) due to blockade of ADH – sensitive adenylcyclase in distal tubules.
- **Toxicity** (course tremor, ataxia, confusion, diarrhea, vomiting…).

Drug interactions: Several drugs increase lithium concentration and may lead to Lithium toxicity: Thiazide diuretics / Non - steroidal anti – inflammatory drugs (NSAID)/Angiotension - converting enzyme inhibitors e.g. lisinopril / Haloperidol high doses (e.g. 40 mg/day). Lithium may potentiate the effect of muscle relaxants. This is important when a patient undergoes an operation or ECT. It may potentiate extrapyramidal side effects of antipsychotics. It may precipitate 5 - HT syndrome if given with SSRIs.

The recommended plasma concentrations are:
- 0.9 - 1.2 mmol / liter (during acute phase)
- 0.4 - 0.8 mmol / liter (for prophylaxis)

Dose is 300 - 450 mg twice or three times a day.
Plasma concentration requires continuous measurement because the narrow therapeutic index of lithium (therapeutic and toxic levels are close). Toxic levels ≥ 1.5 mmol / liter.
Plasma level should be measured 12 hours after the last dose.

Carbamazepine (Tegretol)

Carbamazepine (Tegretol) was first used to treat epilepsy and trigeminal neuralgia. Then, it has been used for decades as a first-line agent for acute and maintenance treatment for bipolar I disorder**.** Studies suggest that carbamazepine may be especially effective in persons who are not responsive to lithium.
In acute mania: carbamazepine is typically effective within the first 2 weeks of treatment in 50 -70 % of cases.
Prophylaxis: carbamazepine is effective in preventing relapses, particularly among patients with mood disorders and schizoaffective disorders.
It is effective in controlling **impulsive and aggressive** behavior in persons of all ages who are not psychotic (e.g. borderline personality disorders, mentally retarded, head trauma Sequelae).
Doses: starting dose is usually 200 mg two times a day. (in children 100 mg / day). It can be increased gradually to 600 – 1000 mg. Therapeutic concentration for psychiatric indications is 8 – 12 ug per mil.
Side effects: It is relatively well tolerated. The most common side effects are mild and transient; Mild GI (gastric discomfort, nausea, vomiting, constipation, diarrhea, and anorexia) and CNS (sedation, drowsiness, vertigo, blurred vision and ataxia). It occasionally causes syndrome of secretion of inappropriate antidiuretic hormone (SIADH) through activation of vasopressin receptor function (hyponatremia +/- water intoxication).
Rarest but serious adverse effects: hepatitis, pancreatitis, serious skin reactions **(**Stevens-Johnson syndrome**),** and blood dyscrasias (agranulocytosis and aplastic anemia).
Drug Interactions: As a result of prominent induction of hepatic CYP 3A4, It decreases serum concentrations of numerous drugs (e.g. oral contraceptives, warfarin, haloperidol, valproate). When carbamazepine and valproate are used in combination, the dosage of valproate may need to be increased and the dosage of carbamazepine should be decreased, because valproate displaces carbamazepine binding on proteins.
Monitoring for a decrease in clinical effects is frequently indicated because of autoinduction.

Valproate (Depakine Depakene, Depakote): It is used for the treatment of manic episode associated with mood and schizoaffective disorders.

Doses: starting dose is usually 250 mg twice/day. It can be increased gradually to 2500 mg**/**day.
Common side effects include Mild GI (gastric discomfort, nausea, vomiting, and anorexia) and CNS (sedation, drowsiness, dysarthria, and ataxia).
Rarest but serious adverse effects; fatal hepatotoxicity, pancreatitis, and fetal neural tube defects (e.g., spina bifida) , 2-4% in women who take valproate during the first trimester of the pregnancy. Daily folic acid supplements reduce the risk of neural tube defects.

Other anticonvulsants used as mood-stabilizers: Lamotrigine (Lamictal), Topiramate (Topamax), Gabapentin (Neurontin), Pregabalin (Lyrica), Levetiracetam (Keppra), and Tiagabine (Gabitril).

Questions:

1- AQ1: Which episode is favorable to make more benefit from lithium?

A. Psychosis B. Acute depression C. Acute mania D. Generalized anxiety disorders

Ans: C

2- Patient w/ CKD stage 3 and has Bipolar. Which of the following is correct about Lithium in this patient?

A. Contraindications for lithium B. Use lithium until reach end stage renal failure C. Use lithium 3 times daily

Ans: A

3- 24 year old boy office worker presented to the psychiatrist with 1 week history of increased activity irritability, sleep deprivation, over talkativeness, believe of having special power (in short manic episode). no history of any psychiatric illness.

A. bipolar I B. bipolar II C. dysthymic disorder D. substance induced manic episode

Ans: A

4- A 34 y/o male came with 4 days history reduced sleep overconfidence, talkativeness what is the most important immediate management?

A . Clonazepam B . Depot IM haloperidol C . Quetiapine D . Risperidone

Answer: C

5- 25-year-old male with a 2-week history of agitation, unrealistic ambitions and reduced need for sleep. What's the treatment? (Doctor mentioned that they mean the immediate)

A. Carbamazepine B. Olanzapine C. Lithium D. valproic acid

Answer: B

6- A 42-year-old man had 3 episodes of disturbed mood, one of which was characterized by talkativeness and reduced need to sleep. He was admitted to a psychiatry ward and treated with paroxetine. What is the most appropriate drug to be added?

A. Fluoxetine B. Clonazepam C. Clozapine D. Carbamazepine

Answer: D

7- Patient Came with hypomanic features ,other than that she has no sign of depression and doesn't have the full manic feature, what is the next step to do ?

A. Do nothing B. Give her mood stabilizers C. give antipsychotics D. give antidepressant

Answer: A

8- A 38 year old man has 10 year history of bipolar I mood disorder, with no history of chronic medical problems. At present, he suffers a severe major depressive episode with suicidal ideas. His treating psychiatrist decided to hospitalize him for ECT. The psychiatrist was so concerned in this case that ECT may precipitate which of the following?

A. Resistant psychosis. B. Amnestic syndrome. C. Epilepsy D. Manic episode induction

Answer: D

1- Case 4: Video link: https://youtu.be/DrzvsRqlgdc

Scenario:“Lady believes that she is on top of the world and a messenger from Allah and can control the wind”

Q1: List 3 clinical features:

1- grandiose delusions

2-agressive behavior

3- euphoric mood

4- Disinhibited

Q2: List 2 differentials:

Bipolar type 1

Substance induced psychosis

Schizoaffective disorder

Q3:What is your management plan:

Take full history and examination, screen for substance abuse (urine drug screen)

For acute episode: olanzapine or haloperidol

For maintenance: lithium

الحالة الرابعة: إمرأة كلامها كثير وأطراف حديثها متعددة (مرة عن سواق صدمها ومرة عن عمرة ومرة عن اختها) تنط من موOوع

لموضوع بطريقة سريعة .المطلوب:

-اذكر علامتين من اللي شفته بالفيديو؟

-pressure of speech

-flight of ideas

سؤالين تسألها وليه ؟-

-The duration for how long? (If 1 week or more it fit the criteria of manic episode)

-association symptoms like decrease sleep? (Criteria of manic episode)

-Previous episodes or low mood symptoms? (For the dx of Bipolar)

-Take any substance abuse? (Rule out substance induced mania)

التشخيص؟

Bipolar disorder