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Depressive & Mood Disorders

- Introduction/Definitions.
- Major Depressive Episodes/Disorder.
- Postpartum Depression
- Dysthymic Disorder.

Antidepressants

Suicide - Parasuicide

- Manic-Hypomanic-Mixed Episodes.
- Bipolar I & II Disorders

Mood stabilizers

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

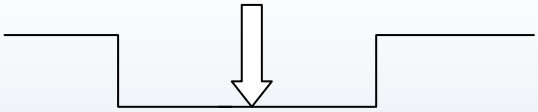
Objective affect: observer's evaluation of expression of affect, through nonverbal signs; facial expression, eye contact, tone of voice, posture & movements.

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

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

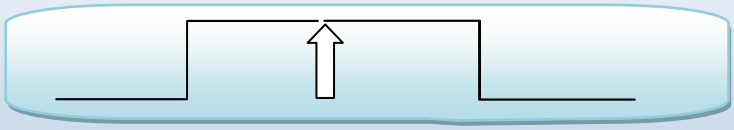
1.Major depressive episode (MDE):

≥ 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:

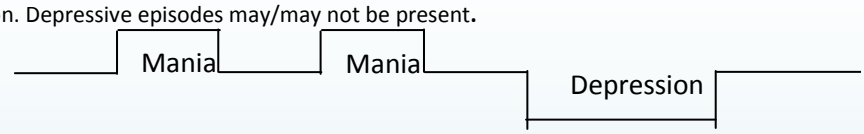
≥ 1 week of both depressed and manic mood + other features

4.Hypomanic episode:

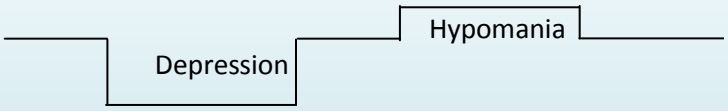
≥ 4 days less severe elevated mood + other features -----  --------

Disorders (longitudinal view / diagnostic term)

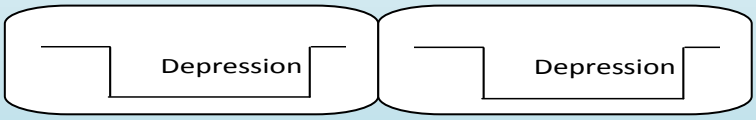
1.Bipolar I disorder: patient has met the criteria for a full manic or mixed episode, usually sufficiently severe to require hospitalization. Depressive episodes may/may not be present**.**



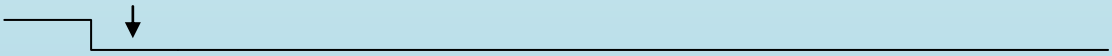
2.Bipolar II disorder: patient has at least one major depressive episode and at least one hypomanic episode, but ***NO*** manic episode.



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).

Depressive features; range / analysis

Appearance & Behavior:
Neglected dress and grooming.
Facial appearance of sadness:
Turning downwards of corners of the mouth.
Down cast gaze**/**tearful eyes/reduced rate of blinking.
Head is inclined forwards.
Psychomotor retardation (in some patients agitation occurs):
Lack of motivation and initiation.
Slow movements**/**slow interactions.
Social isolation and withdrawal.
Delay of tasks and decisions.

Biological Features (Neuro-vegetative Signs): Change in appetite (usually reduced but in some patients increased).
Change in sleep (usually reduced but in some patients increased)
Early morning (terminal) insomnia; waking 2 - 3 hours before the usual time, this is usually associated with severe depression.
Change in weight (usually reduce but may be increased).
Fatigability, low energy level (simple task is an effort). Low libido and /or impotence. Change in bowel habit (usually constipation).
Change in menstrual cycle (amenorrhea).
Diurnal variation of mood (usually worse in the morning).
Several immunological abnormalities (e.g. low lymphocytes) increasing the risk to infection.

Mood (Affective) Changes:
Feeling low (more severe than ordinary sadness).
Lack of enjoyment and inability to experience pleasure (anhedonia).
Irritability /Frustration/Tension

Cognitive Functions & Thinking:
Subjective poor attention, concentration and memory.
In elderly this may be mistaken as dementia ***(pseudo dementia***).
Depressive cognitive triad (pessimistic thoughts) as suggested by Beck;
Present: patient sees the unhappy side of every event (discounts any success in life, no longer feels confident, sees himself as failure). *Past*: unjustifiable guilt feeling and self-blame. *Future*: gloomy preoccupations; hopelessness, helplessness, death wishes (may progress to **suicidal ideation and attempt**).

Psychotic Features Associated with Severe Depression.

A. Hallucinations (mood-congruent)

1. Usually second person auditory hallucinations (addressing derogatory repetitive phrases).
2. Visual hallucinations (e.g. scenes of death and destruction) may be experienced by a few patients.

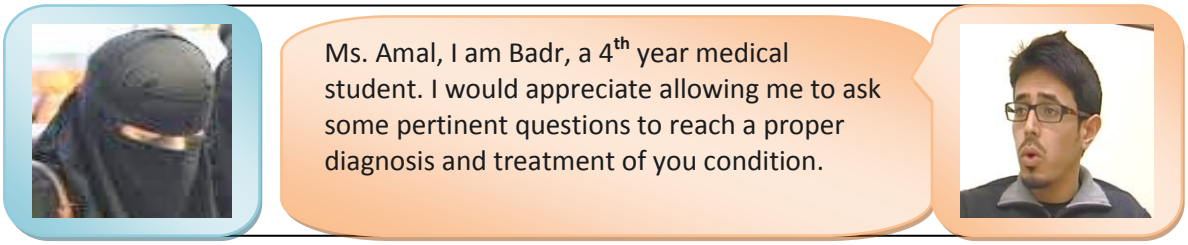
B. Delusions (mood-congruent)

1. Delusion of **guilt** (patient believes that he deserves severe punishment).
2. **Nihilistic** delusion (patient believes that some part of his body ceased to exist or function, e.g. bowel, brain…).
3. Delusion of **poverty** and impoverishment.
4. **Persecutory** delusion (patient accepts the supposed persecution as something he deserves, in contrast to schizophrenic patient).

Diagnostic Criteria for Major Depressive Disorder (MDD)

A. Presence of major depressive episode (s).
B. Not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.
C. There has never been a manic episode, a mixed episode, or a hypomanic episode.

If the full criteria are currently met for a major depressive episode, specify its current clinical status and/or features:
Mild, moderate, severe without psychotic features/severe with psychotic features
Chronic - With catatonic features - With melancholic features
With atypical features - With postpartum onset



What to assess	How to assess
MDE	1. Do you feel marked low mood most of the day for ≥ 2-week period? 2. Do you feel markedly diminished interest or pleasure during the same 2-week period? 3. Do you feel markedly decreased appetite in nearly every day and significant weight loss, when not dieting? Or weight gain. 4. Do you feel markedly disturbed sleep (insomnia or hypersomnia) nearly every day? 5. Do you feel marked fatigue or loss of energy nearly every day? 6. Do you experience feelings of worthlessness or excessive guilt?
MDD / Bipolar MD	1. Have you ever had any similar episode in the past? When/what/for how long/how was it treated? 2. Have you ever had any period of elevated, expansive, or irritable mood? When /for how long/how was it treated?

☐ **Differential Diagnosis of Major Depressive Disorder (MDD) :**

- Depression secondary to ***medical diseases***:

- Hypothyroidism - Diabetes mellitus - Cushing's disease - Parkinson's disease.
- Stroke; see post stroke depression (PSD) p 46.
- Carcinoma (especially of the pancreas and lungs).
- Autoimmune diseases; SLE, multiple sclerosis.

- Depression secondary to ***medications:***

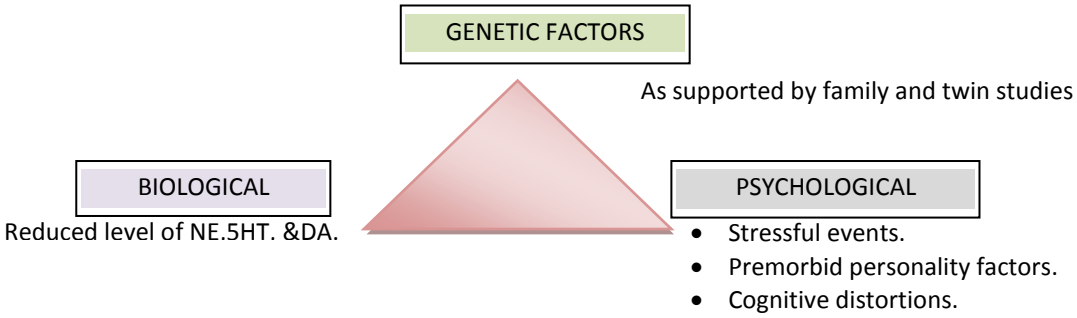
- Antihypertensives (e.g. beta-blockers, methyldopa, reserpine & Ca-channel blockers).
- Steroids.
- Bromocriptine & L - dopa.
- Indomethacin.
- Isotretinoin (Roaccutane); treatment of acne.
- Progestin-containing contraceptives (compared to estrogen-containing contraceptives, which can reduce depression risk).
- Tamoxifen (estrogen-receptor antagonist used in breast cancer): it may induce depression that can be difficult to treat with antidepressants.
- Chemotherapy agents e.g. vincristine, interferon (may induce severe depression with suicidal ideas).
- Antipsychotics.

- Depression secondary to ***substance abuse*** (upon discontinuation of stimulants / cannabis).

- **Psychiatric disorders**:
  - Dysthymic disorder (chronic& less severe depression- see later-).However, both may occur together; dysthymic disorder complicated by major depressive episodes ***(double depression***).
  - Adjustment disorder with depressed mood (see later).
  - *Schizophrenia, schizoaffective disorder.*
  - Somatization disorder
  - Anxiety disorder.

Etiology of MDD:

The causative factors are multifactorial (interacting together);



Epidemiology of Major Depressive Disorder (MDD)

- It is more prevalent than bipolar mood disorder (more in women).
- Lifetime risk is in the range of 10 - 15 %.
- Lifetime prevalence is in the range of 15 - 25 %.
- The mean age of onset is about 40 years (25 - 50 years).
- It may occur in childhood or in the elderly.
- In adolescents, it may be precipitated by substance abuse.
- More common in those who lack confiding relationship (e.g. divorced, separated, single…).

☐ Management of Major Depression: Bio-Psycho-Social Approach.

Hospitalization is indicated for:

- Suicidal or homicidal patient.
- Patient with severe psychomotor retardation who is not eating or drinking (for ECT).
- Diagnostic purpose (observation, investigation…).
- Drug resistant cases (possible ECT).
- Severe depression with psychotic features (possible ECT).

Electroconvulsive therapy (ECT):. The effect of ECT is best seen in severe depression especially with marked biological (neurovegetative), suicidal and psychotic features. It is mainly the speed of action that distinguishes ECT from antidepressant drug treatment. In pregnant depressed patient ECT is safer than antidepressants.

Psychosocial: Supportive therapy. Family therapy. Cognitive-behavior therapy- CBT- ; for less severe cases or after improvement with medication (see later;)

Prognosis of Unipolar Depressive Disorders; About 25 % of patients have a recurrence within a year. Ten percent will eventually develop a manic episode. A group of patients have chronic course with residual symptoms and significant social handicap.

Antidepressants have proven to be very useful in the treatment of severe depression. They shorten the duration in most cases (see antidepressants later).

- **Avoid Tricyclics / Tetracyclics in suicidal patient because of cardiotoxicity in overdose.**

- Selective Serotonin Reuptake Inhibitors **(SSRIs**) e.g. fluoxetine, paroxetine.

-Selective serotonin – Norepinephrine Reuptake Inhibitors **(SNRIs)** e.g. venlafaxine, duloxetine. Other new agents e.g. mirtazapine.

- Desirable therapeutic antidepressant effect requires a period of time, usually 3-5 weeks. Side effects may appear within the first few days.
- After a first episode of a unipolar major depression, treatment should be continued for six months after clinical recovery, to reduce the rate of relapse.
- If the patient has had two or more episodes, treatment should be prolonged for at least a year after clinical recovery to reduce the risk of relapse.
- Lithium Carbonate can be used as prophylaxis in recurrent unipolar depression.

Post-partum Depression

– About 10 - 15 % recently delivered women develop disabling depression within 6 weeks of childbirth (10–14 days after delivery) which if not treated may continue for six months or more and cause considerable family disruption. It is associated with increasing age, mixed feelings about the baby, physical problems in the pregnancy and prenatal period, family distress and past psychiatric history.
– Depressed mood may be associated with irritability, self-blame and doubt of being a good mother, excessive anxiety about the baby's health and death wishes.
– Counseling, additional help with child-care may be needed. Antidepressants or ECT are indicated if there are biological features of depression.

DYSTHYMIC DISORDER (*Persistent Depressive Disorder* in DSM-5)

- Dysthymia (ill-humored) was introduced in 1980 and changed to dysthymic disorder in DSM-IV.
- It was also called "**depressive neurosis**" and "**neurotic depression**" compared to major depression (psychotic or endogenous depression)
- Dysthymic disorder is a chronic depressed mood that lasts most of the day and presents on most days.

Diagnostic Criteria

- ≥ 2 years history of chronic low mood.
- No remission periods more than two months.
- During low mood there should be ≥ 2 out of the following:

2. low energy or fatigue.
3. low self-esteem.
4. feeling of hopelessness.
5. insomnia (or hypersomnia).
6. poor appetite (or overeating).
7. poor concentration or difficulty in making decisions.

- Not better accounted for by any other psychiatric or medical diseases (e.g. major depression, hypothyroidism).
- It leads to impairment in functioning or significant distress.

Differential Diagnosis

This is essentially identical to that of major depression. However, two disorders require consideration:

1. Chronic Fatigue Syndrome / Neurasthenia
• Disabling chronic fatigue of uncertain etiology associated with variable extent of somatic and / or psychological symptoms.
2. Recurrent Brief Depressive Disorder:
Brief (less than two weeks) periods during which depressive features are present with greater severity than that of dysthymic disorder. The course is episodic and recurrent.

Treatment: The most effective treatment is the combination of pharmacotherapy and cognitive or behavior therapy (CBT).

A. Pharmacological:
Selective serotonin reuptake inhibitors (SSRI).
Selective serotonin – Norepinephrine Reuptake Inhibitors(SNRIs) e.g. venlafaxine,duloxetine.
Or Monoamine oxidase inhibitors (MAOI). Avoid combining with SSRI or tricyclic antidepressants.
These groups may be more beneficial than tricyclic drugs in the treatment of dysthymic disorders.

3. Psychological:
Supportive therapy.
Cognitive therapy; to replace faulty negative self-image, negative attitudes about self, others, the world, and the future.
Behavior therapy; to enable the patient to meet life challenges with a positive sense by altering personal behavior through implementing positive reinforcement.

Course and Prognosis

The onset is usually insidious before age 25; the course is chronic. Some patients may consider early onset dysthymic disorder as part of life. Patients often suffer for years before seeking psychiatric help.

About 25 percent never attain a complete recovery

ANTIDEPRESSANTS

Antidepressants have therapeutic effects in depressive disorders but do not elevate mood in healthy people (they are not mood elevators in healthy people but may precipitate mood elevation in patients who have predisposing factors to mood disorders). They are usually commenced in small doses, which are then increased gradually (to reduce the risk of side effects). Sudden withdrawal may lead to restlessness, insomnia, anxiety and nausea. Antidepressant action may take 2-4 weeks to appear. They have to be continued for several months (six months is a usual period) after symptoms have been controlled, to avoid relapse. Some patients may require long treatment (years).

Selective-Serotonin- Reuptake Inhibitors (SSRIs):

E.g. paroxetine (seroxat), fluoxetine (prozac), citalopram (cipram), escitalopram (cipralex), sertraline (lustral), fluvoxamine (faverin). Selectively inhibit serotonin reuptake into presynaptic neurons. No significant interactions with muscarinic, or histaminergic receptors. Relatively safe in overdose.

- **Uses :**
  - Depressive disorders.
  - Anxiety, phobia & panic disorders.
  - Obsessive compulsive disorder.
  - Trichotillomania.
  - Tic disorders.
  - Premature ejaculation.
  - Others.

- **Side Effects:**
  - Gastrointestinal upset, nausea, reduced appetite, diarrhea / constipation.
  - Headache/ irritability/sweating/fine tremor.
  - Sexual dysfunction (delayed orgasm).
  - Insomnia (mainly with Fluoxetine).
  - Sedation (mainly with Fluvoxamine).
  - Withdrawal syndrome (mainly with paroxetine).
  - **Serotonin syndrome**; Rare but serious S/E. It is due to combination of a number of drugs that potentiate brain serotonin function. The most common combination is MOAIs (which inhibit the catabolism of serotonin) with SSRIs, clomipramine and fenfluramine. **Features**; myoclonus, nystagmus, tremor, irritability, confusion, and hyperpyrexia. **Treatment;** Stop Rx and support vital signs.

Selective-Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs):

E.g. Venlafaxine (Effexor-Efexor), desvenlafaxine (Pristiq), duloxetine (Cymbalta).

***Venlafaxine*(Efexor)** has a potential to induce **higher rates of remission in depressed patients** than do the SSRIs. This difference of the venlafaxine advantage is about 6 %. The most common **adverse reactions** are dry mouth, nausea, anorexia, somnolence, dizziness, nervousness, constipation, asthenia, anxiety, blurred vision, abnormal ejaculation or orgasm, erectile disturbances, and impotence. Sweating is also more common with venlafaxine than the SSRIs. Venlafaxine can cause an increase in diastolic BP, but this was seen more often in patients treated with doses of venlafaxine **>** 225 mg /day. ***Desvenlafaxine*(Pristiq) has fewer and less troublesome side effects than venlafaxine.**

Mirtazapine (Remeron)

It increases both NE and 5HT through a mechanism other than reuptake blockade. It is effective for the treatment of depression. It is often combined with SSRIs or venlafaxine to augment antidepressant response or counteract serotonergic side effects of those drugs, particularly nausea, agitation, and insomnia.

Advantages: It is highly sedating, making it a reasonable choice for use in depressed patients with severe or long-standing insomnia. No significant pharmacokinetic interactions with other antidepressants and more likely to reduce rather than cause nausea and diarrhea (the result of its effects on serotonin 5-HT_3 receptors). No effect on sexual functions. **Side effects:** increased appetite, weight gain, and sedation.

Bupropion (Wellbutrin); Norepinephrine and dopamine reuptake inhibitor.
Used as an antidepressant monotherapy, but a significant percentage of its use occurs as add-on therapy to other antidepressants, most commonly SSRIs (it counteracts sexual side effects, sedation, wt. gain).
Advantages: no significant drug-induced orthostatic hypotension, weight gain, daytime drowsiness, withdrawal syndrome or anticholinergic effects.
Side effects: dry mouth, constipation, weight loss, and hypertension in some patients.

Old antidepressants:

Tricyclic Antidepressants (TCAs)

E.g. Amitriptyline, imipramine, clomipramine.

They are of proven effectiveness and commonly used though they have many side effects. They are generally less expensive than other antidepressants.

Uses:

- Depressive disorders.
- Anxiety, phobic disorders and panic disorders.
- Obsessive compulsive disorders (*clomipramine* in particular because it regulates serotonin in the CNS).
- Nocturnal enuresis (imipramine in particular).
- Pruritis (H_1 blockade e.g. doxepin).
- Gastric ulcer (H_2 blockade e.g. amitriptyline)

Side Effects:

- Anticholinergic: constipation, urinary retention, dry mouth , impaired visual accommodation, worsening of glaucoma central anticholinergic toxicity(delirium)
- Antiadrenergic (alpha-receptors):Postural hypotension, delayed ejaculation and drowsiness
- **Others:** sweating, weight gain, arrhythmia, tremor, precipitation of mania in susceptible patients.

- If a patient has insomnia, a sedative tricyclic antidepressant (e.g. amitriptyline or doxepin) is preferred.
- Tricyclics are **dangerous** in overdose and should be avoided with **suicidal patients.**

Monoamine Oxidase Inhibitors (MAOIs)

Because of their serious interactions with tyramine – containing foodstuffs and other drugs, they are almost obsolete nowadays and seldom used as first choice drugs. They have been found effective in patients who have not responded to other antidepressants, those with atypical depression and in patients with phobic and panic disorders. Narcolepsy is another indication.
They should not be given to patients who cannot understand or comply with dietary restrictions.
Side effects:

- Dry mouth/urinary retention/constipation.
- Postural hypotension.
- Sexual dysfunction.
- Headache/ Dizziness/ Tremor.
- Sleep disturbances.
- Weight gain
- Ankle edema.
- Hepatotoxicity.
- Hypertensive crisis.

Patients already on MAOIs should not be started on another type of antidepressant (except in resistant cases, under supervision of a psychiatrist). At least a two- week interval should separate the last dose of any MAOI and initiation of tricyclic or SSRI therapy.

Precautions and Contraindications :

Liver failure. cardiac disease, acute confusional states, Pheochromocytoma, and conditions that require patient to take any of the drugs which interact with MAOIs

Moclobemide (Reversible Inhibitors of Monoamine Oxidase – A "RIMA"

It has clear advantages over conventional MAOIs due to its freedom from tyramine reactions and its quick offset of activity. It is better tolerated than conventional MAOIs or tricyclics.
Side effects include nausea and insomnia.
It must not be combined with SSRI or clomipramine.

SUICIDE (international self-murder) Sui: self, Cide: murder

Ms. Amal's mother reported that; Amal sometimes experiences death wishes, and suicidal ideation.

Common Underlying Factors: Depressive disorder- Substance abuse - Schizophrenia - Personality disorder - Serious chronic physical disease - Social isolation and lack of support - Financial problems

Suicide Methods: Hanging / Shooting / Burning / Poisoning/Rushing in front of running vehicles/Jumping from high places.

Who requires suicide evaluation? Any patient who

- has recently attempted suicide.
- presents with suicidal ideation.
- reveals suicidal ideas only when asked.
- has behavior indicating possible suicidality.

Risk Factors for Suicide: These risk factors should be recognized, assessed and utilized in conjunction with careful clinical assessment in deciding the suicidality of a patient.

1. Age > 45 years old.
2. Male > Female.
3. Separated, divorced, widow > single > married.
4. Previous suicide attempts or behavior.
5. Family history of suicide behavior.
6. Current psychopathologic conditions: Severe depression/Substance abuse/Psychosis/Personality disorder
7. Concurrent serious or chronic medical condition.
8. Lack of social support.
9. Suicide note.
10. Planning with precautions against discovery.
11. Strong intent to die.

Assessment of Suicide Risk

1. **Evaluation of intentions:** Asking about suicidal intentions is very important. It will not make suicide more likely. Sympathetic approach, which also helps the patient feel better understood and hence may reduce the risk of suicide. Systematic enquires (thought/feeing >> intention >> act): Thoughts whether life is worth living/ hopeless towards the future >> any wishes to die >> suicidal ideation >> suicidal intent >> suicidal specific preparatory acts (e.g. planning with precautions against discovery) >> actual suicidal trial.

2. **History of intentional self-harm.** Serious deliberate self-harm. Repeated dangerous attempts. Continuing wish to kill or harm self. Writing a farewell suicidal note.

3. **Presence of mental disorders:** Severe depression with guilt feelings hopelessness and helplessness. Depressed patient may not be able to plan and commit suicide while severely depressed. However, it was found that suicide might occur during recovery from severe depression. Schizophrenia: on recovery from acute phase or in chronic schizophrenic illness. Substance abuse with psychiatric and physical complications. Personality disorders (e.g. borderline personality disorder; these patients have poor impulse control and chronic emotional instability).

4. **Presence of adverse social and medical conditions:** Social factors (e.g. home, work, finances…) should be assessed. Medical problems (especially if they are painful disabling or rapidly deteriorating in spite of medical interventions).

5. **Presence of homicidal ideation:**
   E.g. to kill the spouse, children or parents, in order to spare them intolerable suffering after committing suicide (some severely depressed suicidal patients have homicidal ideas).

youtube.com/watch?v=IkA7TN44Q2Q

youtube.com/watch?v=bXefWSTZ74U

Management of suicide :

- Proper assessment of suicidal risk.
- Every suicidal ideation, impulse, gesture or attempt should be taken seriously.
- Hospitalization: for patients with serious suicidal risk.
  - Prevent access to all means of harm (sharp objects, ropes, drugs…). Search the patient thoroughly.
  - Appropriate close one to one observation: vigilant nursing staff with good communication.
  - Treat any psychiatric disorder (**ECT**/ antidepressants/ antipsychotics)

If the risk does not seem to require hospitalization:

- Counseling /Problem solving/Ensure good support &positive view of the future.
- Relatives: responsible, reliable and understanding.
- Treat underlying psychiatric condition and keep regular follow up visits.

For only limited periods suicidal persons remain suicidal, thus the value of early detection and restrain.

Whatever carefully the correct procedures have been followed, some patients commit suicide.

PARASUICIDE; إيذاء الذات بما دون القتل

PARASUICIDE; also called: "Attempted suicide" & "Non-fatal deliberate self-harm".

Definition: any act of self-damage carried out with the apparent intention of self- destruction; yet ineffective, half-hearted and vague.

- **Etiology**:
  - Impulsive behavior: seen commonly in borderline personality disorder.
  - Unconscious motives: to influence others, a signal of distress or a cry for help seen commonly in histrionic personality disorder.
  - Failed suicide: 25 % of cases.
  - Risks Factors: young (15 – 35 years), commoner in females, personality problems (e.g. borderline personality disorder) and Situational stress (e.g. arguments with parents, spouse…).
- **Methods**:
  - Drugs overdose (e.g. paracetamol) is the most common method.
  - Self-injury e.g. laceration of wrist.
  - Jumping from heights.
- **Management:** each case should be assessed thoroughly;
  - Thoughts /intentions /plans /psychosocial stresses /personality problems /available support/possibility of repetition
- Treat any psychiatric disorder
  - Inpatient or outpatient depending on the case.
- Problem solving and counseling
  - To resolve current difficulties.
  - To deal better with future stresses.
- Prolonged follow up is required for some cases who are at risk of repetition of self-harm and suicide those with personality disorders and long-term adverse psychosocial situations.

youtube.com/watch?v=KY7GKUD31UY

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).

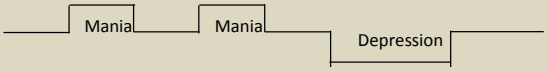
Epidemiology: onset usually 18-30 years. Lifetime prevalence: 1% . ♂ = ♀.

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

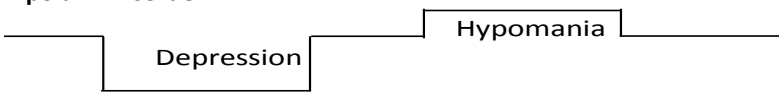
Patients who are having their first episode of bipolar I disorder MDE cannot be distinguished from patients with MDD. Thus, according to DSM-IV-TR, patients must be experiencing their ***first*** manic episode to meet the diagnostic criteria for bipolar I disorder (Bipolar I Disorder, ***Single*** Manic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

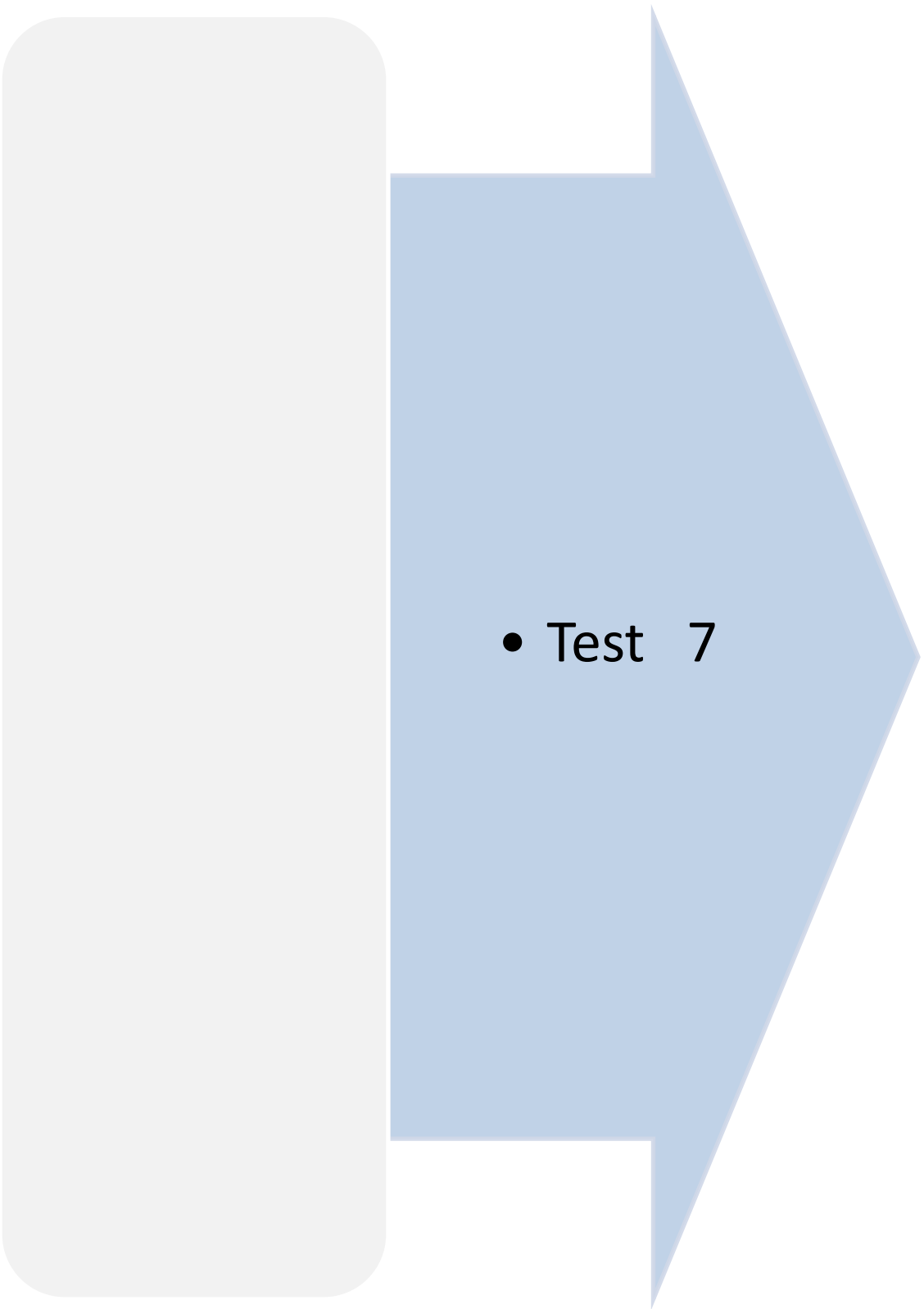
Carbamazepine (Tegretol)

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).


• Test 7

1. A 41-year-old man presented with a 3-week-history of lack of motivation, fatigue, excessive self-blame, poor appetite, social isolation, and delaying his tasks. He has no previous history of psychiatric or medical disorders. What is the most likely diagnosis?
    a. Major Depressive Disorder, recurrent type.
    b. Dysthymic disorder.
    c. Major depressive Disorder, single episode.
    d. Depression due to underlying medical problem.

2. A 27-year-old woman has been suffering lack of enjoyment, low self-esteem, insomnia, poor concentration, and fatigue for more than 3 years. She has no medical diseases. What is the most likely diagnosis?
    a. Bipolar II mood disorder.
    b. Bipolar I mood disorder.
    c. Cyclothymic disorder.
    d. Dysthymic disorder.

3. A 28-year-old university graduate had 3 episodes of disturbed mood one of which characterized by being very energetic, and impulsive to the degree of being admitted to a psychiatry ward where he was treated with Olanzapine 10 mg daily. After discharge, he has been completely normal for the past 4 months. He does not abuse drugs and healthy otherwise. What is the most pertinent drug to add?

    a. Clozapine.
    b. Valproate.
    c. Imipramine.
    d. Alprazolam.

4. A 47-year-old businessman alcoholic for more than 10 years, has marital problems. Recently he lost 3 million SR in the stock market. He became insomniac, and agitated. He sent a message to his wife asking her to forgive him. His son brought him to Emergency Department. What is the most urgent step?

    a. Amitriptyline 50 mg.
    b. Hospitalization.
    c. Lorazepam 2mg.
    d. Reassurance and explanation.

5. A 32-year old man has a long history of a recurrent mental illness maintained on a medication that helped in reducing the number and the severity of his relapses. Three days before, he abruptly discontinued his medication upon the request of a faith- healer. Then, he developed repeated fits. The best management is:

    a. Prescribe him haloperidol 10 mg.
    b. Resume his previous medication
    c. Admit him in the psychiatric ward.
    d. Give him alprazolam 2 mg,3 times/day.

6. A 31-year-old man has been complaining of nausea, abdominal discomfort, loss of appetite, and sexual dysfunction. Three weeks before, his doctor started him on a medication for depression. The most likely medication was:

a. Lamotrigine.
b. Mirtazapine.
c. Risperidone.
d. Paroxetine.

7. A 53-year-old hypertensive man on antihypertensive medications was referred to psychiatry clinic for evaluation of loss of pleasure, poor erection, poor appetite, and disturbed sleep. The most appropriate management step:

a. Start him on paroxetine 50 mg.
b. Investigate him for hypothyroidism.
c. Review side effects of his medications.
d. Add Propranolol to his medications.

8. A 29-year-old woman noticed by her husband, over the last two weeks, to have excessive talking, overambitious ideas, tense mood, and decreased need for sleep. The most appropriate drug is:

a. Procyclidine.
b. Lithium.
c. Quetiapine.
d. Paroxetine.

9. A 26-year-old married man has a 4-year-history of tiredness, low self-confidence, lack of enjoyment, difficulty making decisions, and insufficient sleep. The most appropriate treatment is:

a. Carbamazepine.
b. Amitriptyline.
c. Electroconvulsive therapy.
d. Escitalopram.

10. A 44-year-old woman had 3 episodes of lack of motivation, fatigue, excessive self-blame, poor appetite, social isolation, and chest tightness. Each episode last for about 2 months. What is the most likely diagnosis?

a. Major depressive disorder.
b. Dysthymic disorder.
c. Bipolar mood disorder.
d. Cyclothymic disorder.

Answers:

1	**2**	**3**	**4**	**5**
C	D	B	B	B
6	**7**	**8**	**9**	**10**
D	C	C	D	A