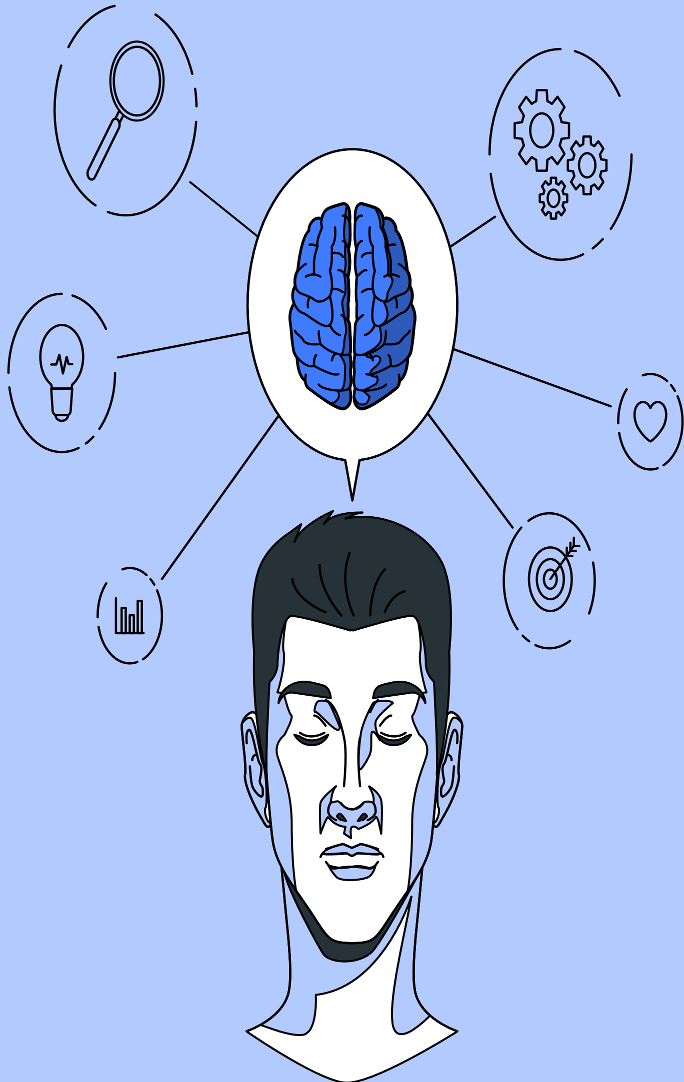
King Saud University

جامعة الملك سعود

MED437 KING SAUD UNIVERSITY



Depressive disorders

Objectives:
Not provided

Done by: Reema Alenezy, Rahaf Althnayan and Norah Alkadi.

Major Depressive Disorder (MDD)

DSM-5 criteria for Major Depressive Episode	
A	**Five (or more)** of the following symptoms during the same two week period and represent a change from previous functioning, at least **one of the symptoms is (1) depressed mood or (2) loss of interest or pleasure**: 1. **Depressed mood** most of the day, nearly every day. 2. Marked **diminished interest or pleasure**. 3. **Significant weight loss** when in all, or almost all, activities, most of the day, nearly every day. We are not talking about diet here. 4. **Insomnia** (not sleeping) or hypersomnia (sleeping all day). 5. **Psychomotor agitation or retardation**. (Thoughts > slow thinking and only having few thought). (Motor > slow movement or restlessness). 6. **Fatigue** or loss of energy. 7. Feelings of **worthlessness or excessive or inappropriate guilt**. Negative self talk. 8. Diminished ability to **concentrate** or **indecisiveness**. 9. Recurrent thoughts of **death**, recurrent **suicidal** ideation, suicide **attempt** or plan.
B	The symptoms cause **significant distress or impairment in functioning**. Any psych illness should be leading to significant distress or impairment in relationship, in work or in studie.
C	The episode is not attributable to the physiological effects of a substance or another medical condition.
D	The occurrence is not better explained by another mental disorder.
E	There has **never been a manic episode or a hypomanic episode**. had If ever been manic or hypomanic then we are talking about bipolar not MDD.

Depressed mood, either:

- **Subjective** report (sad, depressed, empty, hopeless, discouraged, down in the dumps).
- **Observed** by others (apparent tearful).

Other symptoms, include:

- We ask about them even though they are not part of the criteria.

- Boredom.
- Tearful.
- Irritability.
- Anxiety or phobia.
- Excessive worries about physical health.
- Pain.
- Menstrual problems.
- Sexual dysfunction, decrease interest in sex.

Children & adolescent

- Mood can be **irritable** mood.
- Children may refer to depressive feelings in terms of **anger**, or feeling "**mad**" rather than sad.
- Children tend to present with **somatic symptoms**. Like stomach aches or headaches.
- Can have **failure to make expected weight gain** rather than weight loss.

In elderly

- Symptoms of **depression are not part of normal aging**. Never normal in any age group.
- Symptoms compared to adult:
  - **Minimize** sadness. They tend to not talk about it.
  - More **agitation.**
  - **Higher rate of completed suicide** and more **lethal methods.** Very dangerous.

Specifiers

- Things that we take into consideration to help us in the management. Not part of the criteria.

"With melancholic features"specifier:

- A case of very severe depressive symptoms.
- No need to memorize this.

A- One of the following:

1. **Loss of pleasure** in all or almost all activities.
2. **Lack of reactivity** to usually pleasurable stimuli (does not feel better even temporarily when something good happens).

B- **Three (or more)** of the following:

1. Distinct quality of mood (profound despondency, despair, empty mood).
2. Depression is worse in the morning.
3. Early morning awakening (at least 2 hours before usual awakening).
4. Marked psychomotor agitation or retardation.
5. Significant anorexia or weight loss.
6. Excessive or inappropriate guilt.

Melancholic features are more frequent in:

- **Inpatients**.
- More **severe** depressive episodes.
- Those with **psychotic** features.
- **Older** individuals.

"With Psychotic features" specifier:

Delusions (unusual through to and beliefs) **and or hallucinations** (unusual experiences related to senses) are present:

- **Mood-congruent** psychotic features: content of the delusions and hallucinations consistent with depressive themes (guilt, inadequacy, etc.).

- **Mood-incongruent** psychotic features: does not involve typical depressive themes. Like when the Pt. Says that he/she have special powers for example.

“With atypical features” specifier:

- The typical features are the ones mentioned in DSM-5 criteria.

A. Mood **reactivity** (mood brightens in response to positive events).

B. **Two (or more)** of the following:
   1. Significant weight gain or increase in appetite.
   2. Hypersomnia.
   3. Leaden paralysis (heavy, leaden feelings in arms or legs).
   4. Long Standing pattern of interpersonal rejection sensitivity causing functional impairment.

C. Criteria are not met for "with melancholic features" or "with catatonia"

- Atypical features may be more **common in Bipolar Depression** than MDD.

- Compared with patients with typical depression features, the patients with atypical features are;
  - found to have a **younger** age of onset.
  - have **long-term** course.
  - more frequent **coexisting diagnosis** of panic disorder, substance abuse or dependence, and somatization disorder.

“With catatonia” specifier:

- Diagnosis of group of symptoms that appear in bipolar, depression and psychosis.

- **3 (or more)** of the following symptoms:
  - Stupor (no psychomotor activity). No movement at all.
  - Catalepsy (passive induction of a posture held against gravity). If you position the pt. They will stay in that position.
  - Waxy flexibility (slight resistance to positioning by examiner).
  - Mutism. Not talking at all.
  - Negativism (no response to instructions or external stimuli).
  - Posturing (spontaneous adoption of posture against gravity). If the pt. Position themselves in a certain position and freeze. Active not passive.
  - Mannerism (odd caricature of normal actions). Non goal directed movement.
  - Stereotypy (repetitive, abnormal non-goal directed movements).
  - Agitation.
  - Grimacing. العبوس
  - Echolalia. Mimicking others talking.
  - Echopraxia (mimicking another's movements).

“With peripartum onset” specifier:

- If mood symptoms occur **during pregnancy** or in the **4 weeks following delivery.**

Epidemiology

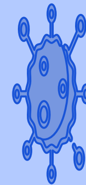
- MDD is among the **leading causes of global disability**.

- Prevalence in adults:
    - Lifetime: approximately 10 to 17 %.
    - 12-Month: approximately 4-7 %.

- Gender:
    - In adult: 1.5-3:1 **F**:M ratio.
    - Age of Onset: Incidence **peaks in 20s**, likelihood increases markedly after puberty, but can still have first onset in late life (onset **later than for BAD**). Bipolar starts earlier (teenage years). They come first with depression not mania or hypomania, with time we realize it is in fact bipolar.

Differential Diagnosis

Medical Conditions:



- Hypothyroidism.
- Cushing's Disease or Addison's disease.
- Anemia, Vitamin B12 or Folate Deficiency.
- Infectious Etiology: Mononucleosis, HIV, etc.
- Pancreatic cancer, brain tumors and other neoplasms.
- Epilepsy.
- CVA.
- Multiple Sclerosis.
- Parkinson's Disease.

Substance Induced:

- Stimulants withdrawal: Amphetamine, MDMA, Cocaine.
- Sedatives: Alcohol, benzodiazepines, barbiturates. Occurs in chronic use of these substance.
- Medications induced. Like corticosteroids and immunosuppressants.

Differential Diagnosis (Cont.)

Grief

Will be explained in anxiety lecture

- Affect is feelings of **emptiness and loss**. Not sadness.
- **Dysphoria** likely **decrease in intensity over days to weeks**. Pt. Is still functioning to a certain degree unlike MDD.
- Functional impairment is usually **transient**.
- May be accompanied by **positive emotions and humor**.
- In grief, self-esteem is usually **preserved**.
- If thoughts about death and dying, limited to **thoughts of joining the deceased** but **not on ending one's life because of worthlessness or pain of depression**.
- Survivor **does not have** morbid feelings of **guilt** and **worthlessness**, **suicidal ideation**, or **psychomotor retardation**.

Adjustment Disorder

Will be explained in anxiety lecture

- When you have a clear stressor.
- Does not fulfill the criteria (pt. have some symptoms).
- Pt. most likely will recover after the stressor is removed.

- Some symptoms overlap.
- Doesn't involve as many of the physical and emotional symptoms of clinical depression.
- Less levels of severity.

Schizoaffective Disorder

- Pt. sometimes fulfill the criteria of schizophrenia other times fulfill criteria of MDD or bipolar.

DSM-5 criteria for schizoaffective disorder	
A	An uninterrupted duration of illness during which there is a **major mood episode (manic or depressive) in addition to criterion A for schizophrenia**; the major depressive episode must include depressed mood. - Criterion A for schizophrenia is as follows: Two or more of the following presentations, each present for a significant amount of time during a 1-month period (or less if successfully treated). At least one of these must be from the first three below. 1. Delusions. 2. Hallucinations. 3. Disorganized speech. 4. Grossly disorganized or catatonic behavior. 5. Negative symptom
B	**Hallucinations and delusions for two or more weeks in the absence of a major mood episode** (manic or depressive) during the entire lifetime duration of the illness. In MDD or bipolar you treat and everything goes away.
C	Symptoms that meet the criteria for a major mood episode are present for the majority of the total duration of the active as well as residual portions of the illness.
D	The disturbance is not the result of the effects of a substance (e.g., a drug of misuse or a medication) or another underlying medical condition.

ADHD (Attention deficit hyperactivity disorder):

- Onset of clear-cut symptoms before age 7.
- Onset of hyperactivity or disruptive behaviors.
- Continuous.
- Family history of disruptive disorders.

Other differential diagnoses, include:

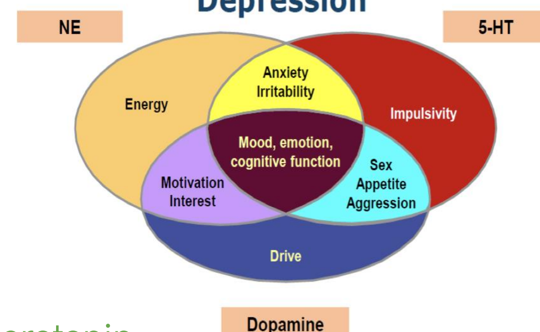
- Normal Sadness.
- Dysthymia.
- Bipolar I & Bipolar II Disorder.
- In elderly, consider: electrolyte imbalance, glucose abnormality, and pain..

Risk factors

- Early-Onset adversity.
- Stressful life events.
- Family history (first degree relatives have 2-4x greater chance of having MDD).
- Female gender.
- Neuroticism (negative affectivity). Negative thinking.
- Chronic medical conditions.
- Substance use.
- Anxiety disorders. Long standing.
- Certain personality disorders.

Depression & neurotransmitters

Functional Overlap Between Aminergic Systems: Features of Depression



- 5-HT is serotonin.

Courtesy of S.M. Stahl

Scales

- No need to memorize them.
- Evaluation tools. Never used to diagnose. Diagnosis is clinical.

Self-report scales, such as:

- Beck Depression Inventory II (BDI-II).
- Zung Self-Rating Depression Scale.
- Patient Health Questionnaire (PHQ-9).
- Quick Inventory for Depressive Symptomatology, Self- Rated(QIDS-SR).

Clinician Rated Scale, such as:

- Hamilton Depression (HAM-D).
- Montgomery-Asberg Depression Assessment Scale (MADRAS).
- Inventory for Depressive Symptomatology (IDS).

Comorbidities

- Substance Use Disorders.
- Anxiety Disorders. Most common.
- Eating Disorders.
- Borderline Personality Disorder.
- Attention-deficit/hyperactivity disorder (ADHD), Learning disabilities, oppositional defiant disorder, and conduct disorder.

- Men more frequently present with substance use disorders.
- women more frequently present with comorbid anxiety and eating disorders.

Prognosis

- Untreated depressive episodes last **6 to 13 months**, treated episodes last **3 months**. These is a significant difference.
- Course is quite **variable**, but 80% will recover within 1 year.
- Can get both absenteeism and presenteeism at work.
- About two-thirds of all depressed patients contemplate suicide and 10 to 15 percent commit suicide.
- **MDD increases the risk of Type II diabetes** and is an independent risk factor for cardiovascular disease and mortality.
- Increased rates of emphysema, COPD, migraine, multiple sclerosis, back problems, cancer, epilepsy, asthma, stroke, thyroid disease, diabetes, and heart disease in patients with MDD.

Low recovery rate, with:

- Long duration of current episode.
- Symptom Severity.
- Psychotic features.
- Prominent anxiety.
- Personality Disorders.

Risk of recurrence, with:

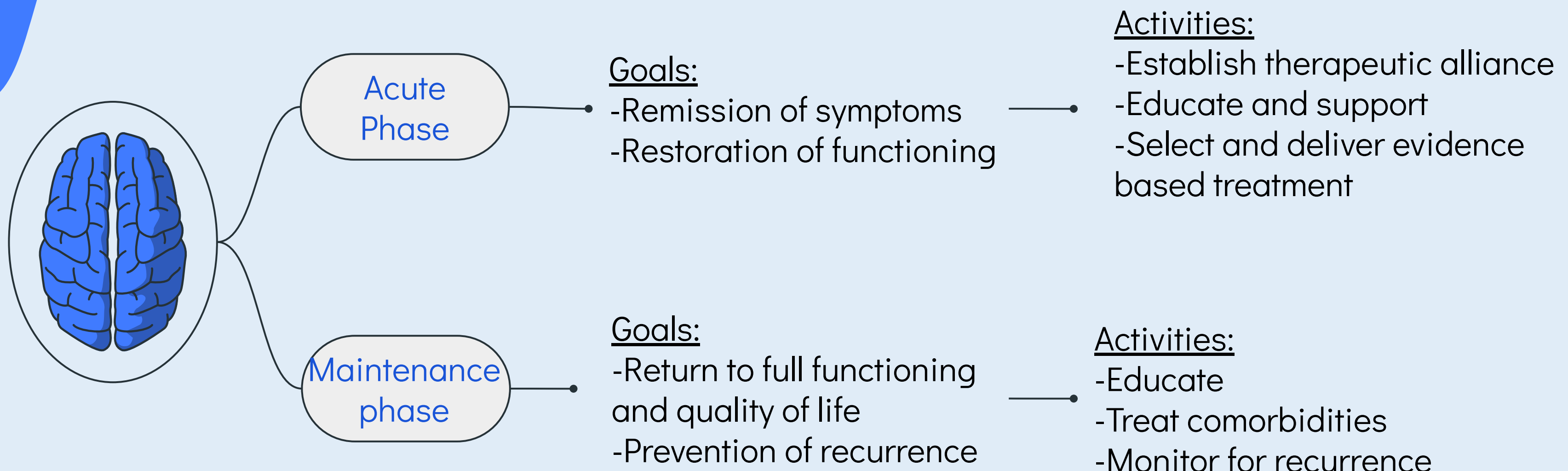
- Multiple prior episodes.
- Previous severe episode.
- Mild depressive symptoms persist during remission. That is why our goal in treatment is full recovery (zero symptoms).
- Younger individuals.

Residual symptoms:

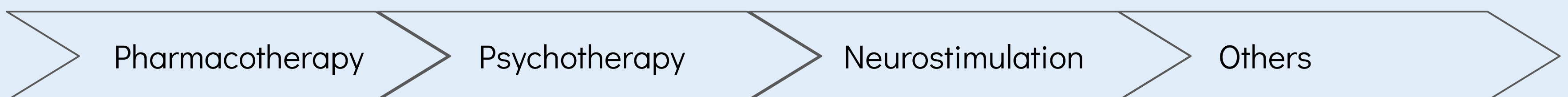
- The least common residual symptoms are **depressed mood**, **suicidality**, and **psychomotor retardation**.

Management

Phases of treatment



Treatment Modalities:



Pharmacotherapy

Antidepressant choice based on multiple factors:

- Patient preference
- Past response
- Drug-drug interaction
- Comorbid Disorders
- Side-effect profile and tolerability
- Cost
- Availability

Length of Treatment:

Risk factors supporting long-term (***2 years*** to lifetime) antidepressant maintenance:

- ***Older*** age
- ***Recurrent*** episodes
- ***Chronic*** episodes
- **Psychotic** Episodes
- ***Severe*** episodes
- ***Difficult to Treat*** Episodes
- Significant ***Comorbidity*** (psychiatric or medical)
- ***Residual*** Symptoms (during remission)
- History of ***recurrence during discontinuation*** of antidepressant

Major medication classes:

-SSRI (Selective serotonin reuptake inhibitors)

-SNRI (Serotonin–norepinephrine reuptake inhibitors)
- VENLAFAXINE, DULOXETINE, and DESVENLAFAXINE

-MAOIs (Monoamine oxidase inhibitor)

-TCA (Tricyclic antidepressants)

-Others
- (bupropion, mirtazapine, trazadone)
- Other newer medications

Adjunctive agents:
- Certain antipsychotics
- Lithium
- T3
- Stimulants
- Others

Major medication classes

Medication Class	SSRIs	MAOIs	TCAs
Mechanism of Action	Selectively block reuptake of 5-HT	Inhibit the metabolism of neurotransmitters DA, NE, 5-HT	Affect multiple receptor systems
Notes	**Include:** -Fluoxetine -Sertraline -Paroxetine -Fluvoxamine -Citalopram -Escitalopram **Compared to MAOIs and TCAs;** -Less cardiotoxicity -More sexual dysfunction	**Common uses:** **-Atypical depression** -Refractory patients **Most of the medications in this class, needs dietary monitoring** (especially types of cheese) NB: Not used as first line because many side effects and drug interactions.	-Multiple side effects (not 1st line) -Several drug- drug interactions **-Lethal in overdose (arrhythmias; seizures)** (Avoid TCAs in suicidal patients) Helpful in cases of (physical symptoms): -Pain -Fibromyalgia -Migraine -Sedative/hypnotic -Severe depression
Common Side Effect	-GI side effects (nausea, vomiting, diarrhea, appetite, weight) -headache -Insomnia -Sexual dysfunction -Agitation, restlessness, anxiety	-Cardiovascular (orthostatic hypotension, peripheral edema) -Weight gain -Sexual side effects -Neurological (headache, insomnia, sedation, paresthesias) -Other (dry mouth, constipation, urinary hesitancy) (anticholinergic side effects)	-Drowsiness, dizziness, falls, fracture **-Cardiac side effects** -Blurred vision, mydriasis (pupillary dilation) -Dry mouth -Constipation -Urinary retention -Memory impairment -Sexual dysfunction -Fever -Weight gain -Neurological side effects (myoclonus, confusional state, **seizure** in **overdose**)
Other Side Effects	-Serotonin syndrome -Abnormal bleeding (Caution with anticoagulants, NSAIDs, ASA) -Cardiotoxicity (citalopram, escitalopram) -The syndrome of inappropriate antidiuretic hormone secretion (SIADH)	**Hypertensive crisis:** (When taking MAOIs with interacting foods or drugs) • Hypertension, neurological symptoms, fever, nausea, palpitations, tachycardia, cardiac arrhythmias, confusion • Possibly CVA and death **Serotonin syndrome:** (psychiatric emergency) • neurological symptoms, GI symptoms, restlessness, MSE changes, confusion, tachycardia, hypertension, fever • In severe form: Hyperthermia, rhabdomyolysis, renal failure, cardiovascular shock, coma, seizures, death	

Other Treatment Modalities

<table>
<tr><td>Psychotherapy</td><td colspan="2">-Several modalities exists
-Examples:
● CBT (cognitive behavioural therapy) *GOLD STANDARD*
● IPT (interpersonal therapy)
● Behavioural activation
● Others</td></tr>
<tr><td rowspan="2">Neurostimulation</td><td colspan="2">Include:
-ECT (electroconvulsive therapy)
-rTMS (repetitive transcranial magnetic stimulation)
-others</td></tr>
<tr><td>ECT

A medical procedure that is delivered under controlled conditions (general anesthesia). It involves the use of electrical stimulus to depolarize cerebral neurons thereby produce a generalized seizure

Helpful in; (strong tx used in severe cases)
● Elderly
● Psychotic depression
● Catatonia
● Severe depression
● Treatment resistant depression</td><td>rTMS

Compared to ECT:
-No anesthesia
-No negative effects on neurocognitive functioning
-No driving restrictions
-Does not affect memory (unlike ECT)

Used mainly for treatment resistant depression that is not necessarily severe.

NB. Use in patients with mild/moderate depression that is not responding to medication (2-3 trials) and do not want to do psychotherapy.</td></tr>
<tr><td>Other Therapies</td><td colspan="2">● Exercise (3 times per week, moderate intensity, 45 minutes each time. More useful in mild/moderate depression)
● Light therapy (high intensity lights of certain specifications. Used more in colder countries were daylight (sun) is scarce during the winter)
● Others</td></tr>
</table>

Other Depressive Disorders

1- Persistent Depressive Disorder (Dysthymia) Chronic depressio

A. **Depressed mood** for most of the day, for more days than not, as indicated by either subjective account or observation by others, **for at least 2 years**

B. **Presence, while depressed, of two (or more)** of the following:
   1. Poor appetite or overeating
   2. Insomnia or hypersomnia
   3. Low energy or fatigue
   4. Low self-esteem
   5. Poor concentration or difficulty making decisions
   6. Feelings of hopelessness

C. During the 2-year period (1 year for children or adolescents) of the disturbance, **the individual has never been without the symptoms in Criteria A and B for more than 2 months at a time**

D. Criteria for a major depressive disorder may be continuously present for 2 years

E. There has **never been a manic episode or a hypomanic episode,** and criteria have **never been met for cyclothymic disorder**

F. The disturbance is **not better explained** by other mental illnesses such as schizoaffective disorder, etc.

G. The symptoms are **not attributable** to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hypothyroidism).

H. The symptoms cause **clinically significant distress or impairment** in social, occupational, or other important areas of functioning.

2- Substance/ Medication- Induced Depressive Disorder

Diagnostic Criteria

A. A prominent & persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities.

B. There is evidence from the history, physical examination, or laboratory findings of both (1) and (2):

   o The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to a medication.

   o The involved substance/medication is capable of producing the symptoms in Criterion A.

C. The disturbance is not better explained by a depressive disorder that is not substance/medication-induced.

D. The disturbance does not occur exclusively during the course of a delirium. (delirium is acute)

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

NB. When diagnosing make sure to add “Due to (particular drug)”. Eg. “Substance-Induced Depressive Disorder due to cocaine intoxication”

Other Depressive Disorders Cont

3- Depressive Disorder Due to Another Medical Conditio

Diagnostic Criteria:

A. A prominent and persistent period of depressed mood or markedly diminished interest or pleasure in all, or almost all, activities that predominates in the clinical picture

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

Examples;

- Neurological: (stroke, Huntington's disease, multiple sclerosis, Parkinson's disease, traumatic brain injury)
- Endocrinological: (Cushing's disease, hypothyroidism)
- Others

4- Other Specified Depressive Disorder

This category applies to presentations in which symptoms characteristic of a depressive 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 depressive disorders diagnostic class.** The other specified depressive 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 depressive disorder.**

Examples:

- Short-duration depressive episode
- Depressive episode with insufficient symptoms

5- Unspecified Depressive Disorder

This category applies to presentations in which symptoms characteristic of a depressive 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 depressive disorders diagnostic class.** The unspecified depressive disorder category is used in **situations in which the clinician chooses not to specify the reason that the criteria are not met for a specific depressive disorder,** and includes presentations for which there is insufficient information to make a more specific diagnosis (e.g., in emergency room settings)

Summary

Major depressive disorder;

- Is a **major psychiatric illness** that can affect several life domains
- In adults, it tends to occur more in **female** than males
- Its onset is **later than for BAD (bipolar disorder)**
- **Psychiatric and medical comorbidities** are common
- About **10 to 15 percent of depressed patients commit suicide**
- 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

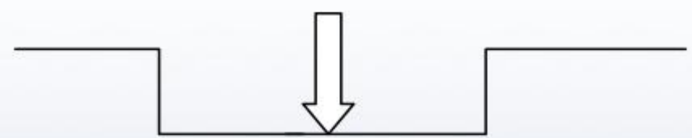
Objective affect: observer's evaluation of expression of affect, through nonverbal signs; facial expression, eye contact, tone of voice, posture & movements.

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:

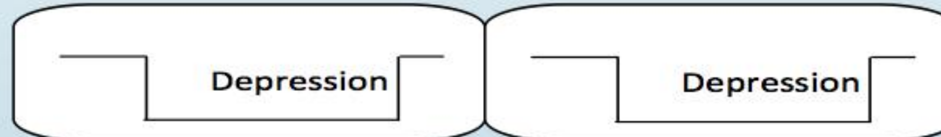
≥ 4 days less severe elevated mood + other features

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).

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

Ms. Amal, I am Badr, a 4th year medical student. I would appreciate allowing me to ask some pertinent questions to reach a proper diagnosis and treatment of you condition.

What to assess	How to assess
MDE	1. Do you feel marked <u>low mood</u> most of the day for ≥ 2-week period? 2. Do you feel markedly <u>diminished interest</u> or <u>pleasure</u> during the same 2-week period? 3. Do you feel markedly <u>decreased appetite in nearly every day</u> and significant weight loss, when not dieting? Or weight gain. 4. Do you <u>feel markedly disturbed sleep</u> (insomnia or hypersomnia) nearly every day? 5. Do you feel <u>marked fatigue or loss of energy</u> nearly every day? 6. Do you experience feelings of <u>worthlessness</u> or excessive <u>guilt</u>?
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?

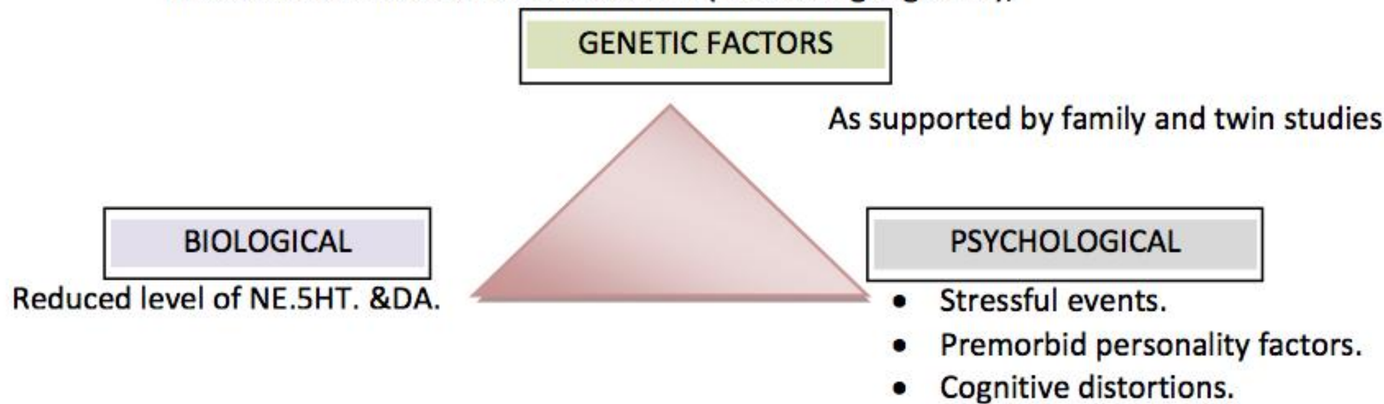
☐ **Differential Diagnosis of Major Depressive Disorder (MDD) :**

- <u>Depression secondary to ***medical diseases***</u>:
- 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.
- <u>Depression secondary to ***medications:***</u>
- 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.
- <u>Depression secondary to ***substance abuse***</u> (upon discontinuation of stimulants / cannabis).

- <u>**Psychiatric disorders**</u>:
  - 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);



- Stressful events.
- Premorbid personality factors.
- Cognitive distortions.

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.

B. 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.

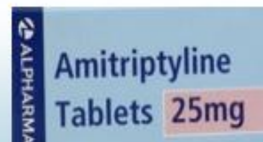
Advantages: It is highly sedating, making it a reasonable choice for use in depressed patients with severe or long-standing insomnia. No significant pharmacokinetic interactions with other antidepressants and more likely to reduce rather than cause nausea and diarrhea (the result of its effects on serotonin 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.

Questions:

1- You were consulted in 12 Y/O girl that the doctor want to diagnose her with MDD, Which of the following mood features is acceptable to be instead of low mood?"

A. Euphoric B. Irritability C. Elated D. Euthymic

Ans: B

2- 30 married male has 5-years history of low mood and lose of interest what is your management?

A. CBT B. Psychoanalysis C. Gradual exposure D. Marital therapy

Ans: A

3- A 41-year-old man has 3 months history of severe major depressive episode with very poor appetite, weight loss. What is the best rapid treatment?

A. Behavioral therapy B. Cognitive therapy C. ECT D. Escitalopram

Answer: C

4- A woman came with seasonal recurrent major depressive disorder, what is the treatment of choice?

A. Fluoxetine B. Fluvoxamine C. Paroxetine D. Sertraline

Answer: A

5- A 23-year-old single Saudi female presented with a two weeks history of anhedonia, late insomnia and weight loss. Before starting the treatment, what would be the most relevant step?

A. Ask about visual hallucinations. B. Ask about family history of depressive disorders. C. Ask about past history of manic episode. D. Ask about pregnancy.

Answer: C

6- A 43-year-old married man has a 9-year history of mild low mood, reduced interest, lethargy and hesitation. What is the most appropriate management?

A. CBT. B. Clomipramine. C. Imipramine. D. Interpersonal psychotherapy

Answer: A

7- A 45 years old patient presented to the psychiatry clinic complaining of ejaculating quickly. Which drug would you give to treat his condition ?

A. Bupropion B. Sildenafil C. Amitriptyline D. Paroxetine

Answer: D

9- Patient Came with chronic episodic depression lasting 3 years, the episode lasts for not more than 2 weeks, which of the following is the dx?

A. Dysthymic disorder B. Recurrent brief depressive disorder C. major depressive disorder D. bipolar

Answer: B

10-Patient with chest tightness, agitation, insomnia, weight loss and delusion of self accusation, what is the treatment of choice for him?

A. Clozapine B. Carbamazepine C. Paroxetine

Answer: C

11- Patient came to you with second person auditory hallucinations and visual, he claims he sees scenes of death and destruction,which of the following is associated with this psychotic features?

A. Bipolar type 1 B. Bipolar type 2 C. severe depression D. Dysthymic disorder

Answer: C

12-: Patient Came with chronic episodic depression lasting 3 years, the episode lasts for not more than 2 weeks, which of the following is the dx?

A. Dysthymic disorder B. Recurrent brief depressive disorder C. major depressive disorder D. bipolar

Answer: B

13-: Patient diagnosed with depressive disorder ,now comes to you complaining of insomnia, which of the following SSRI drugs best to treat his problem?

A. fluvoxamine B. fluoxetine C. escitalopram D. paroxetine

Answer: A

14- Patient Came to you complaining of hypersomnia weight gain and increased fatigue, he claims that it always come in the winter but when the summer begins his symptoms go away. How would you treat this Patient .?

A. give him artificial light B. give him antidepressant C. give him antipsychotic D. do nothing

Answer: A

15-: A mother of 3 children came to you complaining of hopelessness, crying and agitation for 1 month, she says it started after her uncle came to live with her and her husband, what is the most likely dx?

A. Adjustment disorder B. acute stress disorder C. Dysthymic disorder D. major depressive disorder

Answer: A

16: a 35.year old women with Rheumatoid arthritis presented in psychological clinic with Low mood, poor concentration, low appetite and insomnia. Which of the following drug is the best in management?

A. Amitriptyline B. Olanzapine C. Fluoxetine D. Lorazepam

Answer: A Because of the sedative effect

17: What does it mean to have double depression?
A. Depression caused by medications over one developed by substance
B. Depression caused by physical illness over one developed by medications
C. Two major depressive episodes occurring at the same time D. One major depressive episode over persistence depression
Answer: D

1. A depressed man is lying on the couch with a debilitating illness (possibly paralyzed) crying while telling the doctor he feels very sad and useless. He mentioned suicidal ideation.

Give observations you would find in his MSE.

poor grooming, sad facial expression, Avoid eye contact, psychomotor retardation, low and depressed mood, low blinking.

Give 2 differential diagnoses and why?

Major depression disorder (due to his sadness, debilitating medical condition and suicidal ideation)

Bipolar disorder (it could be that he has bipolar but in depressed episode)

Case three- رجل أتى إلى الدكتور يشتكي من حزن شديد وسبب هذا الحزن وفاة أخته وقال ياليت لو أني ميت ولكن لم تأتيه أفكار الإنتحار:

1- Ask 3 questions you would like to ask in history and why?

-Duration and When did she die? (To see if it undergo with normal stages of bereavement or not)

-How did she die? (Possible ASD or PTSD)

-Does the pt have loss of interest or low mood or feeling of guilt? (Rule out depression)

2- Give two differential diagnosis?

-Normal physiological response (grief/bereavement)

-Depressive disorder

كانت مقابلة الدكتور الصغيّر مع واحد يقول صار حزين وما في شي يفرحه مثل اول من ٥ سنين بس انه ما في محاولات أو أفكار انتحارية.

What will you ask? Any hypomania episode? (To Exclude cyclothymic disorder)

Affect his functioning level in life significantly? (To assess the severity)

Medical Hx of chronic disease? (To Exclude other medical causes)

DDX?

Dysthymic disorder

Cyclothymic