433 Teams

# PSYCHIATRY

Lecture 1

## Major depressive disorder (MDD)

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**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.

## Depressive Disorders (DSM-5)

1. **Major Depressive Disorder, Single and Recurrent Episodes**
2. **Persistent Depressive Disorder (dysthymic Disorder & chronic major depressive disorder)**
3. **Disruptive Mood Dysregulation Disorder**
4. **Premenstrual Dysphoric Disorder**
5. **Substance/Medication-Induced Depressive Disorder**
6. **Depressive Disorder Due to Another Medical Condition**
7. **Other Specified Depressive Disorder**

## ☒ Major depressive disorder (MDD):

### ❖ Etiology of MDD:

The causative factors are **multifactorial** (interacting together);

- ✓ **GENETIC FACTORS** : As supported by family and twin studies
- ✓ **BIOLOGICAL** : Reduced level of NE,5HT, &DA.
- ✓ **PSYCHOLOGICAL** : Stressful events.

### ❖ Epidemiology

- more prevalent than bipolar mood disorder (**more in women**).
- The mean age of onset is about **40 years** (25 - 50 years).
- In adolescents, it may be precipitated by substance abuse.
- More common in those who **lack confiding relationship**

## ❖ Signs and symptoms

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).

## ❖ Episodes

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

## ❖ Depressive features;

- **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 libido and /or impotence.

- ✓ Change in bowel habit (usually constipation).
- ✓ (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).

## ❖ Differential Diagnosis of Major Depressive Disorder (MDD) :

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

- **Hypothyroidism** - Diabetes mellitus - Cushing's disease - Stroke
- **Parkinson's disease**. - 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).However, both may occur together; dysthymic disorder complicated by major depressive episodes *(double depression*).
  - Adjustment disorder with depressed mood.
  - *Schizophrenia, schizoaffective disorder.*
  - Somatization disorder
  - Anxiety disorder.

## ❖ 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

- **Pharmacological**:

✓ **Antidepressants** have proven to be very useful in the treatment of severe depression. They shorten the duration in most cases .

- ✓ 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.

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

### ❖ Prognosis of Unipolar Depressive Disorders;

About 25 % of patients have a recurrence within a year. Ten percent will eventually develop a manic episode.

## ☒ DYSTHYMIC DISORDER

### ❖ 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:

- ✓ low energy or fatigue.
- ✓ low self-esteem.
- ✓ feeling of hopelessness.
- ✓ insomnia (or hypersomnia).
- ✓ poor appetite (or overeating).
- ✓ poor concentration or difficulty in making decisions.

**It leads to impairment in functioning or significant distress.**

### ❖ Differential Diagnosis

**1. Chronic Fatigue Syndrome / Neurasthenia**
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**.
- Monoamine oxidase inhibitors (MAOI).

**Avoid combining with SSRI or tricyclic antidepressants.**

**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.**
- ✓ About 25 percent never attain a complete recovery

## ☒ 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.**

## ☒ ANTIDEPRESSANTS

- ✓ Antidepressants have therapeutic effects in depressive disorders but **do not elevate mood in healthy people**
- ✓ they 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.
✓ 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-HT3 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 (H1 blockade e.g. doxepin)**.**
  - Gastric ulcer (H2 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.
- ✓ 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.

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

- **Precautions and Contraindications :**
  Liver failure. cardiac disease, acute confusional states, Pheochromocytoma

- **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**

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