433 Teams

PSYCHIATRY

1. Depression

Lecture contents:

1. Introduction/Definitions
2. Major Depressive Episodes/Disorder
3. Postpartum Depression
4. Dysthymic Disorder
5. Antidepressants Disorders
6. Clinical assessment (OSCE)

- Manual of Basic Psychiatry
- Doctor's notes
- Important

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1. Introduction and Definitions

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.
- ✓ 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.

- **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.
- **Objective affect:** observer's evaluation of expression of affect, through nonverbal signs; facial expression, eye contact, tone of voice, posture & movements.
- **Subjective affect:** one's verbal expression of feelings.

- **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.

2. Major Depressive Episode (MDE)

Major depressive episodes if more than one time = disorder

MDE, which can be a presentation of MDD, Bipolar I or Bipolar II disorders.

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.	5. Psychomotor agitations or retardation.
2. Loss of interest in pleasurable activities (anhedonia).	6. Fatigue or loss of energy.
3. Appetite or body weight change (increased or decreased).	7. Feelings of worthlessness or excessive guilt.
4.Insomnia or hypersomnia.	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.

Mood (Affective) Changes:

- ✓ Feeling low (more severe than ordinary sadness).
- ✓ Lack of enjoyment and inability to experience pleasure (anhedonia).
- ✓ Irritability /Frustration/Tension
- ✓ 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).
- ✓ Delay of tasks and decisions.
- ✓ Diurnal variation of mood (usually worse in the morning).
- ✓ Several immunological abnormalities (e.g. low lymphocytes) increasing the risk to infection.

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).
- ✓ **Severe depression with psychosis usually present with auditory hallucinations**

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.

Differential Diagnosis of Major Depressive Disorder (MDD) :

Depression secondary to medical diseases:

- ✓ Hypothyroidism - Diabetes mellitus - Cushing's disease - Parkinson's disease.
- ✓ Stroke; **50% of stroke patients would get 2ry depression**
- ✓ 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).

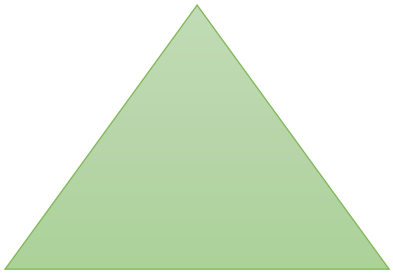
Psychiatric disorders:

- ✓ 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.
- ✓ Stressor with depression = adjustment disorder.
- ✓ Schizophrenia, schizoaffective disorder.
- ✓ Somatization disorder
- ✓ Anxiety disorder.

Etiology of MDD:

GENETIC FACTORS

As supported by family and twin studies



BIOLOGICAL

Reduced level of NE,5HT, &DA

PSYCHOLOGICAL

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: hallucination – pregnant – electrolyte imbalance

- ✓ 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): in acute cases

- ✓ 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.

- **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.

3. 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.

4. 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.
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Diagnostic criteria:

- ≥ 2 years continuous 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.

Note: In children and adolescents, mood can be irritable and duration must be at least 1 year.

- 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).

Pharmacological:

- ✓ **Selective serotonin reuptake inhibitors (SSRI). (drug of choice)**
- ✓ 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.

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.

5. Antidepressants Disorders

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).
Prozac: fatigability.
Mirtazapine: insomnia

Serotonin syndrome;

EMERGENCY 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.

STOP TREATMENT + IV FLUIDS + CONTROL VITALS

- **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-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.

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.

Uses:

- 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, and conditions that require patient to take any of the drugs which interact with MAOIs.

6. Clinical assessment (OSCE)

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	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?

- ✓ Take a detailed past psychiatric history especially previous manic, mixed, or depressive episodes.
- ✓ This is very essential in such a case.
- ✓ 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.

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