MOOD DISORDERS

- **Mood is defined as a pervasive emotional tone that profoundly influences one's outlook and perception of self, others and the environment in general.**
- ***MOOD DISORDERS*** encompass a large group of disorders in which pathological mood and related disturbances dominate the clinical picture
- The mood disorders include:
    - Major depressive disorders
    - Bipolar disorders (I and II)
    - Dysthymic disorder
    - Cyclothymic disorder
    - Mood disorders due to a medical condition
    - Substance-induced mood disorder

MAJOR DEPRESSIVE EPISODE:

- See DSM-IV criteria p149 of Kaplan and Sadock Handbook
- Information obtained from the history is crucial:
    - **Depressed mood:**
        - Subjective feeling of sadness for a prolonged period of time
    - **Anhedonia** (inability to experience pleasure)
    - **Social withdrawal**
    - **Lack of motivation**
    - **Little tolerance of frustration**
    - **Vegetative symptoms:**
        - Decrease in libido
        - Weight loss and anorexia
        - Weight gain and increased food intake
        - Low energy levels
        - Abnormal menses
        - Early morning awakening
            - ~75% depressed patients have sleep disturbance (too much or too little)
        - Symptoms worse in the morning
    - **Constipation**
    - **Dry mouth**
    - **Headache**
- MENTAL STATE EXAMINATION:
    - **General appearance and behaviour:**
        - Patient may exhibit:
            - Agitation
            - Poor eye contact
            - Tearful
            - Downcast
            - Inattentive to personal appearance
    - **Affect:**

        - Constricted
        - Labile
    - **Mood:**
        - Depressed
        - Irritable
        - Sad
    - **Speech:**
        - Little or no spontaneity
        - Monosyllabic
        - Long pauses
        - Soft
    - **Thought content:**
        - Suicidal ideation affects 60% (15% commit suicide)
        - Obsessive rumination
        - Hopelessness
        - Worthlessness
        - Guilt
        - Indecisiveness
        - Mood congruent hallucinations and delusions
    - **Cognition:**
        - Distractible
        - Difficulty concentrating
        - Apparent disorientation
        - Abstract thought may be impaired
    - **Insight and judgment:**
        - Impaired due to either:
            - Cognitive distortions
            - Personal worthlessness
- AETIOLOGY AND PATHOPHYSIOLOGY:
    - The neurobiology of unipolar depression is poorly understood
    - **Genetic factors:**
        - Evidence for genetic transmission is not as strong as in bipolar disorder
            - MZ twins have higher concordance rates (~45%) compared to DZ twins (~20%)
    - **Biogenic amines hypothesis:**
        - Suggests that heterogeneous dysregulation of biogenic amines may be responsible for depression
        - Based on the findings of abnormal levels of monoamine metabolites in the blood, urine and CSF of patients:
        - Serotonin depletion is associated with depression:
            - Thus accounting for the efficacy of serotinergic agents in treatment of depression
    - **Neuroendocrine regulation:**
        - May simply relate to disruptions in biogenic amine input to the hypothalamus

        - Abnormalities include:
            - Increased cortisol and CRH
            - Increase in adrenal size
            - Decrease inhibitory response of glucocorticoids to dexamethasone
            - Blunted response of TSH to TRH infusion
            - Decreased release of LH, FSH, GH and testosterone
            - Decreased nocturnal secretion of melatonin
        - Normalisation occurs with effective anti-depressive therapy
    - **Sleep:**
        - Diurnal variations in symptom severity and alterations in circadian rhythmicity of a number of neurochemical and neurohumoral factors suggest that biological differences may be secondary to a primary defect in regulation of biological rhythms
        - Abnormalities in depression include:
            - Delayed sleep onset
            - Shortened REM latency (time between falling asleep and first REM period)
            - Decreased length of REM sleep
            - Abnormal delta sleep
    - **Neuroanatomic:**
        - PET studies show decreased metabolic rate in caudate nuclei and frontal lobes in depressed patients which normalises with recovery
    - **Psychosocial factors:**
        - Learned helplessness:
            - Attributes depression to a person's inability to control events
        - Stressful life events:
            - Often precedes first episodes of mood disorders
    - **IT IS CRUCIAL TO NOTE THAT ALTHOUGH ANTIDEPRESSANT DRUGS RESULT IN IMMEDIATE BLOCKADE OF TRANSMITTER UPTAKE WITHIN HOURS, THEIR THERAPEUTIC EFFECTS TYPICALLY EMERGE OVER SEVERAL WEEKS:**
        - This may suggest neuroadaptive changes in second messenger systems and transcription factors as possible mechanisms of action of these agents.

- Major depression can occur alone or as part of BIPOLAR DISORDER:
    - When it occurs alone it is also known as UNIPOLAR depression
        - Symptoms must be present for 2 weeks and represent a change from previous functioning
- TREATMENT:
    - The most effective approach is to integrate pharmacotherapy with psychotherapeutic interventions

- Maintenance treatment for at least 5 months with antidepressants helps to prevent relapse
- Long term pharmacological therapy may be indicated in patients with recurrent major depressive disorder
- **PSYCHOPHARMACOLOGICAL METHODS:**
  - **SSRI:**
    - First choice of most physicians
    - Early transient side effects include:
      - Anxiety
        - Early anxiogenic effects may increase suicidal ideation
        - Either reduce the dose or add an anxiolytic
      - GIT upset
      - Headache
      - **Education improves compliance**
    - **Sexual dysfunction** is often a persistent and common side effect (may respond to a change in drug or a change in dosage)
    - **It is important to note that there is an increased risk of suicide as suicidally depressed patients begin to improve**
      - This is due to the fact that they have the energy and will they previously lacked to perform the act
      - Known as PARADOXICAL SUICIDE
  - **Bupropion:**
    - Noradrenergic and dopaminergic drug with stimulant-like properties
    - Particularly useful for depression marked by anergy and psychomotor retardation
    - Devoid of sexual side effects
    - May exacerbate anxiety and agitation
    - Its dopaminergic properties may exacerbate psychosis
    - Tendency to cause seizures has been alleviated by availability of sustained release preparation
  - **Serotonin and Noradrenaline reuptake inhibitors:**
    - **Venlafaxine and Duloxetine**
    - May be particularly effective in severe or refractory cases
    - Side effects similar to SSRIs
  - **Nefazodone:**
    - 5HT-2 blockade
    - Beneficial effects on sleep
    - Low rates of sexual side effects
  - **Mirtazapine:**
    - Antihistamine, noradrenergic and serotonergic actions
    - 5HT-2 and 5HT-3 specifically blocked, thereby decreasing the anxiogenic, sexual and GIT side effects

            - Can be highly sedating and cause weight gain
        - **Tricyclic antidepressants (TCA):**
            - Highly effective but require dose titration
            - Side effects include:
                - Anticholinergic (dry mouth, dry eyes)
                - Orthostasis
                - Potential to cause cardiac conduction delay
            - The secondary amines (e.g. **nortryptiline**) are often better tolerated than the tertiary amines (e.g. **amitryptiline**)
            - Blood levels can be helpful in determining adequate dosage
            - Lethality in overdose remains a concern
        - **Augmentation strategies:**
            - Used in treatment resistant cases
            - Include:
                - Liothyronine
                - Lithium
                - Amphetamines
        - **MAO-I:**
            - Used if symptoms still do not improve
            - Safe if education regarding dietary restriction of tyramine containing compounds is given
            - Atypical depression or depression related to bipolar I disorder may respond preferentially to MAO-I
            - Must not be administered for 2-5 weeks after discontinuation of an SSRI or other serotonergic drug due to the risk of serotonin syndrome
        - **Electroconvulsive therapy (ECT):**
            - Useful in refractory major depressive disorder and major depressive episodes with psychotic features
            - Also used if side effects of antidepressants must be avoided or when rapid response is desired
    - **PSYCHOLOGICAL THERAPIES:**
        - When used in conjunction with antidepressants, it is a more effective treatment strategy than either method in isolation
        - Methods include:
            - **Cognitive:**
                - Aimed at testing and correcting negative cognitions and the unconscious assumptions that underlie them
            - **Behavioural:**
                - Aimed at specific undesired behaviours
                - Positive reinforcement
            - **Interpersonal:**
                - Developed as a specific short-term treatment for non-psychotic, non-bipolar depression
            - **Psychoanalytically oriented:**

        - Insight-oriented
        - Aimed at achieving understanding of unconscious conflicts that may be fuelling or sustaining depression
    - **Supportive:**
        - Primary aim is provision of emotional support
    - **Group:**
        - Not indicated for acutely suicidal patients
        - May be of benefit for some patients
    - **Family:**
        - Particularly indicated when patient's depression is related to family events, or if depression is causing disruption to the family unit

BIPOLAR DISORDER:

- A common problem, but quite difficult to diagnose
- It is characterised by unpredictable swings in mood from **mania (or hypomania)** to **depression**
- **MANIA:**
    - A distinct period of abnormally and persistently elevated, expansive or irritable mood, lasting for at least one week (or any duration if hospitalisation is required)
    - See Kaplan and Sadock handbook (p150) for DSM-IV criteria for manic episode.
    - Clues from history:
        - Erratic or disinhibited behaviour:
            - Excessive spending or gambling
            - Impulsive travel
            - Hypersexuality or promiscuity
        - Overextended in activities and responsibilities
        - Low frustration tolerance with irritability, outbursts of anger
        - Vegetative symptoms:
            - Increased libido
            - Weight loss, anorexia
            - Insomnia (expressed as no need to sleep)
            - Excessive energy
    - Clues from mental state examination:
        - General appearance and behaviour:
            - Psychomotor agitation
            - Seductive
            - Colourful clothing
            - Excessive makeup
            - Inattention to personal appearance or bizarre combinations of clothes

        - Intrusive
        - Entertaining
        - Threatening
        - Hyperexcited
    - Affect:
        - Labile
        - Intense (may have rapid depressive shifts)
    - Mood:
        - Euphoric
        - Expansive
        - Irritable
        - Demanding
        - Flirtatious
    - Speech:
        - Pressured
        - Loud
        - Dramatic
        - Exaggerated
        - May be incoherent
    - Thought content:
        - Highly elevated self esteem
        - Grandiose
        - Extremely egocentric
        - Delusions and less frequently hallucinations
            - Mood congruent themes of inflated self-worth and power
    - Thought process:
        - Flight of ideas (if severe, can lead to incoherence
        - Racing thoughts
        - Neologisms
        - Clang associations
        - Circumstantiality (indirect speech that is delayed in reaching the point)
        - Tangentiality
    - Sensorium:
        - Highly distractible
        - Difficulty concentrating
        - Memory is generally intact (but being easily distracted, it is difficult to assess
        - Abstract thinking is generally intact
    - Insight and judgment:
        - Extremely impaired
        - Often total denial of illness and inability to make any organised or rational decisions

- **Rapid cycling bipolar disorder:**
    - Four or more depressive, manic or mixed episodes within 12 months
    - Bipolar disorder with mixed or rapid cycling episodes appears to be more chronic than bipolar disorder without alternating episodes
- **Hypomania:**
    - Elevated mood associated with decreased need for sleep, hypoactivity and hedonic pursuits
    - Less severe than mania with no psychotic features
- **DIFFERENTIAL DIAGNOSIS:**
    - Toxic effects of stimulant or sympathomimetic drugs
    - Secondary mania induced by:
        - Hyperthyroidism
        - AIDS
        - Neurological disorders:
            - Huntington's
            - Wilson's
            - CVA
    - Comorbidity with alcohol and substance abuse is common
    - Schizophrenia:
        - Can look like a manic, depressive or mixed episode with psychotic features
    - Bereavement = profound sadness secondary to major loss
        - Suicidal ideation absent
        - Feelings of worthlessness/hopelessness often absent
    - Personality disorders
    - Schizoaffective disorder:
        - Signs and symptoms of schizophrenia accompany prominent mood symptoms
    - Primary sleep disorders
- **AETIOLOGY AND PATHOGENESIS:**
    - Concordance rate for monozygotic twin pairs approaches 80%
    - Pathophysiological mechanisms underlying profound mood changes remain unknown:
        - Possibility of dysregulation of Na/K ATPase
        - Disordered signal transduction mechanisms
    - Neurophysiological studies suggest altered circadian rhythmicity
- **TREATMENT:**
    - **Acute manic episodes:**
        - Use lithium and other mood stabilisers:
            - Response rate to lithium is ~80% in acute mania
        - Adjunctive use of potent sedative drugs:
            - Usually clonazepam and lorazepam
            - May use olanzapine and risperidone
    - **Biological therapies:**

- Lithium is the first-line drug of choice for mood stabilisation:
  - Can also use valproic acid and carbamazepine
  - Pre-lithium work-up includes:
    - FBC
    - ECG
    - TFT
    - EUC
    - Pregnancy test
  - A blood level of 0.8-1.2 is required for therapeutic effect
    - A level of 2 or higher is considered toxic
  - Response may take 4 days after a therapeutic level has been achieved
  - Typical side effects include:
    - Thirst
    - Polyuria
    - Tremor
    - Metallic taste
    - Cognitive dulling
    - GIT upset
    - Weight gain
    - Acne
  - Rare side effects:
    - Hypothyroidism
    - Renal toxicity
    - Neurotoxicity
    - Hypercalcaemia
    - ECG changes
  - Blood levels are increased by:
    - Thiazide diuretics
    - Tetracyclines
    - NSAIDs
  - Blood levels are decreased by:
    - Bronchodilators
    - Verapamil
    - Carbonic anhydrase inhibitors
- The range of psychological therapies used for depression can also be used in bipolar disorder