

Affective disorders

- Characterized by disturbance of mood
- Clinical depression: feeling sad for more than two weeks.

Core symptoms of depression

- Decreased mood
- Loss of energy and interest
- A feeling of physical illness
- Poor concentration
- Altered appetite and sleep
- Decreased mental and physical functions
- Physical problems e,g, heartburn, indigestion, constipation, headaches
- Feelings of hopelessness, helplessness, guilt and anxiety

DEPRESSION IS THE MOST COMMON CAUSE OF SUICIDE

Causes of depression

- Not clear

An imbalance of certain neurotransmitters in brain (Decreased NA or Decreased serotonin), triggered by:

1. Genetic factors (due to a gene that increases the risk of depression)
2. External triggers e.g. bereavement, social isolation, severe physical illness(reactive or exogenous depression)
3. No obvious reason(biological or endogenous depression)

Classification of Depression

- A) According to number of symptoms and degree:
 1. Mild depression-----self-limiting
 2. Moderate depression-----difficulties at home and work
 3. Severe depression-----serious, associated with suicidal thoughts

- B) According to type:
 1. Unipolar depression (major depression)
 - repeated episodes of depression
 - mood returns to normal at the end of episode
 2. Chronic depression (dysthymia)
 - Low grade, long-term depression
 - resembles chronic fatigue
 3. Bipolar depression (manic-depressive)
Alternating depression and mania

4. Psychotic depression----- delusions and hallucinations
5. Seasonal affective disorder (SAD)= depression due to absence of sunlight
6. Post-partum depression

Manic symptoms

- Boundless energy
- Grandiose ideas
- Flight of ideas or racing thoughts
- Decreased need for sleep
- irritability

Treatment of depression

1. Psychological treatment
2. Pharmacological treatment----70 % of depressed patients respond to antidepressants
3. ECT (electroconvulsive therapy)----- for very severe depression, which has not responded to other treatments or for patients who cannot take antidepressants

Antidepressants

- Antidepressants do not act immediately (after 2 weeks).
- Affect only people who are depressed.
- Effect does not increase with increasing doses.
- Antidepressants are not habit-forming.
- Efficacy of antidepressants is similar.
- Antidepressants differ widely in side effects.

General Mechanism of Action

- Mood elevating effect is correlated with changes in the concentrations of catecholamines and/ or serotonin in the CNS and the long-term receptor down regulation caused by these changes (Beta or 5-HT2 receptors).
- Antidepressants are either:
 - MAO inhibitors
 - Monoamine reuptake inhibitors

Monoamine oxidase inhibitors

- Include:
 - phenelzine
 - tranylcypromine
 - isocarboxazid
 - moclobemide

Mechanism

- Inhibition of MAO
- no anticholinergic effect

Adverse effects

- Xerostomia, blurred vision, drowsiness, dizziness, impotence
- Insomnia, agitation and headache
- The cheese reaction due to tyramine content (causes hypertensive crisis); moclobemide does not cause the cheese reaction (because it is a selective inhibitor of MAO type A, which inactivates noradrenaline and 5-HT).
- Weight gain, hepatitis.
- Serious interactions with tricyclics, fluoxetine and decongestants like pseudoephedrine.

Therapeutic uses

- Depression
- Migraine prophylaxis
- Obsessive compulsive disorders
- Panic disorders
- Phobic disorders
- Orthostatic hypotension

Tricyclics(3-membered ring)

- Include:
 - amitriptyline
 - desipramine
 - clomipramine
 - nortriptyline
 - doxepin
 - trimipramine
 - imipramine
 - protriptyline

Tricyclic antidepressants

- **Mechanism :**
 - Blockade of NA & 5-HT reuptake
 - They are anticholinergics (decrease memory , concentration and intellect)
 - They are antihistamines

Adverse effects

- Xerostomia, blurred vision, drowsiness, dizziness, impotence
- Harm the cardiac function :. They are dangerous in overdose (tachycardia ,heart failure , arrhythmias , myocardial infarction)
- Agranulocytosis , anaemia , thrombocytopenia
- sun sensitivity
- Many drug-drug interactions

Therapeutic uses

- depression
- enuresis
- pain
- obsessive compulsive disorders
- May be useful in:
ADHD , bulimia , insomnia , migraine
prophylaxis , panic and phobic disorders.

Heterocyclic antidepressants

- Very dissimilar medications
e.g. venlafaxine , trazodone , maprotiline ,
bupropion

Mechanism :

Inhibit reuptake of both 5-HT & NA but no
anticholinergic or antihistaminic activity

- Adverse effects:
 - Xerostomia, blurred vision, drowsiness, dizziness, impotence
 - Headache , nausea , weight loss , constipation
 - bupropion also blocks dopamine reuptake but reduces dopamine release . It does not induce mania (useful in bipolar disorders) also it does not reduce sexual function .

- Therapeutic uses :

Depression

Also useful in anxiety, ADHD & insomnia

Selective serotonin reuptake inhibitors [SSRIS]

Include:

- fluoxetine (prozac)
- fluvoxamine (luvox)
- paroxetine (paxil)
- sertraline (zoloft)

- **Mechanism :**

Selectively block serotonin reuptake .

- **Side effects :**

- acne , alopecia , anorexia , cough, GIT disturbances
- decreased libido and sexual performance
- flat emotions .

- **Therapeutic uses**

Depression , obsessive – compulsive disorder, bulimia , anorexia nervosa , alcoholism , obesity, post – traumatic stress disorder

Other antidepressants

Buspirone

- partial agonist at 5-HT type 1A receptors (decrease 5HT activity) but enhances dopaminergic and noradrenergic activity .
- An anxiolytic that is useful in anxious depressive state .
- Has no abuse potential .

reboxetine (edronax)

- **Noradrenaline reuptake inhibitor (NARI)**
- well tolerated
- improves drive and motivation in chronically depressed patients .
- may reverse the cheese reaction seen in MAOI users .
 - NARIS + MAOIS → potent from of combination therapy .
- **Mirtazepine :**
 - Releases both NA & serotonin in brain

- **Use of antidepressant in bipolar disorders :**

- antidepressants induce mania in patients who are genetically susceptible to bipolar disorder .
- give a mood stabilizer (lithium , valproate , carbamazepine)prior to beginning antidepressant therapy.

Antidepressant-induced hypo (mania)

- Shown by tricyclics
- Less by SSRIS
- Least seen with bupropion and MAOIS .

Lithium carbonate or citrate

- Mood stabilizer
- **Mechanism :**

Not known .

It may interfere with the synthesis , storage ,
release and reuptake of monoamines .

Adverse effects

Anorexia , diarrhoea , hypothyroidism ,
seizures , leukocytosis , nephrotic
syndrome and polyuria , impotence .

A toxic drug ; adverse reactions are dose-
and conc-dependent .

Therapeutic uses

- Bipolar disorder
- Mania
- Major depression
- Neutropenia (chemotherapy - & zidovudine–induced neutropenia)
- SIADH (syndrome of inappropriate secretion of ADH) .