Medications used in psychiatry are called psychotropic drugs, which have effects mainly on mental symptoms. According to their principal actions, they are classified into several groups:

### 1. Antipsychotics (Formerly Major Tranquilizers /Neuroleptics)

<table>
<thead>
<tr>
<th>Typical / Conventional</th>
<th>Atypical / Non-conventional</th>
</tr>
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<tbody>
<tr>
<td>They block dopamine receptors improving positive psychotic features, but they are associated with significant extrapyramidal side effects (EPSE), e.g. chlorpromazine, haloperidol.</td>
<td>They act on dopamine and serotonin receptors to improve both positive and negative symptoms of psychosis. They produce an antipsychotic effect without causing extrapyramidal side-effects. e.g. olanzapine, risperidone</td>
</tr>
</tbody>
</table>

### 2. Mood Stabilizing Drugs

Indications: mania (acute phase and prophylaxis), schizoaffective disorder, unipolar recurrent major depressive episodes (as an adjunct treatment), impulsive and aggressive behavior. E.g. lithium, carbamazepine, sodium valproate.

### 3. Antidepressants

Besides their common use as antidepressants, they have several other uses. Some antidepressants are used in anxiety, panic disorder phobias, obsessive-compulsive disorder, premature ejaculation, insomnia, eating disorders, and others.

Antidepressants include many groups:

- **Monoamine Oxidase inhibitors:**
  - Irreversible (phenelzine, tranylcypromine, isocarboxazid)
  - Reversible (moclobemide).
- **Tricyclics:** E.g. amitriptyline, imipramine, clomipramine, doxepin.
- **Tetracyclics:** e.g. maprotiline.
- **Selective-Serotonin Reuptake Inhibitors (SSRIs):**
  E.g. fluoxetine, fluvoxamine, paroxetine, citalopram, escitalopram sertraline.
- **Selective-Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs):**
  E.g. venlafaxine, duloxetine.
- **Others:** mirtazapine, trazodone, nefazodone, bupropion.
4. **Antianxiety (Anxiolytic) Drugs**
   - Benzodiazepines: e.g. lorazepam, alprazolam, diazepam.
   - Buspirone.
   - Beta-adrenergic antagonists e.g. propranolol.

5. **Sedative - Hypnotics (for insomnia)**
   - Benzodiazepines e.g. Nitrazepam.
   - Chlormethiazole.
   - Zolpidem, zopiclone.
   - Ramelteon (It is a new drug. It targets melatonin receptors)
   - Antihistamines e.g. hydroxyzine.

6. **Antiparkinsonian/Anticholinergic drugs (used in case of EPSE)**
   - E.g. procyclidine.

7. **Others:**
   - Medications used in dementia: cholinesterase Inhibitors (donepezil, rivastigmine, galantamine), and memantine.
   - Psychostimulants e.g. methylphenidate, modafinil.
   - Disulfiram.

**Common misconceptions about psychotic drugs**
1. Dangerous drugs.
2. Mere tranquilizers.
3. Full of side effects that outweigh any benefit.
5. Always lead to addiction.

**ANTIPSYCHOTICS**

- **Indications:**
  - Functional psychosis: schizophrenia, mania, schizoaffective disorders, schizophreniform disorder, brief psychosis, and delusional disorders.
  - Organic psychosis: delirium intoxication with substances, dementia, others.
  - Violence, agitation and excitement
  - Medical uses: e.g. nausea, vomiting, poor appetite
  - Others e.g. tic disorders, ADHD.
• **Mechanism of action:**
  
  **A-Antipsychotic effects:**
  1. In mesolimbic tract; pathological hyperactivity of this pathway accounts for active psychotic features: hallucinations, delusions, aggression, and disorganized behavior. Postsynaptic blockade of CNS dopamine receptors type 2 (D2) in this pathway reduces active psychotic features.
  2. In mesocortical tract; primary dopamine neuron defect or serotonergic overactivity is responsible for most negative features and cognitive defects seen in some schizophrenic patients. Atypical antipsychotics act on dopamine and serotonin receptors to improve negative symptoms of psychosis: lack of motivation, restricted affect, poor self-care, and others.

  **B – Side effects:**
  1. In Nigrostriatal tract; they induce extrapyramidal effects due to antidopaminergic effect (these side effects are better treated with anticholinergic medications rather than dopaminergic drugs (compared to Parkinson's disease).
  2. In Tuberoinfundibular tract; dopamine inhibits prolactin release from the anterior pituitary. Antidopaminergics induce excessive prolactin secretion.

• **Adverse Effects:**
  
  **(1.) Extra-Pyramidal Side Effects (EPSE)**
  
  **• Acute dystonia:**
  – Appears within days after antipsychotics.
  – Severe painful spasm of neck muscles (toricollis), ocular muscles (oculogyric crisis) muscles of the back (opisthotonus) and tongue protrusion. Treated with anticholinergic drugs (e.g. procyclidine 5 – 10 mg IM or P.O.).

  **• Parkinsonism:**
  – Appears within weeks after treatment, its features: stooped posture, akinesia, muscle rigidity, masked face, and coarse tremor. Treated with anticholinergic drugs
(e.g. procyclidine)

- **Akathisia** (inability to keep still, associated with unpleasant feelings of inner tension)
  - Appears within days – weeks.
  - Generally disappears if the dose is reduced.
  - Benzodiazepine or beta-blockers may help in the treatment, whereas anticholinergics have no therapeutic effect.

- **Rabbit Syndrome** (perioral tremor)
- **Tardive Dyskinesia**
  - occurs in about 10 – 20 % of patients on long-term antipsychotics for several years.
  - chewing, sucking or choreo-a-thetoid movements of the facial and neck muscles.
  - may be due to super-sensitivity of dopamine receptors resulting from prolonged dopamine blockade.
  - no specific treatment, the only agreed treatment is to discontinue the antipsychotic drug when the patient’s state allows this.

(2.) **Antiadrenergic:**
  - postural hypotension
  - inhibition of ejaculation

(3.) **Anticholinergic:**
  - dry mouth.
  - blurred vision.
  - constipation.
  - urinary retention.
  - precipitation of closed – angle glaucoma.
  - Poor erection.

(4.) **Others:** weight gain, galactorrhea, amenorrhea, sedation (antihistamine effect)

Toxic Effect: Neuroleptic Malignant Syndrome (NMS) see psychiatric Emergencies (chapter 19).
The therapeutic effect of antipsychotics may take up to 6 weeks to appear.
Antipsychotics can be classified according to their potency into:

**High potency drugs:**
- More antidopaminergic effect.
- Less anticholinergic effect.
- EPSE are prominent. e.g. haloperidol, triflouperazine.

**Low potency drugs:**
- More anticholinergic effect.
- Less antidopaminergic effect.
- EPSE are less prominent.
- Postural hypotension and sedation are marked, e.g. chlorpromazine.

- **NEW ATYPICAL ANTIPSYCHOTICS:**
  Compared to the typical antipsychotics (which bind strongly to postsynaptic D2 receptors) these new agents bind in varying degrees to dopamine D2, D4, 5HT2, alpha adrenergic and muscarinic receptors.
  - They are less likely to cause extrapyramidal side effects.
  - These include:
    1. Olanzapine  
    2. Risperidone  
    3. Paliperidone  
    4. Quetiapine  
    5. Aripiprazole  
    6. Ziprasidone  
    7. Sertindone  
    8. Clozapine

**Clozapine** was the first atypical antipsychotic drug. It is indicated for resistant psychosis not responding to traditional antipsychotics, schizophrenia with negative features or in patients who cannot tolerate the adverse effects associated with those drugs. Its side effects include: Neutropenia and agranulocytosis. Therefore, regular blood tests are required. These are not dose dependent. Risk is about 2%. Others: seizure, sedation, weight gain, sialorrhea, hypotension, constipation and tachycardia (all are dose dependent).

**DEPOT (SLOW RELEASE) ANTIPSYCHOTICS:**
These are long-acting antipsychotic drugs, given as deep intramuscular injections to patients who improve with drugs but cannot be relied on to take them regularly by mouth (i.e. poor
Basic Psychiatry

compliance). Such patients usually suffer from either; chronic schizophrenia, delusional disorders, or schizoaffective disorder.

**Depot Antipsychotics:**

- Fluphenazine decanoate (Anatensol – Modecate): e.g. 25 – 75 mg / month.
- Flupenthixol decanoate (Depixol – Fluansol): e.g. 20 – 100 mg / month.
- Zuclopenthixol decanoate (Clopixol): 200 – 600 mg. /month.
- Risperdal consta: 25-50 mg./2weeks.

A test dose is usually given (¼ - ½ the dose) to check patient’s tolerability. Depot injections are released slowly in 1 – 8 weeks.

**ANTICHOLINERGIC ANTIPARKINSONIAN DRUGS**

- They are used in psychiatry to control the extra-pyramidal side effects of antipsychotic drugs.
- The commonly used compounds are:
  - procyclidine (kemadrin) 5 mg. P.O. / IM injections are available and commonly used in the treatment of acute dystonia.
  - benztropine (cogentin).
  - trihexyphenidyl / benzhexol (artane).
  - biperiden (akinetone).
- Their side effects include:
  - dry mouth
  - blurred vision
  - constipation
  - urinary retention
  - precipitation of glaucoma (closed – angle)
  - anticholinergic intoxication (delirium, dry skin, hyperthermia…)
MOOD STABILIZERS

LITHIUM

- **Mechanism of action:**
  The exact mechanism is unknown, however it is thought that it stabilizes neuronal activities (decreases sensitivity of postsynaptic receptors and inhibits release of neurotransmitters).
- **Before starting lithium,** a note should be made of any other medications taken by the patient and a physical examination should be carried out.
- **Prerequisite laboratory test:**
  - Renal functions and electrolytes.
  - Thyroid functions.
  - ECG if cardiac disease is suspected.
  - Pregnancy test (if indicated).
- **Contraindications:**
  - Renal or cardiac failure.
  - Recent myocardial infarction.
  - Chronic diarrhea sufficient to alter electrolytes.
  - First trimester of pregnancy
  Lithium is not recommended in children.
- **Side effects:**
  - Fine tremor.
  - Gastric discomfort and diarrhea.
  - Dry mouth, metallic taste.
  - Fatigue
  - Weight gain
  - Reversible hypothyroidism.
  - Reversible nephrogenic diabetes insipidus (polyuria – polydipsia) due to blockade of ADH – sensitive adenylcyclase in distal tubules.
  - Toxicity (course tremor, ataxia, confusion, diarrhea, vomiting…).
Drug interactions:
- There are several drugs that increase lithium concentration and may lead to Lithium toxicity:
  - Thiazide diuretics.
  - Non-steroidal anti-inflammatory drugs (NSAID).
  - Angiotension - converting enzyme inhibitors e.g. lisinopril.
  - Haloperidol high doses (e.g. 40 mg/day)
- Lithium may potentiate the effect of muscle relaxants. This is important when a patient undergoes an operation or ECT.
- It may potentiate extrapyramidal side effects of antipsychotics.
- It may precipitate 5-HT syndrome if given with SSRIs.
- The recommended plasma concentrations are:
  - 0.9 - 1.2 mmol / liter (during acute phase)
  - 0.4 - 0.8 mmol / liter (for prophylaxis)
- Dose is 300 - 450 mg twice or three times a day.
- Plasma concentration requires continuous measurement because the narrow therapeutic index of lithium (therapeutic and toxic levels are close). Toxic levels ≥ 1.5 mmol / liter.
- Plasma level should be measured 12 hours after the last dose.

CARBAMAZEPINE (Anticonvulsant)
- Doses:
  - Starting dose is usually 200 mg two times a day. (in children 100 mg / day).
  - It can be increased gradually to 600 – 1000 mg.
  - Therapeutic concentration for psychiatric indications is 8 – 12 ug per mil.

- Side effects:
  - Nausea
  - Drowsiness
  - Dizziness
  - Double vision
  - Skin rash
– Agranulocytosis (rare 1 in 20,000 patients but serious)
– Jaundice.

**SODIUM VALPROATE (Anticonvulsant)**

**• Doses:**
– Starting dose is usually 250 mg twice/day. It can be increased gradually to 2500 mg./day

**– Common side effects include:**
- Gastrointestinal disturbances (nausea, vomiting …)
- Sedation
- Weight gain
- Tiredness
- Neurological: tremor, ataxia, and dysarthria.

**– Rare side effects:**
- Fatal hepatitis.
- Platelets dysfunction

**ANTIDEPRESSANTS**

Antidepressants have therapeutic effects in depressive disorders but do not elevate mood in healthy people. 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.

**TRICYCLIC ANTIDEPRESSANT:**
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 (especially clomipramine because it regulates serotonin in the CNS).
- Nocturnal enuresis.
- Pruritis (H\textsubscript{1} blockade e.g. doxepin).
- Gastric ulcer (H\textsubscript{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 in suicidal patients.

II. SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)
- 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.
  - sexual dysfunction (delayed orgasm).
  - insomnia (mainly with Fluoxetine).
  - sedation (mainly with Fluvoxamine).
  - sweating.
  - tremor.
  - serotonin syndrome (see psychiatric emergency chapter 19).

II. **MONOAMINE OXIDASE INHIBITORS (MAOIs)**

• Because of their serious interactions with tyramine – containing food stuffs and other drugs, they are 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 prescriptions.

**Side effects:**
  - Constipation.
  - Dry mouth.
  - Urinary retention.
  - Postural hypotension.
  - Sexual dysfunction.
  - Headache.
  - Sleep disturbances.
  - Weight gain
  - Dizziness.
– Tremor.
– Ankle edema.
– Hepatotoxicity.
– Hypertensive crisis (see chapter 19).

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 the 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 it’s freedom from tyramine reactions and it’s quick offset of activity.
- It is better tolerated than conventional MAOIs or tricyclics.
- Side effects include nausea and insomnia.
- It should not be combined with SSRI or clomipramine.

**BENZODIAZEPINES**
- They act on specific receptor sites (benzodiazepine receptors) linked with gamma aminobutyric acid (GABA) receptors in the C.N.S. They enhance GABA action which has an inhibitory effect.
- They have several actions:
  - Sedative & hypnotic action.
  - Anxiolytic action.
  - Anticonvulsant action.
  - Muscle relaxant action.
They differ in potency and half-life.
- Long acting (more than 24 hours) e.g. diazepam, nitrazepam.
- Relatively short acting e.g. alprazolam, lorazepam.

**Side effects:**
- Dizziness and drowsiness (patient should be warned about these side effects which may impair functions e.g. operation of dangerous machinery, driving).
- Release of aggression due to reducing inhibition.
- Dependence and withdrawal:
  - If given for several weeks.
  - Short acting drugs have more risk of dependence.

**Withdrawal Syndrome:**
- It generally begins 2 – 3 days after cessation of short acting, and 7 days after cessation of long acting benzodiazepines and then diminishes in another 3 – 10 days.
- Features:
  - Anxiety, irritability, apprehension
  - Nausea
  - Tremor and muscle twitching
  - Heightened sensitivity to stimuli
  - Headache
  - Sweating
  - Palpitation
  - Muscle pain
  - Withdrawal fit may occur when the dose of benzodiazepine taken has been high.

Withdrawal is treated with a long acting benzodiazepine (e.g. diazepam) in equivalent doses before withdrawal then the dose is reduced gradually by about 10 – 20 % every 10 days.
**BUSPIRONE**

- It has anxiolytic activity comparable to that of benzodiazepines. However, it is pharmacologically unrelated to benzodiazepines.
- It stimulates 5HT – 1A receptors and reduces 5HT (serotonin) transmission.
- It’s onset of action is gradual (several days – weeks) therefore, it is not effective on PRN basis.
- It does not cause functional impairment, sedation nor interaction with CNS depressants.
- It does not appear to lead to dependence.
- **Adverse effects:**
  - Headache.
  - Irritability.
  - Nervousness.
  - Light-headedness.
  - Nausea.

**MEDICATIONS USED IN DEMENTIA**

See Chapter 6 (dementia).

**ELECTROCONVULSIVE THERAPY (ECT)**

**History and Concept:**

Patients with concomitant schizophrenia and epilepsy were found to improve in psychosis following repeated fits. It was therefore, thought that there is an antagonism between schizophrenia and epilepsy.

In 1938 Cerletti administered an electrically-induced fit to a catatonic vagrant schizophrenic patient who then showed reasonable improvement.

Later, anesthesia was introduced and convulsions were modified using muscle relaxing agents.
Indications for ECT
1. Depression:
   - depressive disorder with suicidal risk.
   - depressive stupor or marked retardation.
   - depressive disorder with delusions
   - inability to take drugs:
     - first trimester of pregnancy.
     - in the elderly.
     - in physical diseases e.g. renal failure.
2. Schizophrenia (catatonic, resistant to drugs).
3. Post partum psychosis.
4. Schizoaffective disorder.
5. Mania and mixed affective states.

Precautions and Contraindications:
Recent research showed no absolute contraindications to ECT. At one time raised intracranial pressure was considered as the only absolute contraindication to ECT. Remember that not all space occupying lesions produce raised intracranial pressure.

Relative Contraindications:
- To ECT itself:
  - Cardiac infarct in the preceding 3 months (some references extend it to 2 years).
  - Other cardiac diseases including arrhythmias.
  - History of cerebral infarction.
  - Brain tumor.
- To anesthesia and muscle relaxants.

Psychiatric disorders that may show deterioration or no response to ECT:
- Phobic disorders
- Conversion disorder
- Primary hypochondriasis (not due to depression)
- Depersonalization disorder.

Mode of Action of ECT:
The exact mode of action is unknown.
The current hypothesis: the beneficial effect which depends on the
cerebral seizures (not on the motor component) is thought to result from neurotransmitter changes probably involving serotonin and noradrenaline transmission.

**ECT Preparations:**
Explanation to the patient (or his caretakers).
ECT consent by the patient or his caretaker.
Hospital admission for full physical assessment (fitness for anesthesia and ECT).
Fasting (midnight).
Oxygenation to overcome succinylcholine-induced apnea, to facilitate seizure activity and to reduce memory impairment.
Muscle relaxant to reduce the consequent motor effects (severe muscle contraction may lead to bone fracture).
Placing a mouth gag in patient’s mouth to prevent tongue or lip bites.
Machine and electrodes preparations.
Decreasing scalp’s resistance with jelly or normal saline.

**ECT Procedure:**
- **Bilateral** (most commonly used procedure)
  - One electrode on each side of the head (fronto-temporal position).
  - It gives a rapid response.
  - Bi-frontal position can be used; it produces less memory impairment but may be therapeutically ineffective.
- **Unilateral:**
  - Both electrodes are placed on the non – dominant side.
  - It produces less memory impairment but less effective than bilateral.
- **ECT is usually given 2 – 3 times a week with a total of 6 – 12 sessions, according to response and progress. Response begins usually after 2 – 4 sessions. If there is no response after 8 sessions, it is unlikely that more sessions will produce a useful change.
In depressed patients antidepressants should be started towards the end of the course of ECT to reduce the risk of relapse.

**Side Effects of ECT**: (ECT in general is a safe procedure)

- Headache (due to temporary increase in intracranial pressure).
- Body aches and myalgias (due to muscle contraction)
- Memory impairment (both retrograde and anterograde amnesia).
  - Duration varies (days – several months).
  - May be due to neuronal hypoxia during seizure.
- Bone fracture and tongue or lip injury.
- Very rarely death (in patients with cardiovascular disease).

**Misconceptions about ECT**

- Dangerous procedure.
- Causes serious brain damages.
- Involves a high voltage (110 – 220 V) current.

Some traditional healers tried 110 V current with some patients assuming that it is the same procedure used by psychiatrist (ECT).