


ANTIPSYCHOTICS



□ Antipsychotic drugs = Neuroleptics= Major tranquilizers

Drugs that are primarily used to treat schizophrenia

- They can also be used for other psychotic states including manic states with psychotic symptoms such as grandiosity, paranoia and hallucinations
- These drugs decrease the intensity of hallucinations and delusions

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- Psychosis: a mental disorder caused by brain dysfunction

 - Schizophrenia
 - ▣ Type of psychosis characterized by:
 - Delusions
 - Hallucinations (often in the form of voices)
 - Thinking or speech disturbances
 - ▣ Schizophrenia is a chronic disorder
 - ▣ It has a genetic component
 - ▣ Biochemical abnormalities include dysfunction of dopaminergic pathways
 - ▣ Associated with D2 type of dopamine receptor

Diagnostic Criteria for Schizophrenia

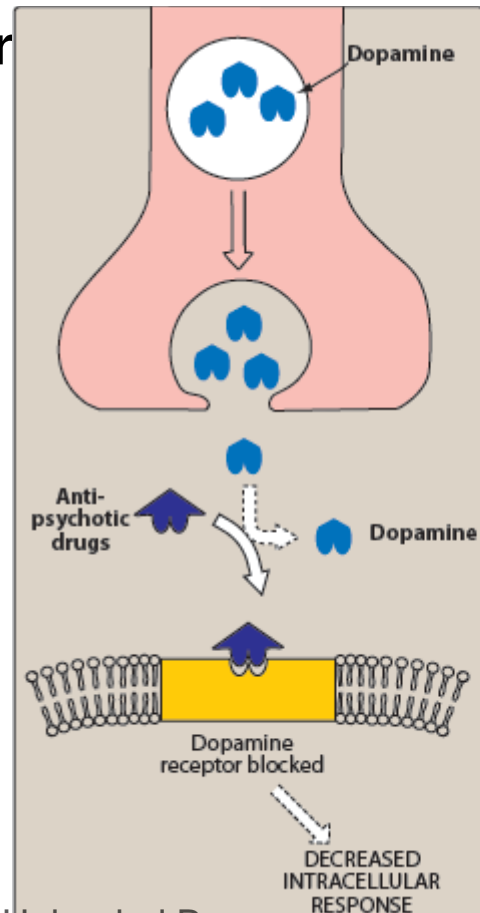
- ❑ At least two of the characteristic symptoms:
 - ❑ Delusions
 - ❑ Hallucinations
 - ❑ Disorganized thoughts and speech
 - ❑ Grossly disorganized behavior
 - ❑ Negative symptoms (blunted affect, anhedonia, apathy, social isolation, poor hygiene, poor memory, impaired attention and poor cognition)

- ❑ Deterioration in function

- ❑ Duration at least 6 months

Antipsychotic drugs

- Affect dopamine by blocking dopamine receptors
- First generation antipsychotics
 - ▣ Chlorpromazine
 - ▣ Haloperidol
 - ▣ Thioridazine
- Second generation antipsychotics
 - ▣ Aripiprazole
 - ▣ Olanzapine
 - ▣ Risperidone
 - ▣ Clozapine



First generation antipsychotics

- ❑ Classified into low potency and high potency based on their affinity to D2 dopamine receptors
- ❑ First generation antipsychotics are also called conventional, typical or traditional antipsychotics
- ❑ Competitive blockers of D2 receptors
- ❑ Associated with movement disorders, especially the ones with stronger binding to dopamine receptors like haloperidol, compared to the weaker binding drugs like chlorpromazine
- ❑ No drug is more effective than the other

Second generation antipsychotic drugs

- ❑ Also referred to as atypical antipsychotics
- ❑ Have fewer extrapyramidal symptoms (EPS) (Parkinson's like symptoms) than first generation drugs
- ❑ Block both dopamine and serotonin receptors
- ❑ Adverse effects include
 - ▣ Hyperglycemia
 - ▣ Hypercholesterolemia
 - ▣ Weight gain

Antipsychotic drugs

- Antipsychotic activity of these agents are due to blockade at dopamine and serotonin receptors
- Many of these drugs also block cholinergic, adrenergic and histaminergic receptors causing undesirable side effects

Antipsychotic drugs

- ❑ Most of these drugs reduce positive symptoms (e.g. hallucinations) by blocking dopamine receptors
- ❑ The negative symptoms (e.g. apathy, poor cognition) are not responsive to first generation antipsychotics
- ❑ Many second generation like clozapine antipsychotics reduce negative symptoms
- ❑ Antipsychotic effects take several days to weeks to occur

Antipsychotic drugs

- ❑ Some antipsychotic drugs (first generation) have antiemetic effects due to blocking of D2 receptors in the chemoreceptors trigger zone of the medulla
- ❑ Antipsychotic treatment should be continued for at least 5 years, or should be taken indefinitely

Antipsychotic drugs

□ Therapeutic uses

- ▣ Treatment of schizophrenia
- ▣ Prevention of moderate to severe nausea and vomiting
- ▣ Tranquilizers to manage agitated behavior
- ▣ Risperidone is approved for management of disruptive behavior and irritability secondary to autism

Antipsychotic drugs

❑ Adverse effects

- ❑ Extrapyrasidal side effects (Parkinson's like symptoms) can be managed by administration of anticholinergic drug like benztropine
- ❑ Tardive dyskinesia: abnormal involuntary repetitive body movements (first generation)
- ❑ Antipsychotic malignant syndrome: Potentially fatal, muscle rigidity, fever and unstable blood pressure (treatment should be stopped)
- ❑ Drowsiness due to CNS depression and antihistamine effects
- ❑ Antimuscaranic side effects with antipsychotics that block cholinergic receptors (blurred vision, dry mouth, constipation)
- ❑ Lowering of seizure threshold (should be used carefully in patients with epilepsy)
- ❑ Metabolic adverse effects: Hyperglycemia, Hypercholesterolemia, weight gain (Second generation)
- ❑ Clozapine can cause agranulocytosis (severe leukopenia)