

# 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

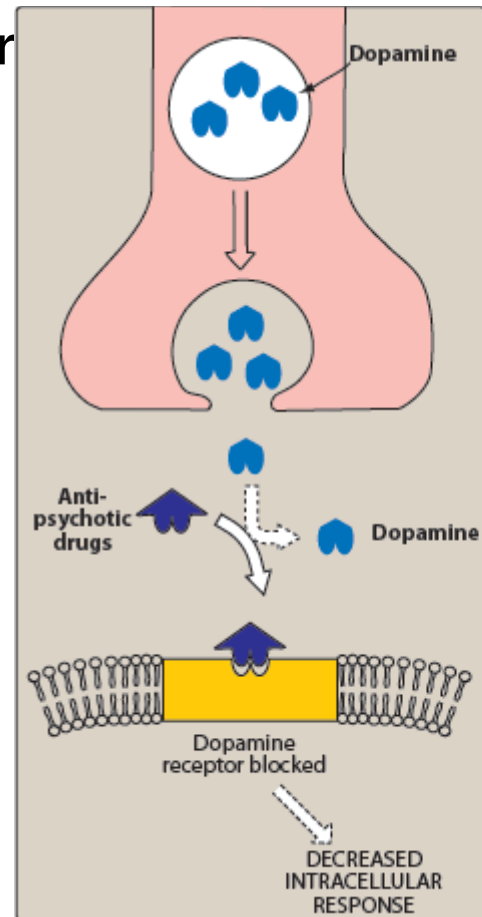
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- **Psychosis: a mental disorder caused by brain dysfunction**
  
  - **Schizophrenia**
    - ▣ Type of psychosis characterized by:
      - Delusions
      - Hallucinations (often in the form of voices)
      - Thinking or speech disturbances
    - ▣ 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

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- 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

- Extrapyrarnidal 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)