

# Schizophrenia

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## Objectives

- Identify positive and negative symptoms used for diagnosis of schizophrenia
- List medications used in treatment of schizophrenia
- Describe some of the side effects associated with schizophrenia medications

## Epidemiology

- U.S. lifetime prevalence = 0.6-1.9%
- Onset typically in late adolescence or early adulthood
- Onset tend to be earlier in males; equal prevalence between sexes

## Diagnosis

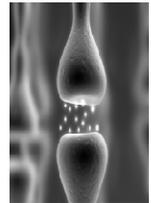
- DSM-IV Criteria:
  - Positive Symptoms
    - Delusions
    - Hallucinations
    - Thought disorders

## Diagnosis(continued)

- Negative Symptoms
  - Loss of interest
  - Lack of emotions
  - Poor hygiene
  - Social Withdrawal
  - Loss of motivation
  - Poverty of speech
- [Schizophrenia Symptoms Video](#)

## Causes of Schizophrenia

- Genetic
- Environmental
- The role of dopamine neurotransmitter is central
- Four dopamine pathways
  - Mesolimbic
  - Nigrostriatal
  - Mesocortical
  - Tuberoinfundibular



## Pharmacotherapy

### First Generation Antipsychotics(AP)

- Bind to D<sub>2</sub> receptors (receptor blockers)
- Low potency versus high potency
  - Describes the affinity of drug for D<sub>2</sub> receptors
  - Thorazine 300 mg/day is equivalent to Haldol 5 mg/day
- Haloperidol (Haldol)
- Thioridazine (Mellaril), Chlorpromazine (Thorazine)

## Second Generation Antipsychotics

- Bind to D<sub>2</sub> receptors and other receptors (blockers)
- Often have greater affinity for serotonin receptors than dopamine receptors
- Control variety of symptoms
- Clozapine (Clozaril), Olanzapine (Zyprexa)
- Risperidone (Risperdal), Ziprasidone (Geodon)
- Aripiprazole (Abilify), Quetiapine (Seroquel)

## Side Effects Consequences due to Receptor Affinity

- Muscarinic acetyl choline blockers
  - Tachycardia, poor memory, blurry vision, dry mouth, constipation, urinary retention
- Alpha -1 receptor blockers
  - Postural hypotension, reflex tachycardia, dizziness, syncope, sedation
- Histamine receptor blockers (H-1 blockers)
  - Sedation, appetite stimulation, weight gain
- Serotonin blockers
  - Hypotension, weight gain, ejaculation difficulties

## Antipsychotic's Receptor Affinity

Medication	mACh	D <sub>2</sub>	Serotonin	Alpha-1	H-1
Haloperidol	+	++++	+	++	No
Chlorpromazine	++	++	++	++	++
Thioridazine	+++	++	++	+++	++
Clozapine	+++	+	+++	++++	+++
Olanzapine	+++	++	+++	+	+++
Risperidone	No	++	++++	+++	++
Ziprasidone	No	+++	++++	++	+
Aripiprazole	No	++++	+++	+	+
Quetiapine	+	+	+	++	++

## Movements Disorders

- Side effect of antipsychotics as a result of blocking dopamine receptors
- Extrapyramidal symptoms
  - Akathisia ([Akathisia video](#))
  - Parkinsonism
  - Dystonia ([Acute Dystonic Reaction Video](#))
- Tardive dyskinesia
  - Abnormal movements of face, peri-oral areas, tongue, extremities ([TD video](#))

## Extrapyramidal Side Effects

Dose	Halop	Risper	Olanz	Quet	Cloza
Low	++	+	-	-	-
High	+++	++	-/+	-	-
Very High	+++	+++	+	-	-

more ← ————— Likelihood of EPS ————— → Less

## Adverse Effects of First Generation Antipsychotic

- Cardiovascular
  - Orthostatic hypotension, QT prolongation
- Dermatologic
  - Photosensitivity
- Endocrine
  - Galactorrhea
- Neurologic
  - Lowered Seizures threshold
- Ophthalmic
  - Pigmentary retinopathy

## Adverse Effects of Second Generation Antipsychotic

- Metabolic side effects
- QT prolongation
- Extrapyramidal side effects (EPS)
- Other side effects

## Metabolic Side Effects

- Weight gain
  - Food craving
  - Alteration in resting metabolic rate
- Predictors of weight gain
  - Dose related to weight gain with risperidone, quetiapine
  - Low initial BMI
  - Sedentary life style
- Concern with weight gain
  - Increase morbidity and mortality
  - Associated with a number of serious medical conditions

## Metabolic Side Effects

- Antipsychotic induced diabetes
  - All labels for second generation antipsychotics must include a warning about hyperglycemia and diabetes
  - Case reports of new onset diabetes leading to DKA
  - Mechanism
    - Insulin resistance related to increased body weight
    - Direct Effect on glucose transporters
    - Decrease pancreatic beta cell responsiveness

## Metabolic Side Effects

- Lipid abnormalities: published trials have examined effect of atypical antipsychotics on fasting blood lipids
  - Clozapine is associated with increased triglycerides
  - Olanzapine is associated with increased
    - Triglycerides and total cholesterol
  - Risperidone and ziprasidone appear to have little to no effect on lipids

## Monitoring Patients for Drug-Induced Metabolic Changes

	Base-line	4 wks	8 wks	12 wks	3 month	12 month	5 years
Personal/ Family History	X					X	
weight	X	X	X	X	X		
Waist Circum	X			X		X	
BP	X			X		X	
FPG	X			X		X	
Lipids	X			X			X

## Other Side Effects

- Q-T prolongation
  - SSRI, Haloperidol, Ziprasidone, Tricyclic antidepressants
- Hyperprolactinemia
  - Common with higher dose risperidone, has been shown to be a transient effect with other atypicals
- Agranulocytosis
  - Frequent lab monitoring required for clozapine
- Lower seizure threshold
  - Should start clozapine at a low dose (12.5 mg qhs) and titrate slowly

