Antipsychotic Medications
used to treat psychoses;
aka “neuroleptics”, “major tranquilizers”, or “anti-schizophrenics”

Schizophrenia Symptoms
• Hallucinations
• Delusions
• Disorganized speech
• Disorganized behavior
• These are called “positive (+) symptoms”
• (abnormalities that have been ‘added’ to the person’s behavior and mental processes)
• Normal emotion lost
• Decreased motivation; apathy
• Decreased social interaction
• Decreased speech
• These are called “negative (-) symptoms” – normal behaviors that have decreased

Phenothiazines:
First Generation Antipsychotics
• 1950’s - chlorpromazine (*Thorazine) became the first and prototypic antipsychotic
• chemically complex – blocks or decreases the action of DA, NE, ACh and histamine
• Others: Mellaril (thioridazine), Stelazine (trifluoperazine), Prolixin (fluphenazine) & ~6 others (all the generics end in “azine”)
• Differ in potency & degree of side effects
• Inexpensive and long-acting; injectable forms are available

Dopamine Hypothesis
• Schizophrenia is associated with excessive response to DA in limbic & cortical regions

Support for the DA Hypothesis
• effectiveness of typical antipsychotics almost perfectly correlated with DA blockade
• drugs which ONLY block DA are highly effective: *butyrophenone (e.g. haloperidol)
• drugs which increase DA can cause paranoid schizophrenic states (e.g. amphetamine psychosis)
• brains of schizophrenics do show some abnormalities in DA activity
• BUT: not the only neurotransmitter affected - growing evidence that serotonin & glutamate also involved
• Blockade of DA receptors by typical antipsychotics primarily decreases “positive” symptoms.
Main Side Effects

• Extrapyramidal Motor Disorders
• Dry mouth, blurred vision, constipation
• Sedation, decreased response to stimuli
• Postural hypotension
• Disturbed hypothalamic functions; skin photosensitivity

• As with mood stabilizers, side effects can lead to significant noncompliance.

Extrapyramidal Motor Effects

• Parkinson’s-like decreased movement (≤30%)
• Involuntary movements of face & limbs (dyskinesia) in 20%
• Compulsive restlessness (akathisia) in 20% (≥2) & internal, emotional sense of agitation
• Sometimes strong involuntary muscle spasms (dystonias) (2%)

• Often must take drugs to control motor side-effects

Tardive Dyskinesia (TD)

• Neurological symptom that may appear after months of use. More common the longer the use, the higher the dose or the older the patient.
• Involuntary movements of lips, tongue, jaw, face, eyelids &; less often, the body
• Unlike other extrapyramidal symptoms, TD may increase if drug is discontinued (may be long-lasting or permanent in some)

http://www.youtube.com/watch?v=BRbjRctgj_k

Second Generation (SGA) or “Atypical” Antipsychotics

• Prototype: Clozaril (clozapine) (1989)
• Block selected D2 & 5HT2 receptors
• Fewer extrapyramidal side effects
• Helped 30-33% previously unresponsive patients
• Improved “negative” symptoms and disorganization; largest decrease in suicides
• Side effect: wt. gain, constipation, sedation
• BUT can cause deadly agranulocytosis in 1-2% so requires blood monitoring

More Atypical Antipsychotics

• Risperidone (Risperdal) But may cause wt. gain, high blood sugar, & diabetes Warning: increased risk of death when used for dementia-related psychosis in elderly
• Olanzapine (Zyprexa)
• Quetiapine (Seroquel)
• Ziprasidone (Geodon)
• Lurasidone (Latuda)
• Aripiprazole (Abilify) may be “new generation” – not a DA blocker

Must weigh side effects/risks against cost
Some will still have EPS

Neuroleptic Malignant Syndrome

- Medical emergency - possibly life-threatening event in 1-2%; may not be recognized
- severe rigidity, may not be able to swallow or speak or move eyes
- catatonia, confusion, agitation, or coma possible
- autonomic effects, high fever; unstable vitals
- Antipsychotics must be stopped; need to be in ICU to control vitals

Other Uses for Antipsychotics

- Other psychotic conditions
- Bipolar disorder; add-on for depression, anxiety
- Borderline personality disorder
- As an add-on for treatment of major depression & some anxiety disorders (SSD, P150)
- Some developmental disorders like autism
- Symptoms of Huntington’s Disease & Tourette syndrome
- Treat aggression, agitation, delusions of dementia
- anti-nausea, anti-itching (e.g. Compazine)
- treat intractable hiccups; slow premature ejaculation
- preanesthetic calming

http://www.youtube.com/watch?v=7IdQYmqqDQ