Antipsychotics

Approach: Start with discussion of dopaminergic pathways, then move to class-wide discussion of mechanism and side effect, then finally a discussion of specific drugs.
Hook: Antipsychotics have been around for a long time, yet their mechanism and efficacy are still somewhat of an enigma. They are also prime shelf exam material and heavily used on inpatient units

What are the four dopaminergic pathways? 1) Mesolimbic (positive symptoms), 2) Mesocortical (negative symptoms), 3) Nigrostriatal pathway (EPS and TD), 4) Tuberoinfundibular (hyperprolactinemia)

	First Generation "Typicals"	**Second Generation "Atypicals"**
Mechanism	Postsynaptic blockade of brain dopamine D2 receptors Examples: Haloperidol (Haldol) Chlorpromazine (Thorazine) Perphenazine (Trilafon)	Block D2 but also Serotonin 5HT2 receptors. 5HT2 activity has been suggested as one basis for the lower overall risk of extrapyramidal side effects (EPS) with the atypical drugs compared with FGAs
Side Effect	**EPS**: The defining difference between FGAs and the newer SGAs is their higher incidence of the following extrapyramidal symptoms: - **Akathisia** — Most common form of EPS. Usually presents as motor restlessness with a compelling urge to move and inability to sit still (Tx = beta blocker, benzo) - **Dystonia -** Involuntary contractions of major muscle groups, characterized by symptoms such as torticollis, oculogyric crisis (Tx = benztropine, diphenhydramine) - **Parkinsonism** - resting tremor, muscle rigidity, bradykinesia, postural instability. (Tx = amantadine, diphenhydramine, benztropine) - **Tardive Dyskinesia -** involuntary movements that occur after chronic use of antipsychotics. These seldom occur after < 6 months of tx, usually = years. Typically: Sucking, smacking of lips, choreoathetoid movements of the tongue, facial grimacing, lateral jaw movements, choreoathetoid movements of extremities (Tx = switch to an antipsychotic with lower risk for TD such as Seroquel/Clozaril)	Weight gain and related metabolic effects, hypotension, sedation, anticholinergic symptoms, extrapyramidal symptoms, cardiac effects, hyperprolactinemia (can lead to gynecomastia, galactorrhea, menstrual disturbances, sexual dysfunction, and infertility) Examples: **Clozapine**: Most effective. Most serious side effects. Agranulocytosis, myocarditis, seizure. Weight gain close 2nd. Weekly CBC needed. **Risperidone**: most EPS of 2nd gen (10-25% risk), most hyperprolactinemia **Olanzapine**: High metabolic syndrome risk; most weight gain **Quetiapine:** Sedation. Approved for bipolar depression. QT prolongation. **Zipraisdone**: Most QTc prolongation. Weight neutral. **Aripiprazole**: Also approved in kids for irritability w ASD, and bipolar in kids. Weight neutral. **Newer**: Paliperidone (Invega), Lurasidone (Latuda), Iloperidone (Fanapt), Asenapine (Sasphris) **Bipolar depression** – Seroquel, Lurasidone, Olanzapine/Fluoxetine

Script by Philip Cawkwell