Psychosis and Antipsychotic Medications

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Psychosis

- Disordered/distorted sense of reality
- Disorganized behavior
Psychotic Disorders

- Schizophrenia
- Delusional disorder
- Schizoaffective disorder
- Psychosis with mood disorders (mania, depression)
- Substance-induced psychosis
- Psychosis due to General Medical Condition (delirium, temporolobal epilepsy)
Schizophrenia

- DSM V: >= 2 symptoms for at least 6 months
  - Delusions, hallucinations, disorganized speech, disorganized behavior/catatonia, negative symptoms

- Paranoid—Disorganized (hebephrenic) spectrum
- 1% prevalence.
- High heritability (First degree relative risk 10%)
- 1:1 gender
- Onset: late teens-early 20s (males earlier)
Schizophrenia Symptom Clusters

• Positive Symptoms
  – Delusions
    • Persecutory, erotomanic, jealousy, poverty, grandiose, nihilism, somatic
  – Hallucinations
    • Auditory, visual, tactile, olfactory, gustatory

• Negative symptoms
  – Apathy, anhedonia, affective flattening, alogia, avolition, asociality
Treatment--Medications

- 1955: First antipsychotic drugs
- 1965: Medicaid & Medicare enacted
Antipsychotic Medications

- 1952: Chlorpromazine/Thorazine
- 1957: Perphenazine/Trilafon
- 1958: Haloperidol/Haldol
- 1959: Trifluoperazine/Stelazine
- 1960: Fluphenazine/Prolixin
- 1962: Thoridazine/Mellaril
- 1967: Thiothixine/Navane
- 1974: Molindone/Moban
- 1975: Loxapine/Loxitane
- 1989: Clozapine/Clozaril
- 1993: Risperidone/Risperdal
- 1996: Olanzapine/Zyprexa
- 1997: Quetiapine/Seroquel
- 2001: Ziprasidone/Geodon
- 2002: Aripiprazole/Abilify
- 2006: Paliperidone/Invega
- 2009: Asenapine/Saphis
Treatment—Medications

Classical/Typical/First Generation Antipsychotics (FGAs)
  D2 Blockers
  Assoc with EPS, hyperprolactinemia,

Atypical/Novel/Second Generation Antipsychotics (SGAs)
  Weaker D2 blocking; stronger HT2 blocking
  Assoc with weight gain, metabolic syndrome
Uses of Antipsychotics

- Primary psychotic disorders
- Substance induced psychosis
- Psychosis in Parkinson’s Disease
- Delirium
- Aggression
- Mania
- Depression
- Borderline Personality Disorder
- Sedation
- Tourette’s syndrome
- Nausea, Hiccups, Vomiting
First Generation Antipsychotics

(aka neuroleptics, typical or classic antipsychotics)

• Haloperidol/Haldol
• Fluphenazine/Prolixin
• Perphenazine/Trilafon
• Chlorpromazine/Thorazine
• Pimozide/Orap
• Thioridazine/Mellaril
• Loxapine/Loxitane
Extrapyramidal Side Effects (EPS)  

**Acute**

- **Parkinsonism**
  - Anticholinergic Rx
    - Trihexiphenidyl/Artane
    - Benztropine/Cogentin
    - Biperiden/Akineton
  - Antihistamine Rx
    - Diphenhydramine/Benadryl
  - Dopaminergic Rx
    - Amantadine/Symmetrel
Extrapyramidal Side Effects (EPS)

**Acute**

- **Acute Dystonia**
  - Anticholinergic Rx
    - Benztropine/Cogentin
  - Antihistamine Rx
    - Diphenhydramine/Benadryl
  - Benzodiazepines
  - Botulinum toxin
Extrapyramidal Side Effects (EPS)  

**Acute**  

- **Akathisia**  
  - Beta Blocker  
    - Propranolol  
  - Benzodiazepines
Extrapyramidal Side Effects (EPS)

Late Onset

- Tardive Dyskinesia
- Tardive Dystonia
Neuroleptic Malignant Syndrome (NMS)

• 1-2% of pts taking FGAs. Also occurs in SGAs
• Fatal in <= 20% of cases
• 80% occur in first 2 weeks of treatment
• Sxs: hyperpyrexia, altered consciousness, dystonia, autonomic NS dysfunction (hypo-/hypertension, tachycardia, diaphoresis.
• Labs: Incr WBC, CPK, myoglobinemia/uria
• Can last up to 14 days
• Discontinue Rx.
Side Effects/Cautions--FGAs

- Seizures
- CVA
- Catatonia
- Hyperprolactinemia
Second Generation Antipsychotics

(aka Atypical Antipsychotics)

• Clozapine/Clozaril
• Olanzapine/Zyprexa
• Quetiapine/Seroquel
• Risperidone/Risperdal
• Aripiprazole/Abilify
• Ziprasidone/Geodon
Clozapine/Clozaril

- Most effective antipsychotic
- Least likely to cause EPS/TD
- Helpful for psychosis with Parkinson’s Disease
- Reduces aggression and suicidality

- Risks
  - Sedation
  - Sialorrhea
  - Weight gain
    - Average 10 pounds
    - Assoc with Diabetes
  - Seizures
    - 5-10% pts (usu at doses >600 mg/d)
  - Agranulocytosis
    - <1%
    - Registry and WBC checks
Olanzapine/Zyprexa

- Derived from Clozapine
- Dose range: 5-30 mg/d
- PO forms (tablet and orally disintegrating form)
- IM form (5x po availability; avoid concurrent use with benzos)
- Effective
- Poorly tolerated (weight gain, sedation)
- Kinetics affected by age and gender
Quetiapine/Seroquel

• Also derived from Clozapine
• Approved for Schizophrenia, mania and bipolar depression
• Dosing: 150-800 mg

• Kinetics affected by age but not gender, smoking, body weight
Risperidone/Risperdal

- Approved in 1984 for Schizophrenia, acute mania
- PO formulation (tabs and orally disintegrating tab)
- Dosing: 0.5-8 mg/d
- IM formulation

- Assoc with akathisia, hyperprolactinemia, sedation
Aripiprazole/Abilify

- Structurally unrelated to other SGAs
- Approved for Schizophrenia, mania, mixed mania and for augmentation of antidepressants

- Dose range 5-20 mg/d
Ziprasidone/Geodon

- Less likely to cause Metabolic Syndrome, EPS, prolactinemia
- PO form
- IM form
- Dosing 80-160 mg/d
Side Effects/Cautions--SGAs

• Weight gain

• Metabolic Syndrome:
• central obesity + (>=2: raised fasting glucose, hypertriglyceridemia, hypertension, reduced HL
Depot (im) Antipsychotics

Loading dose: 20x oral dose (ie 20 x 4-8 mg)
Then, monthly decrease to 15x, 12x, 10x.
Usually, 10x is maintenance dose
injection q 4 wks

Loading dose formula is less worked out
Usual po dose 2-8 mg/d
injection q 3 wks
Monitoring

• Compliance
• Involuntary movements/EPS
  – AIMS
• Health
  – Obesity
  – Drug use
  – Smoking
### Abnormal Involuntary Movements Scale (AIMS)

**Patient's Name (please print)**

**Examiner's Name**

**Current Medications and Total mg/day**

<table>
<thead>
<tr>
<th>Medication #1</th>
<th>Total mg/day</th>
<th>Medication #2</th>
<th>Total mg/day</th>
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**Instructions:** Complete the examination procedure before entering these ratings.

#### Facial and Oral Movements

1. Muscles of facial expression (e.g., movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing)
2. Lips and perioral area (e.g., puckering, posturing, smacking)
3. Jaw (e.g., biting, clenching, chewing, mouth opening, lateral movement)
4. Tongue (Rate only increases in movement both in and out of mouth, NOT inability to sustain movement)

#### Extremity Movements

5. Upper (arms, wrists, hands, fingers) (Include chronic movements (i.e., rapid, objectively purposeless, irregular, sporadaneous); athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT include tremor (i.e., repetitive, regular, rhythmic).)
6. Lower (legs, knees, ankles, toes) (e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot)

#### Trunk Movements

7. Neck, shoulders, hips (e.g., rocking, twisting, squirming, pelvic gyrations)

#### Scoring:

- Score the highest amplitude or frequency in a movement on the 0-4 scale, not the average.
- Score Activated Movements the same way; do not lower those numbers as was proposed at one time.
- A POSITIVE AIMS EXAMINATION IS A SCORE OF 2 IN TWO OR MORE MOVEMENTS or a SCORE OF 3 OR 4 IN A SINGLE MOVEMENT.
- Do not sum the scores: e.g., a patient who has scores 1 in four movements DOES NOT have a positive AIMS score of 4.

#### Overall Severity

8. Severity of abnormal movements
9. Incapacitation due to abnormal movements

#### Patient's awareness of abnormal movements (rate only patient's report)

10. Patient's awareness of abnormal movements

#### Dental Status

11. Current problems with teeth and/or dentures?
12. Does patient usually wear dentures?

**Comments:**

**Examiner's Signature**

**Next Exam Date**