Schizophrenia is the most common psychotic illness

- Prevalence of 1/1000 people
- Poor long-term outcomes in social and vocational realms
- Higher rates of medical illness and mortality than the general population
- Life expectancy is 25 years less than average
- Primarily affected by cardiovascular disease
- Higher rates of suicide (5%–13 times greater than general population)

Clinical Significance

- Patients with schizophrenia die earlier than the general population mostly from preventable and treatable medical illnesses.
- Higher rates of cardiovascular, infectious, respiratory, endocrine, and gastrointestinal disease in patients with schizophrenia.
- Certain antipsychotic medications contribute to metabolic abnormalities more than others.
- Routine physical health monitoring and targeted interventions, especially for cardiovascular disease and its risk factors, are key considerations when caring for this patient population.

What is schizophrenia?

- “Psychosis” is not a diagnosis but a term describing certain symptoms with the most narrow definition including delusions and/or hallucinations.
- May be a part of the presentation of schizophrenia
- Not all psychosis is indicative of a primary psychiatric disorder such as schizophrenia, i.e. infection, endocrinopathies, electrolyte metabolite abnormalities, neurological processes (seizures, and demyelinating diseases, brain lesions), intoxication and withdrawal from drug use.

Screening for psychosis

- Start with a lead-in treatment to normalize the experience.
- Elicit delusional thinking by asking about strange or odd experiences, people following or watching you, feeling like you can hear others thoughts, afraid you will be hurt or harassed.
- Elicit reports of hallucinations by asking “Have your ears her eyes playing tricks on you? Are there times when you heard or saw things that the people could not?”
Six common symptom clusters characteristic of schizophrenia

- Delusions and hallucinations
- Motor system abnormalities
- Affective symptoms
- Negative symptoms
- Cognitive dysfunction
- Disorganization of speech

Characteristics of schizophrenia

- Combination of symptoms, some more prominent than others, lasting for 1 month or more and causing social or occupational dysfunction
- Continuous signs of disturbance must persist for 6 months
- “Positive” symptoms: Delusions, Conceptual disorganization, Hallucinations, Excitement, Grandiosity, Suspiciousness/persecution, Hostility
- “Negative” symptoms: alogia, anhedonia or asociality, avolition or apathy, affective blunting, lack of attention or cognitive deficits (difficulty with abstract thinking, stereotyped thinking)
- Developmentally, negative symptoms often appear first in a patient but are harder to detect.

Antipsychotic medications

- Help to manage symptoms by a blockade of D2 dopamine receptors
- Have little effect on negative or cognitive symptoms
- First-generation antipsychotics are likely to reduce sedation, orthostasis and anticholinergic side effects as well as extrapyramidal symptoms and prolactin elevation
- Second-generation antipsychotics have the potential for troubling weight gain, disturbances in glucose and lipid metabolism
- Clozapine has the risk of agranulocytosis and requires routine monitoring of blood
- Some medications cause prolonged QTc

Treatment of schizophrenia

- Usually requires a multidisciplinary team
- Psychiatrist, PCP, therapist, case manager, outreach worker, visiting nurse, residential staff member, legal guardian

IMPACT

- Assertive community treatment (ACT) is an evidence-based model of treatment for individuals with severe and persistent mental illness for whom traditional approaches have been ineffective. Individuals appropriate for Integrated Multidisciplinary Program of Assertive Community Treatment (IMPACT) are those that have had frequent or prolonged hospitalizations, or experienced homelessness or incarceration by virtue of their mental illness.
- Assertive community treatment programs are typically staffed by a multidisciplinary team of physicians, nurses, social workers, substance abuse counselors, occupational therapists, and rehabilitation therapists. The team provides consistent care and assertive client advocacy by teaching individuals in the program ways to improve quality of life, self and home care, and resource utilization.

Team members may assist individuals in the program with:

- Accessing and maintaining benefits
  - Food stamps
  - Medicaid
  - Social Security
- Gaining and maintaining employment
- Housing
- Maintaining activities of daily living
  - Bathing, grooming, cooking, housekeeping
  - Paying bills
  - Taking medications
  - Transportation
- Managing medications and symptoms
Treatment of an initial presentation of psychosis in primary care setting

- May be an initial presentation or a long-standing psychotic illness
- Primary care provider may elect to start medication after ruling out medical causes for presentation and while waiting for definitive psychiatric assessment
- May be possible to treat on an outpatient basis
- First-line choices are risperidone or perphenazine for treatment-naïve patients
- Risperidone is a second generation antipsychotic with low rates of extrapyramidal symptoms and moderate metabolic side effects
- Perphenazine is a first generation antipsychotic with a better metabolic profile and an increased risk of extrapyramidal symptoms including acute dystonia and tardive dyskinesia
- A baseline metabolic profile should be obtained as well as education about general lifestyle interventions including diet and exercise

Medical care of patients with schizophrenia

- Mortality rate and schizophrenia is 2-3 times higher than in the general population
- Elevated risk is due to mortality from suicide and injury as well as medical illness
- 5% of people with schizophrenia complete suicide
- Making it a 13 time greater risk than in the general population
- Risk assessment should be a routine part of the clinical encounter

Medical illness is highly prevalent in patients with mental illness

- 50-90% of patients having at least one chronic medical condition
- In patients with schizophrenia rates of mortality from medical illnesses are elevated across the following disease categories: infections, respiratory, endocrine, GI, cardiovascular

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Family history of obesity, diabetes, dyslipidemia, hypertension or cardiovascular disease</td>
<td>Baseline, annually</td>
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<td>Smoking status</td>
<td>Each visit</td>
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<tr>
<td>Weight (kg)</td>
<td>Before starting an antipsychotic, then monthly, then quarterly if stable</td>
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<tr>
<td>Waist circumference</td>
<td>Baseline, annually</td>
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<tr>
<td>Blood Pressure</td>
<td>Baseline, 3 months, then at least annually</td>
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<tr>
<td>Fasting glucose and Fasting lipid (Adjusted risk of diabetes and hyperlipidemia with antipsychotic use)</td>
<td>At initiation, 3 months, then at least annually</td>
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<tr>
<td>EKG (antipsychotics may prolong QTc)</td>
<td>No clear consensus</td>
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<tr>
<td>Neurological examination (Parkinsonism and dyskinesia, especially with first generation antipsychotics)</td>
<td>Q6 months</td>
</tr>
<tr>
<td>Prolactin level</td>
<td>When indicated</td>
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Often medical problems are side effects from medications

- Weight gain
- Diabetes
- Hypercholesterolemia
- EPS/TD
- Prolactin elevation
- Sedation
- Anticholinergic side effects
- Orthostatic hypotension
- QTc prolongation

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<th>Effect of Antipsychotics in Clinical Trials (Benzyl-Neuroleptic)</th>
<th>Other Antipsychotics</th>
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<td>Risperidone</td>
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<td>Ziprasidone</td>
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<tr>
<td>Olanzapine</td>
<td>7</td>
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<td>Clozapine</td>
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<th>Assessment</th>
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<td>Clozapine</td>
<td>20</td>
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**Cardiovascular disease in people with schizophrenia**
- Risk factors include obesity, smoking, diabetes, hypertension, dyslipidemia, metabolic symptoms
- Present at rates 1.5-5 times greater than the general population
- In a cohort of chronic schizophrenic patients, 41% had metabolic symptoms
- Second generation antipsychotics often exacerbate these parameters

**Treatment**
- Some risk factors are amenable to intervention, i.e., smoking, diet and exercise
- Using CBT, Motivational Interviewing can be helpful
- Use of metformin to reduce metabolic risks
- Medical management of hypertension

**Management of EPS**
- Risperidone has a greatest risk of EPS especially at doses greater than 4 mg daily
- Clozapine is one of the preferred agents in patients with high risk for EPS
- Patient should be monitored for restlessness, slow movements, shaking and rigidity at baseline and weekly during dose increases

**EPS management**
- Benztropine and beta-blockers
- Benzodiazepines were first-line until 2 studies (2016) reported association between benzodiazepine use and mortality in schizophrenic patients

**Tardive dyskinesia**
- Sucking, smacking of lips
- Choreaathetoid movements of the tongue
- Facial grimacing
- Lateral jaw movements
- Choreiform or athetoid movements of the extremities and/or truncal areas
- Effects can be permanent, even with withdrawal of medication

**Managing TD**
- Reevaluate medication regimen
- Consider use of quetiapine or clozapine
- Clozapine requires monitoring for severe neutropenia
- Can also cause orthostatic, hypotension, bradycardia, syncope, seizures, myocarditis, cardiomyopathy
- Severe dystonias can be treated with intramuscular or intravenous benztropine or diphenhydramine.
- Milder dystonias can be treated with lower, less frequent doses of benztropine.
Secondary parkinsonism
• Consists of mask-like facies, resting tremor, cogwheel rigidity, shuffling gait, and psychomotor retardation
• Benztropine, amantadine

QT prolongation
• Clozapine, thioridazine, iloperidone, ziprasidone, pimozide, and intravenous haloperidol prolong the QT interval, particularly at higher doses. These medications should be avoided in patients with cardiac disease, elderly patients, and in conjunction with other medications that prolong the QT interval such as antiarrhythmics and erythromycin.
• An electrocardiogram (ECG) should be performed prior to starting the medication and periodically (e.g., yearly) during treatment.

Neuroleptic malignant syndrome
• Neuroleptic malignant syndrome, a tetrad of clinical features (fever, rigidity, mental status changes, and autonomic instability), is associated with medications that block dopamine transmission.
• Neuroleptic malignant syndrome is a rare but potentially life-threatening event that can be seen with all antipsychotic drugs with a reported incidence rate of less than 1 to 3 percent of patients taking these medications [25].
• Treatment involves withdrawal of medication and intensive management for cardiovascular support, control of hyperthermia, and fluid and electrolyte balance.

Anticholinergic effects
• Anticholinergic side effects of antipsychotic drugs include dry mouth, urinary hesitancy, constipation, visual disturbance, and cognitive impairment. These effects tend to be worse in older patients.
• Anticholinergic effects are seen with clozapine, chlorpromazine, olanzapine, and, to a lesser extent, with quetiapine, iloperidone, and loxapine.
• Because anticholinergic effects are dose-related, dose reduction is one approach to these side effects.

Sedation
• Although any antipsychotic can cause sedation in some patients, severe sedation is most common with low potency medications such as chlorpromazine, clozapine, and quetiapine.
• These side effects are usually most severe during the first weeks of treatment and often require gradual titration of the antipsychotic. Sedating medications may be best tolerated at bedtime.

Elevated plasma prolactin
• First-generation antipsychotics, risperidone, and paliperidone can elevate plasma prolactin. This elevation can lead to galactorrhea and menstrual disturbances in women as well as sexual dysfunction and gynecomastia in men. This side effect can usually be managed by changing to a medication that is less likely to elevate prolactin.
Obstacles to effective care

- 50% of patients with schizophrenia have substance use disorder
- Symptoms of the disorder may disrupt the process of engagement
  - Paranoia may make waiting in a crowded waiting room difficult
  - Thought disorder and cognitive impairments can obscure a history, interfere with treatment plan
  - Negative symptoms (amotivation) can interfere with adherence

Conclusions

- Vulnerable population with high medical needs that are often missed, undertreated and can lead to premature mortality
- PCPs as frontline clinicians have the potential to reduce disparities
- Focus on cardiovascular care

Works cited

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