Schizophrenia

And other psychotic disorders

Learning Objectives:

1. Diagnosing schizophrenia
2. Epidemiology of schizophrenia
3. Course and prognosis of schizophrenia
4. Etiology of schizophrenia
5. Biological & psychosocial interventions in treating schizophrenia & other psychotic disorders

Outline:

1. Diagnosing schizophrenia
   - What is meant by the term “psychosis”
   - Identifying the “positive” symptoms and the “negative” symptoms of schizophrenia
   - Diagnostic process for schizophrenia-Criteria A, social occupational dysfunction, time duration
   - Downward drift hypothesis
   - Differential diagnosis of schizophrenia/other psychotic disorders

2. Epidemiology of schizophrenia

3. The course & prognosis of schizophrenia
   - What is the prodromal phase, active phase, residual phase
   - Risk of suicide, substance abuse
   - Problem of cognitive impairment
   - Prognosis of schizophrenia, good and bad outcome predictors

4. The etiology of schizophrenia
   - Dopamine Hypothesis, Genetic theory, Infection/Immune theory
   - Theory of illness process: neurodegenerative, developmental

5. The biological & psychosocial interventions in treating schizophrenia & other psychotic disorders
   - Overview of use of anti-psychotic medication in treating psychotic disorders
   - Ongoing treatment issues: medication compliance, issue of assisted treatment
   - Social issues of the illness: food, money, medical care, housing

6. How do patients with schizophrenia present to Medicine
   - Increased risk of cardiovascular disease in schizophrenia patients

Mechanisms Human Disease Course 2010
Schizophrenia & Other Psychotic Disorders

I. Diagnosing Schizophrenia

Criteria A: Active Phase signs and symptoms
Criteria B: Social Occupational Dysfunction How bad is it?
Criteria C: Time Duration
Criteria D: Another Diagnostic Explanation

Criteria A: Signs & Symptoms

1. Hallucinations
2. Delusions
3. Disorganized thinking
4. Disorganized Behavior
5. Negative Symptoms

Psychosis

Grossly impaired reality testing. Persons incorrectly evaluate the accuracy of their perceptions and thoughts and make incorrect inferences about external reality, even in the face of contrary evidence. Psychosis commonly means the patient is experiencing delusions and hallucinations. These are also called the "positive" symptoms of schizophrenia.
Disorganized thinking is also sometimes referred to as psychotic thinking or psychosis.

1. **Hallucinations**-perceptions without stimuli;
   - Auditory hallucinations-"hearing voices"; most common type of hallucination
   - Visual hallucinations-"seeing things that aren't there"; 2nd most common type of hallucination
   - Tactile hallucinations-feeling things that aren't there, like bugs on or under ones skin; less common type of hallucination; may be seen in context of various substance withdrawal syndromes
   - olfactory & gustatory hallucinations- smelling, tasting things; rare type of hallucinations
2. **Delusions**-unfounded, unrealistic belief that is held without supporting evidence;
   a key is the person is feature is the person is totally convinced that what they believe is true; will lead to conflicts with others
   - Non-bizarre delusions-have a certain amount of plausibility when you first hear about it, as you get more and more details it becomes less and less plausible
   - Bizarre delusions-clearly implausible, not understandable, and/or do not derive from ordinary life experiences. Usually easy to identify though can be difficult to judge situations involving different cultures
   - Delusion examples

Non bizarre	Bizarre
My significant other is being unfaithful;	My wife is having an affair with Elvis Presley
Oprah Winfrey is trying to reach you to ask you to be on her show;	Oprah Winfrey (who the I have never met) is desperately in love with me,
I am being watched/monitored, harassed by my neighbors	Alien controlled neighbors are monitoring/harassing me

3. **Disorganized thinking**
   - Symptom must substantially impair effective communication

   Inferences about thinking are based primarily on the individual's speech; one's speech may be disorganized in various ways:

   Derailment or loose associations—person slips off track from one association to another
   Tangential speech-answers are unrelated or only vaguely related to the question

Incoherence or word salad-severely disorganized speech, nearly incomprehensible

4. **Disorganized behavior**

Grossly disorganized; may be seen in wide range of possible behaviors.

Childlike silliness to unpredictable agitation,

Problems with any form of goal directed behavior; leads to difficulties performing activities of daily living (meal preparation, maintaining personal hygiene,

5. **Negative symptoms**

affective flattening-lack of emotion; interpersonal emotional cues (facial expression, eye contact, body language) are lacking

alogia-poverty of speech; brief, laconic, empty replies

avolition-lack of motivation; inability to initiate and persist in goal directed activities

anhedonia-lack of pleasure; unable to enjoy activities

Only need to have one of the four negative symptoms to qualify as having negative symptoms

Meeting the Schizophrenia A criteria

Need to have 2 of the 5 signs and symptoms to meet the A criteria.

If the delusions are so severe that they are bizarre delusions-that is enough to meet the A criteria

If the hallucinations are auditory and are severe (a voice continually commenting, or multiple voices conversing) that is enough to meet the A criteria.

Criteria B: Social Occupational Dysfunction, How Bad Is It?

For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning--work, interpersonal relations, or self-care-- are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

Downward Drift Hypothesis

- It is noted that a disproportionate number of people with schizophrenia are in the low socioeconomic group. The downward drift hypothesis posits that the reason is that the social-occupational dysfunction of schizophrenia results in those who start out with resources available to them gradually lose them and drift downward into the low socioeconomic group.
- A significant number, 33%, of the homeless population have schizophrenia

Criteria C: Time Duration

Continuous signs of the disturbance that persist for at least 6 months—Criteria A does not need to be met for the entire time

At least 1 month where Criteria A (active phase symptoms) is met

If duration of symptoms < 1 month—diagnosis of brief psychotic disorder or psychosis nos (not otherwise specified)

If total duration of symptoms > 1 month, < 6 months—diagnosis of schizophreniform disorder

Onset of illness-most commonly there is a gradual onset and building of the symptoms of schizophrenia, a prodromal phase. Often it is not realized until after the symptoms have gotten serious (the first break of psychosis), that the behaviors were abnormal and part of a prodromal phase.

Criteria D: Another Diagnostic Explanation

Illnesses with psychosis	
1. Another psychotic disorder	Schizoaffective disorder, Delusional disorder, Schizophreniform disorder, Brief Psychotic Disorder, Psychosis N.O.S.,
2. Mood disorder with psychosis	Bipolar disorder w/ psychotic features, Major Depression w/ psychotic features
3. Psychosis due to a substance	Substance Intoxication/Withdrawal, Psychosis secondary to medication reaction

4. General Medical condition	Any medical illness, that effects the CNS-neurological, endocrine, metabolic
5. Developmental Disorders	Autism, Rhett's disorder, Asperger's disorder
6. Personality disorders	Cluster A-paranoid, schizoid, schizotypal

1. Another psychotic disorder
   Schizoaffective disorder-period(s) of time with mood disorder (major depression, a manic episode)
   and Criteria A of schizophrenia ; also there is a period of 2 weeks time of symptoms that meet Criteria A of schizophrenia but there are no prominent mood symptoms
   Delusional Disorder—non-bizarre delusion; most common: persecutory, jealousy
2. Mood disorder with psychosis
   Bipolar disorder with psychosis -symptom overlap: grandiosity (delusions?), flight of ideas (disorganized speech)
   Major depression with psychosis-symptom overlap with negative symptoms: anhedonia, avolution (lack of energy), affective flattening (disturbed mood?)
3. Psychosis due to a substance
   Intoxication with Alcohol, any illicit drug
   Withdrawal: alcohol, sedatives, hypnotics, anxiolytics
   Medications: anesthetics, anti-cholinergics, anti-convulsants, anti-histimines, anti-hypertensive, cardiovascular meds, anti-microbial meds, anti-parkinsonian meds, chemotherapeutic agents, **steroids**, GI meds, muscle relaxants, NSAIDS, OTC, anti-depressants, disulfiram,
4. General Medical condition
   Neurological-neoplasms, dementia, CVA's, epilepsy, CNS infection, Huntington's disease
   Endocrine-hyperthyroid, hypothyroid, hyperparathyroid, hypoparathyroid, hypoglycemia
   Metabolic-delirium: hypoxia, hypercarbia, hepatic diseases, renal diseases, fluid or electrolyte imbalances
5. Developmental disorder
   Autism, Rhett's, Aspergers: symptom overlap: poor communication skills (disorganized thinking/speech), poor reciprocal social skills (affect is flat, anhedonia?)
6. Personality disorders
   Paranoid-pattern of distrust and suspiciousness of others (delusion?)
   Schizoid-social detachment & restricted affect (negative symptoms?)
   Schizotypal-odd beliefs/unusual perceptual experiences (psychosis?), odd speech (disorganized thinking?), odd/eccentric behavior (disorganized behavior)

II. Epidemiology

The incidence of schizophrenia in the U.S. is 0.3 - 0.6 per 1000 individuals.
The lifetime prevalence is about 1%. Ranges reported in different studies vary between 0.5%-1.5%.
Prevalence Male vs Female? About equal M = F
US population of ~ 300 million; ~ 2.2 million people in the country have schizophrenia

Impact on Society: *Where do 2.2 million patients with Schizophrenia live?*

• 750,000 (~33%) live independently	• 135,000 (~6%) live in jail/prison o This is 15-30% of all people in jail/prison
• 550,000 (~25%) live with family member	• 100,000 (~4.5%) live in hospitals
• 400,000 (~18%) live in group home or other supervised living situation	• 100,000 (~4.5%) are homeless-live in shelters/streets o This is over 33% of homeless population
• 165,000 (~7.5%) live in nursing homes	

III. Course of Illness

A. Prodromal phase: vague symptoms-social isolation/withdrawal, peculiar behavior, impaired personal hygiene,
inappropriate affect, abnormal speech, odd beliefs; often the prodromal phase is not identified until after an

the first active phase (psychotic break) takes place;

B. Active phase (relapse): Patient meets the "A" criteria for schizophrenia

C. Residual phase (remission): after active phase(s) have taken place; no longer clearly meets the "A" criteria; much overlap with the Prodromal phase

1. Peak age of onset of 1st time in Active phase:

Male-earlier age 15/18-25 years; > 50% have 1st hospitalization by age 25

Female-later, age 25-35/45; ~33% have 1st hospitalization by age 25

2. Severity of illness, in general, M > F

10-15% have single active phase

25-30% have intermittent active phases

50-55% have chronic course of illness

3. Suicide

- Completed suicide: different studies give range of 8-10%
  General population complete suicide rate 1%
- Attempted suicide: different studies give different ranges, but ~40% make suicide attempts
  ~50x's higher than general population risk for suicide attempts
- Risk factors
  - Young, male, higher functioning, good insight into illness, med non-compliance/poor response to medication, substance abuse, social isolation/depression
  - Most common time is during remission of illness just following a relapse (post hospitalization discharge is a high risk period)

4. Cognitive Impairment

- SMART
  Speed, **M**emory (working, visual, verbal) **A**ttention, **R**easoning, **T**act (social cognition)
- Patients are moderately to severely impaired compared with general population
- Appears early in course of illness, persists, and is stable
- Wisconsin Card Sort
- Anosognosia-lack of awareness of illness. Also called lack of insight into illness
  Some patients have awareness of their illness. Often, as illness progresses they lose their awareness.
  Some patients have no awareness of their illness.
  Some patients have partial awareness of their illness.
  Finally, for patients with illness awareness or partial awareness, there may be variability in their awareness as their illness goes into and out of the active phase.

5. Substance Abuse

- 30-50% alcohol abuse/dependence
  10-15% marijuana abuse/dependence
  5-10% cocaine abuse/dependence
- About 50% of patients with schizophrenia have, or have had, a problem with alcohol or illicit drugs

6. Prognosis/Outcome predictors

Predictor of Worse Outcome	Predictor of Better Outcome
Insidious onset (premorbid phase)	Acute/sudden onset (no premorbid phase)
Family history of schizophrenia	No family history
Earlier age of onset—teen years	Later age of onset—30's
Male	Female
Negative symptoms	Lack of negative symptoms
Initial lack of response to medications	Initial response to medications**

Initial minimal response to medications	**Strongest correlation with outcome**
Substance abuse	

Please note, predictive factors are statistical and indicate increased likelihood. No factor or combination of factors makes one a lock to have a good or bad outcome.

Other Treatment Issues

- Medication compliance
  - Medication side effects
  - Majority (70%) are non-compliant within 2 years post hospital discharge
  - Availability of long term injectable form of medication—depot anti-psychotics

- Psychosocial problems
  - Money, Food, Housing
  - Employment
  - Social Skills training
  - Medical & Dental Care

- Victimization
  - Vulnerable to criminals, cognitive deficits make them "easy marks" for theft, assault, and rape. Often the victims have difficulty giving a coherent narrative to police of what happened.

- Concerns about Assaultive/Violent Behavior

  Surgeon General 1999 report conclusions:

  1. To date nearly every modern study indicates that public fears are way out of proportion to the actual risk of violence from patients with mental illness
  2. Magnitude of violence associated with mental illness is comparable to that associated with age, educational attainment, and gender and is **limited to only some disorders and symptoms constellations**
  3. Because serious mental illness is relatively rare and the excess risk modest, the contribution of mental illness to overall levels of violence in our society is miniscule

  Risk factors for violence from schizophrenia patients

  - Concurrent alcohol and/or substance abuse
  - Noncompliance with medication
  - Past history of assaultive behavior

  Patients with schizophrenia are at much higher risk of harming themselves than others

- Sex, Pregnancy, Parenthood
  - Side effects of anti-psychotic medications may decrease sexuality, fertility; but ~50% of women with schizophrenia become mothers (almost equals general population)
  - Those who are cognitively impaired may not have ability to consent to sexual behavior
  - For pregnant patients, the ability to get/follow prenatal care is often a problem
  - Ability to be a parent can be greatly impaired; many opt for adoption; about 33% of mothers with schizophrenia lose custody of their children to family members, ex-partners, foster care, even adoption

- Legal issues

  Question/debate/conundrum can perhaps be summed up this way:
  - Does freedom include the right to be sick such that it interferes with or prevents one's

ability to exercise that freedom and make further choices?
- ACLU, others oppose various state laws that allow forced treatment
  Argue that it's a violation of civil liberties and/or the right to privacy

- Need for ongoing Assisted Treatment
  Various programs throughout the country to address situations where patients with schizophrenia lack awareness about their illness, are without medications, and are unable to provide for themselves or are a danger to themselves/others; legal issues effect their efforts
  - Advanced directives, Assertive case managers, Representative Payee, Conditional Release, Out-patient commitment, Conservatorship, Substituted judgment, "Benevolent coercion", Threat of Incarceration
- Confidentiality-prevent family from being able to help pt
- Hospitalization/Involuntary hospitalization

7. Outcome

Life expectancy: General population 78 years Schizophrenia 48-53 years

- General population ~1% die from suicide; Schizophrenia pts ~10%
- General population ~50% die from Cardiovascular disease; Schizophrenia pts ~75%

Schizophrenia pts-have higher rates of obesity, dyslipidemia, hypertension, diabetes, & cigarette smoking compared to general population

	Schizophrenia pts	General population	Comparison: more common is schizophrenia patients
Obesity	42% BMI ≥ 27	27% BMI ≥ 27	1.5 to 2x's more common
Dyslipidemia			up to 5x's more common
Hypertension	~27%	~17%	1.5 to 2x's more common
Diabetes Mellitus	~13%	~3%	2 to 4x's more common
Cigarette Smoking	~75%	~25%	2 to 3x's more common

Patients with schizophrenia untreated for medical problems-from NIMH CATIE study
30% untreated for diabetes mellitus
62% untreated for hypertension
88% untreated for dyslipidemia

- 75% can't work, are unemployed; schizophrenia is among the top 10 causes of disability
- 60-70% do not marry, most have limited social contacts
- Only about 33% live independently

Quality of life associated with schizophrenia ranks among the worst of chronic medical illness

IV. Etiology: What causes Schizophrenia?

A. Theories on the Cause of Schizophrenia

1. Neurochemical theory
   Dopamine hypothesis
   Other neurochemical-glutamate, GABA,
2. Infection/Immune theory
   Viral cause-slow virus? May remain latent for long period of time before causing illness
   Many viruses are seasonal, could account for seasonality of births in schizophrenia
   - Many studies consistently show more patients (~5-8%) with schizophrenia were born in the winter or spring months.
3. Nutritional theory
   Other vitamin deficiency illnesses (beriberi, pellagra, pernicious anemia) may have psychiatric

symptoms, could schizophrenia also?

- abnormality in metabolism of lipids/fatty acids that are neuron components
- abnormality in protein metabolism

4. Endocrine theory
   Dysfunction of thyroid, adrenal gland, pituitary
5. Genetics theory

Risk if no family history of schizophrenia	1 : 100	1%
Risk if parent or sibling has schizophrenia	1 : 10	10%
Risk if both parents have schizophrenia	4 : 10	40%
Risk if identical twin has schizophrenia	1 : 2	50%

B. Theories on Process of schizophrenia development

Neurodegenerative theory-brain deterioration over time from the psychotic episodes

Developmental theory

Something goes awry during the process of brain development in utero; neuronal wiring is wrong; Something goes awry with the pruning process of neurons during late teen years

- Strong agreement that a single gene is not the cause
- Combination of genes is a more likely cause than a single gene
- More likely still, a person's genetics make them more susceptible to schizophrenia; in combination with other factors, (virus? neurochemical? other) leads to development of the illness.

Process of schizophrenia development (?)

Genetic predisposition

Early environmental insults-prenatal, perinatal

Neurodevelopmental abnormalities

Later developmental insults-substance abuse, psychosocial stressors

Late adolescence neuronal pruning mistakes

Further brain dysfunction

Periods of psychosis

Neurodegeneration

Bottom line: Cause of Schizophrenia is not known

V. Overview: Treating psychotic illnesses

Mood disorder with psychosis

Major depression with psychosis-treat with anti-depressant & anti-psychotic; when patient no longer psychotic may eventually stop anti-psychotic; continue anti-depressant indefinitely

Bipolar disorder with psychosis-treat with mood stabilizer & anti-psychotic, when patient no longer psychotic, may discontinue anti-psychotic; note 2nd generation/atypical anti-psychotics can be used as mood stabilizers

Medical illness with psychosis (delirium)-treat with anti-psychotic to help with psychosis and agitation/prevent unintentional patient injury; ultimately must find & treat underlying medical illness; discontinue anti-psychotic once delirium resolved

Dementia with psychosis-treat with low dose anti-psychotic, ideally treat only temporarily

Substance induced psychosis-treat acutely with anti-psychotic; most commonly psychosis resolves in 24-48 hours once substance is out of patient's system; when no longer psychotic, discontinue anti-psychotic

Schizoaffective disorder-typically the patient is treated indefinitely with anti-psychotic medications

Schizophrenia-typically the patient is treated indefinitely with anti-psychotic medications