Schizophrenia and Related Psychotic Disorders

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Schizophrenia

- Kraepelin – 1896 “Dementia Praecox.” Single, Homogenous Disorder Separates From Manic-Depression
- Bleuler – 1911 “Schizophrenia” (the Split Mind). Group of Disorders
- Prevalence – 1% World-Wide, ~3 Million Affected in the USA
- Onset: Late Adolescence or Early Adulthood
- Course – Chronic. Episodic or Continuous Symptoms
- Outcome – Variable. Some Decline is Typical. Rule of 3: Approximately 33% improve, 33% stable & 33% decline significantly.

Genetic:
- Multiple Genes, Variable Penetration
- 5-8% Prevalence in 1st Degree Relatives including Adopted-Away Children of a Parent with Schizophrenia,
- 40-50% Prevalence in Identical Twins
- Linkage studies currently point to locations on 5q, 6p, 8p,10p, 13q, 15q, 18p, 22q, Xpter

Environmental:
- Prenatal Infection (?Virus – Influenza, Measles, Herpes I & II), Obstetric Trauma, Head Injury

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Schizophrenia – Causes

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Schizophrenia – Costs, Burden

Cost: ~$20 Billion in Annual Direct Costs (USA)
~$45 Billion in Annual Indirect Costs (USA)

Burden:
- Personal Suffering*, Family Burden**, Societal Loss
- Persons with schizophrenia live 20% shorter than their healthy counterparts
- 20-50% attempt suicide. 10-15% commit suicide.

* First Person Account - Schizophrenia Bulletin
** National Alliance For The Mentally Ill - NAMI

Schizophrenia Challenges in Treatment

- 30% respond poorly to current treatments
- Noncompliance rate ~50% at one year
- High relapse rate
  - Treated ~15-20% per year
  - Untreated/non-compliant ~ 40-70% per year
- 50% of patients with schizophrenia have history of substance abuse
- 20-50% of patients attempt suicide at least once
  - 10-15% commit suicide

Schizophrenia Morbidity & Mortality

- High mortality rates with schizophrenia
  - 1.6 times higher than all cause mortality risk
  - 4.3 times higher risk for all unnatural causes
    - Suicide, accidental death
  - 1.4 times higher risk from Illness
    - Cardiovascular
    - Infectious
    - Respiratory
    - Endocrine disorders
- Overall life expectancy is 20% shorter than that of the general population
Schizophrenia

Positive Symptoms

Hallucinations: Hearing Voices is common. Visual, Olfactory, Tactile & Gustatory experiences may occur.

Delusions: Persecutory, Grandiose, Somatic etc

Formal Thought Disorder: Convoluted Train of Thinking, Loose Associations

Disorganized Behavior: Stupor, Excitement, Repetitive Behaviors – verbal & motor, Regressed & Primitive Behavior

Response of a 28-year-old patient with schizophrenia to the question “What kind of problems are you experiencing?”

Schizophrenia

Negative Symptoms

Blunted Affect: Emotions Restricted in Depth & Range

Alogia: Brief Speech, Limited Content

Apathy: No Interest, No Pleasure

Avolition: Lack of Initiative & Drive

Schizophrenia

Cognitive Symptoms

Impaired Attention: Distractable, Hyperarousal, Hypersensitive

Impaired Abstraction: Poor Planning, Impaired Problem Solving

Impaired Memory: Difficulty in Using Discrete Episodic Memory or Semantic Memory in Application Tasks

Course of Schizophrenia

Theoretical Model

In each type of course, there are two prognostic groups—those who recover well and those who don’t. As a rule of thumb, 33% of patients have good recovery, 33% show moderate recovery and 33% show significant decline.
**Schizophrenia: Neurobiology**

**NEURODEVELOPMENTAL THEORY**

- **CNS INSULT DURING EARLY IN-UTERO LIFE (10-18 weeks of pregnancy)**
  - DISTURBED NEURONAL MIGRATION
  - DISTURBED NEURONAL CIRCUITRY
  - PRECURSORS IN CHILDHOOD (attention deficits & soft neurological signs)
  - PSYCHOTIC SYMPTOMS IN ADOLESCENCE

**Brain Morphology**

- Enlarged Lateral Ventricles
- Decreased Brain Size
- Loss of Neurons in Prefrontal Cortex
- Loss of Neurons in Hippocampus
- Loss of Neurons in Medial Temporal Cortex
- Reduction in Size of Thalamus
- ? Cerebellar Vermis Dystrophy

**Neurochemistry**

- Increased DA activity in mesolimbic and mesocortical regions
  - Upregulation of D2 receptors
- Increased 5-HT activity in prefrontal cortex
  - Upregulated 5-HT2 receptors
- Altered glutamate input from impaired NMDA receptors in prefrontal cortex

**Dopamine Theory of Schizophrenia**

- **Mesocortical pathway**
  - Hyperactivity: positive symptoms
- **Mesolimbic pathway**
  - Hyperactivity: positive symptoms
- **Nigrostriatal pathway** (part of EP system)
- **Tuberoinfundibular pathway**
  - Hypoactivity: negative symptoms

*Slide courtesy of BMS*
Dopamine Antagonism: Positive Symptoms and EPS

- Improvement of positive symptoms
- EPS
- Hyperprolactinemia
- DA inhibition

Slide courtesy of BMS

Schizophrenia Related Psychotic Disorders
- Schizoaffective disorder
- Delusional disorder
- Brief psychotic disorder
- Psychosis not otherwise specified

Antipsychotic Medications - Typical
Neuroleptic Agents:
- Low D2 potency: Chlorpromazine (Thorazine)
  Thiotodazine (Mellaril)
- Medium potency: Loxapine (Loxitane)
  Molindone (Moban)
  Thiothixene (Navane)
- High potency: Haloperidol (Haldol)
  Fluphenazine (Prolixin)

Antipsychotic Medications - Atypical

- Clozapine (Clozaril) - 1989
- Risperidone (Risperdal) - 1994
- Olanzapine (Zyprexa) - 1996
- Quetiapine (Seroquel) - 1997
- Ziprasidone (Geodon) - 2001
- Aripiprazole (Abilify) - 2002

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All the above atypicals are modest D2 blockers and heavy 5HT2 blockers, except Aripiprazole which is a partial D2 agonist and heavy 5HT2 blocker.

Schizophrenia
- Supportive Psychotherapy
- Psychoeducation
- Social Skills Training
- Reduction of Expressed Critical Emotions
- Cognitive Enhancement

Antipsychotic Medications
Long Acting Injections
- Haloperidol decanoate injection
- Fluphenazine decanoate injection
- Risperidone depot injection

Psychosocial Therapy
- Supportive Psychotherapy
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• Schizophreniform disorder
• Schizoaffective disorder
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Schizophrenia Management

It is recommended that the management of a person with schizophrenia be performed by a team including a physician, counselor, and case manager in liaison with the person’s family AND that pharmacotherapy be judiciously combined with supportive psychosocial therapy and a structured program of rehabilitation.