Schizophrenia and Related Psychotic Disorders

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Schizophrenia

• Kraeplin – 1896 “Dementia Praecox.” Single, Homogenous Disorder Separate 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

Schizophrenia – Costs, Burden

Cost: ~$20 Billion in Annual Direct Costs (USA)
~$45 Billion in Annual Indirect Costs (USA)
(1994 estimate)

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


Negative Symptoms

Blunted Affect: Emotions Restricted in Depth & Range

Alogia: Brief Speech, Limited Content

Apathy: No Interest, No Pleasure

Anhedonia

Avolition: Lack of Initiative & Drive

Amotivation

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

Years

Function

Good

Premorbid

Prodromal

Progression

Stable relapsing

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

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**Schizophrenia**

**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

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**Schizophrenia**

**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 pre-frontal cortex

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**Dopamine Theory of Schizophrenia**

- **Hyperdopaminergic** pathways
- **Hypodopaminergic** pathways

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**Dopamine Theory of Schizophrenia – DA pathways**

- Mesocortical pathway
- Hypoactivity: negative symptoms
- Mesolimbic pathway (part of EP system)
- Hyberactivity: positive symptoms
- Nigrostriatal pathway
- Tubero-infundibular pathway (inhibits prolactin release)
Dopamine Antagonism: Positive Symptoms and EPS

EPS
Hyperprolactinemia
 Improvement of positive symptoms

DA inhibition

Slide courtesy of BMS

Schizophrenia Related Psychotic Disorders

- Schizophreniform disorder
- Schizoaffective disorder
- Delusion 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)

Schizophrenia

**Atypical Antipsychotics**

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

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

Antipsychotic Medications

**Long Acting Injections**

- Haloperidol decanoate injection
- Fluphenazine decanoate injection
- Risperidone depot injection

Schizophrenia

**Psychosocial Therapy**

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