

Schizophrenia

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EPIDEMIOLOGY

INCIDENCE - 0.11-0.70 per 1000.

PREVALENCE:

Point prevalence (i.e. number of cases at one moment in time) \approx 1% (0.6-8.3%).

Lifetime prevalence in USA \approx 1.3% (i.e. \approx as of diabetes mellitus).

N.B. schizophrenic patients in developing countries tend to recover from their illness at higher rate (than do schizophrenic patients in industrialized nations) \rightarrow lower prevalence rates!

Gender

Western world: men \approx women; *men tend to develop earlier and more severe disease** (\rightarrow men with schizophrenia tend never to have been married; affected women tend to be divorced or separated).

*may be because of antidopaminergic influence of estrogen.

Developing countries: men \gg women.

Role of socioeconomic status

- PREVALENCE and INCIDENCE as well as DISEASE COURSE correlate with socioeconomic status.

- in USA highest rates are found in **lower socioeconomic classes** (schizophrenic patients tend to drift downward in socioeconomic status [*drift hypothesis*]; parents of schizophrenics have social class distribution similar to that of general population).
- in India, highest rates occur in **upper castes** (social stress on class of people, rather than drift, may be major factor in precipitating schizophrenia).
- in cities with populations $>$ 100,000, INCIDENCE increases in proportion to **size of city**.

Premorbid personality

- research has not demonstrated specific personality features that reliably predict development of schizophrenia.

ETIOPATHOPHYSIOLOGY

- complex and yet undetermined.

NEURODEVELOPMENTAL VULNERABILITY to schizophrenia (genetic predisposition; intrauterine, perinatal complications) + triggering ENVIRONMENTAL STRESSORS (biochemical* or social**)

*e.g. substance abuse (esp. marijuana)

**e.g. leaving home for college, breaking off romantic relationship

No evidence that schizophrenia is caused by poor parenting!

A. Genetic predisposition theories

- *genetic factors clearly play role*, but actual manner of genetic transmission of schizophrenia is complicated (*simple single gene transmission* is no longer plausible; schizophrenia *transmission in families* does not fit any known pattern of pure genetic transmission; *polygenic transmission* is likely).
- risk of schizophrenia is elevated in **biological relatives** but not in **adopted relatives**.
- studies show high rates of mental illness* in relatives of patients with schizophrenia.
*not necessarily schizophrenia.
- **monozygotic twins** have \approx 53% risk (risk higher if twins are raised together); dizygotic twins \approx 10-14%.
- if individual has **1st-degree relative with schizophrenia**, his risk \approx 10% (vs. \approx 1% in general population).

B. Developmental (perinatal) insult theories

- *developmental factors play major role* (schizophrenia is **neurodevelopmental disorder**, perhaps sometimes beginning in utero or at birth).
- **season of birth** - schizophrenia risk is greatest for individuals born in **late winter \div early spring** (prenatal exposure to virus such as **influenza** is implicated).
- **prenatal malnutrition**, **low birth weight** are also associated with increased risk.
- **preeclampsia** \rightarrow ninefold increased risk.

C. Psychological theories

- no longer play etiologic role:

1. **Family interaction** theories:
 - a. mistakes in mothering by so-called "**schizophrenogenic mother**".
 - b. "**expressed emotions**" (high level of affect with criticism and overinvolvement) cause exacerbation of schizophrenia (were once thought to cause schizophrenia).
2. **Cultural causes** (to explain differences in incidence between industrialized and rural areas); economic factors that affect access to nutrition, sanitation, and health care are more likely to account for any cultural differences!

D. Biologic mechanisms

- abnormal cell development / cell damage in **multiple brain regions** mediated by **multiple chemical messenger systems** cause disease (i.e. no one abnormality appears to account for spectrum of symptoms).

1. Neurotransmitter abnormalities

Dopamine \uparrow (one of oldest theories - **overactivity of MESOLIMBIC dopaminergic neurons**).

- D₂ receptors are found in abnormal numbers in brains of schizophrenics.

- D₂ receptor blockade is sine qua non of antipsychotic effects of neuroleptics.
- PET shows *increased activity* of dopaminergic neurons in limbic system (strongly correlated with hallucinations and other positive symptoms) and *decreased activity* in frontal lobes and prefrontal cortex (correlated with negative symptoms).

Serotonin↑ (transmethylation hypothesis of schizophrenia – certain methylated serotonin derivatives [formed as metabolism errors] may cause psychosis)

- some psychotomimetic compounds (psilocybin, LSD) show high levels of serotonergic activity.
- abnormal levels of serotonin (and its metabolite 5-hydroxyindoleacetic acid) have been found in CSF of schizophrenics.

Glutamate↓

- glutamate levels are reduced in CSF of schizophrenics.
- phencyclidine is glutamate receptor antagonists.

γ-aminobutyric acid (GABA)↓

- low levels of GABA are found early in course of schizophrenia.
- benzodiazepines (GABA agonists) can relieve some symptoms of schizophrenia.
- baclofen (GABA antagonist) can exacerbate schizophrenia.

2. Structural abnormalities see *Neuroimaging (below)* >>

3. Functional abnormalities

- **limbic system activity**↑ closely correlates with *positive symptoms*; **neuroleptics** can reverse this overactivity.
- **activity**↓ in frontal lobes closely correlates with *negative symptoms*; **atypical neuroleptics** can sometimes reverse this hypoactive state.

CLINICAL FEATURES & DIAGNOSIS

Established biologic markers or pathognomonic clinical features do not exist!

Schizophrenia involves:

- 1. Positive symptoms** (appear added to presentation) – delusions*, hallucinations, catatonia, agitation.
- 2. Negative symptoms** (appear missing from presentation) – affective flattening, apathy, social withdrawal, anhedonia, poverty of thought and content of speech.
- 3. Cognitive symptoms** – deficits in attention and executive functions (such as ability to organize and abstract, understand viewpoints of other people, learn from experience).
- 4. Disorganized symptoms** – thought disorder, bizarre behavior (e.g. childlike silliness, agitation, inappropriate appearance, hygiene, or conduct).

*most characteristic feature of schizophrenia!

Symptoms of schizophrenia typically impair ability to function and markedly interfere with work, social relations, and self-care*.

*unemployment, isolation, deteriorated relationships, and diminished quality of life are common outcomes.

DSM-IV Diagnostic Criteria for Schizophrenia:

A. Two of following for **most of 1 month**:

1. **Delusions**
2. **Hallucinations**
3. **Disorganized speech**
4. **Grossly disorganized or catatonic behavior**
5. **Negative symptoms**

(Note: only one of these is required if *delusions* are bizarre or if *hallucinations* consist of voice keeping up running commentary on person's behavior or thoughts, or if there are two or more voices conversing with each other)

B. Marked **social / occupational dysfunction**: for significant portion of time since onset of disturbance, one or more major areas of functioning (work, interpersonal relations, self-care) is markedly below level achieved prior to onset (or when onset is in childhood - adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. **Duration of at least 6 months*** of persistent symptoms such as **attenuated forms of Group A symptoms** (above) or **negative symptoms**. At least 1 month of this must include Group A symptom.

D. Symptoms of **schizoaffective** and **mood disorder** are ruled out**.

E. **Substance abuse** and **medical conditions** are ruled out as etiological.

*if < 6 months = acute psychotic disorders (**schizophreniform disorder, brief reactive psychosis**).

mood disorders in addition to psychotic symptoms = **schizoaffective disorder, major depression with psychotic features, or bipolar mood disorder.

MOST FREQUENTLY found symptoms (in descending order):

1. Lack of insight
2. Auditory hallucinations
3. Verbal hallucinations
4. Ideas of reference
5. Suspiciousness
6. Flatness of affect
7. Voices speaking to patient
8. Delusional mood
9. Delusions of persecution
10. Inadequate description of problems
11. Thought alienation
12. Thoughts spoken aloud

HIGHEST RELIABILITY of symptoms:

1. Suicidal ideation
2. Elated thoughts
3. Ideas of reference
4. Delusions of grandeur
5. Hearing thoughts aloud
6. Derealization
7. Lack of concentration
8. Hopelessness
9. Delusions of persecution and reference

LOWEST RELIABILITY of symptoms:

1. Negativism
2. Preservation
3. Stereotyped behavior (e.g. lip smacking, chewing)

- **impaired information processing** is most harmful symptom (more disrupting than delusions and hallucinations!) → difficulty dealing with changes.
- even in cases of severe disruption, *some areas of functioning may be reserved* (e.g. patient with chronic schizophrenia who exhibits bizarre behavior and severe disruptions of speech and thinking may retain skills of concert pianist).

A. **FORM OF THOUGHT (formal thought disorder)** - "loosened" thought processes:

1. LOOSENING OF ASSOCIATIONS - connections among patient's ideas are absent / obscure - listeners may feel as if understanding of patients' thought had been suddenly lost*:

*vs. mania and anxiety disorders - tangentiality and flight of ideas - patients express coherent ideas but lose point of string of ideas.

- 1) **word use may be highly idiosyncratic and individualized** (words may be created [neologism] or selected by patients using their own internal logic and special symbolism).
- 2) **abnormal concept formation** (it is perceptual defect) – patient is unable to exclude irrelevant or competing ideas from their consciousness; thinking becomes overinclusive; extraneous items and details that have specific meaning to patients are incorporated into patients' communication but are difficult for listeners to follow.
- 3) **logic follows primitive pattern** (in piagetian sense) - illogical reasoning, exclusion of important information from reasoning process, frank distortion of logical connections; patients assume existence of causal connections when others perceive no such connections; patients may treat symbols as if they were actual objects.
- 4) **concreteness substitutes for abstraction** - simultaneous preoccupation with symbols and abstractions, as well as loss of ability to process these, are common features;
 - severely impaired ability to form abstract ideas.
 - limited ability to discern abstractions within ideas; concrete interpretations of abstract ideas becomes predominant.
 - lost ability to understand metaphors and similes.
 - abstraction ability deterioration is greater in *early-onset schizophrenia*.
- 5) **language structural problems:**
 - (1) *neologisms*
 - (2) *verbigeration* (persistent repetition of words or phrases)
 - (3) *echolalia* (repetition of words or phrases of examiner)
 - (4) *mutism* (functional inhibition of speech and vocalization)
 - (5) *word "salad"* (complete lack of language)

2. Poverty of content and speech - speech may be complex, concrete, or limited in overall productivity, but it generally lacks specific information content.

3. Thought blocking (internal interruption in patients' speech and flow of thought - long pauses before answers to questions or odd pauses in middle of answers).

B. **CONTENT OF THOUGHT** - *delusions*. see p. Psy5 >>

C. **PERCEPTUAL DISORDERS**

- fundamental perceptual defect in schizophrenia is *inability to habituate and suppress* extraneous environmental stimuli or internal thought processes.

1. HALLUCINATIONS. see p. Psy5 >>

- most characteristic **auditory** hallucinations include hearing **voices speaking** about patient in third person, hearing voices making derogatory comments about patient, and hearing one voice telling patient to commit some action (*command hallucinations*)*; patients may hear their own voice spoken aloud.
 - *may be so persistent that become difficult to resist (commands telling to harm themselves or others are dangerous!).
- **visual** hallucinations are more common in other disorders (esp. organic mental disorders); in schizophrenia they are complex and related to patient's delusional system (e.g. visit from aliens).
- **other** (tactile, gustatory, olfactory) are frequently connected to delusional systems.

2. ILLUSIONS. see p. Psy5 >>

- **hypersensitivity to light, sound, smell** is common in schizophrenia.

D. **AFFECT** - blunted, flat, inappropriate.

- little range of expressed emotion.
- during first psychotic episode, up to 75% patients suffer from depressive symptoms! (98% of these symptoms remit with resolution of psychosis without antidepressant treatment).
- 80% schizophrenics experience ≥ 1 episodes of major depression at some time in their life.

E. Disrupted **SENSE OF SELF**:

- 1) loss of self-esteem.
- 2) confusion about sexual identity.
- 3) inability to separate oneself from events in environment (i.e. feeling that one's thoughts have harmed another person).
- 4) projection of one's own fears or suspicions onto others.
- 5) experiencing self and others as dichotomous opposites (i.e. all good or all bad) with little integration of opposing features.

F. **VOLITIONAL SYMPTOMS** (most persistent and intractable features of schizophrenia) - difficulties initiating and maintaining purposeful and goal-directed activity and interest in environment.

1. **Interest** in environment may be difficult to generate and maintain.
2. Difficulties in **initiative** (ability to begin goal-directed activity) is lacking → difficulty finding housing, financial support, etc; also may be unable to initiate spontaneous movement without direction from others.
3. Difficulties in **drive** (ability to pursue goal-directed activity after it has been started).
4. **Ambition** may be preserved in absence of drive and initiative! (unrealistic ambitions + delusions → complex dysfunctional patterns of behavior).

G. Changed **RELATIONSHIP TO EXTERNAL WORLD** - patients become increasingly *preoccupied with internal events* → withdrawal from world (**autism** in its extreme form).

H. Changed **MOTOR ACTIVITY** (patient may make odd movements which may or may not be related to neuroleptic medication).

CATATONIA - extreme psychomotor disturbance – either *markedly retarded motor activity* (maintaining rigid postures and resisting efforts to be moved) or *markedly agitated motor activity* with purposeless and unstimulated motor activity. also see p. Mov1 >>

1. QUANTITATIVE CHANGES - amount of activity ranges from **extremes of agitation** (in excited catatonic states and acute psychotic exacerbations) to **withdrawn and inactive states** (associated with catatonic stupor and chronic institutionalization).

N.B. **akathisia**, **bradykinesia**, and **tardive dyskinesia** are due to neuroleptic effects!

- a. **Catatonic stupor** - dramatic motor inactivity (untreated patients may be immobile for months);
 - as patients recover, it is clear that they have been aware of events in environment.
 - aggressive medical care is required to avoid *dehydration*, *electrolyte disturbances*, and *infections*.
- b. **Catatonic excitement** (psychiatric emergency) - hypermetabolic state - excessive, driven, purposeless activity and speech;
 - patient may be violent.
 - untreated patients die of *acute hyperthermia*.

2. QUALITATIVE CHANGES

- a. **Catatonic posturing** - patients assume strange postures and hold them for long periods:

- **catatonic rigidity** - patients resist being moved from their unusual rigid postures.
- **waxy flexibility** - patients' limbs may be moved like wax, and they hold newly assumed position for long periods of time.
- b. Echopraxia** (behavioral equivalent of echolalia) - patients involuntarily mimic movements of another person.
- c. Automatic obedience** - following of directives in unquestioning, robotlike manner.
- d. Mannerisms & grimacing** - patients' artificial and stilted appearance.
 - particular mannerisms may have special meanings that are connected to delusions or hallucinations.
 - grimacing movements may be mistaken for orofacial dystonias of tardive dyskinesia.
- e. Stereotyped behaviors** - purposeless* repetitive movements (or verbalizations); may involve entire body such as rocking or may involve repetition of complex gestures.
 - *may have magical significance or may be purposeless to patient.
- f. Perseveration** - involuntary repetition of task.
 - e.g. patients who are asked to copy series of circles may continue to copy figures until they run off page; patients may repeat answer to question until asked to stop.*

I. Impaired SOCIAL BEHAVIOR - loss of social skills, body language, and empathic abilities.

- severely socially debilitated schizophrenic patients may live on fringe of society as severely dysfunctional "street people" (in past, these same individuals may have been long-term institutionalized patients).

PSYCHOLOGICAL TESTING

- clearly abnormal (also in some asymptomatic relatives):

- 1) **lack of creativity and imagination** (i.e. preservation of verbal intelligence but not performance intelligence).
 - 2) **attention deficits** (easy distractibility)
 - 3) **loss of executive function** (difficult to make choices and decisions about simple things such as what to wear and when to eat).
- **orientation** (time, place, self) is usually intact.

NEUROIMAGING

- important to consider for every person with new onset of psychotic illness (or, perhaps, marked change in symptomatology) - to exclude treatable causes (e.g. brain tumor, subdural hematoma).
N.B. up to now, it has been impossible to identify any one brain region as primary site of neuron loss.

Because of *large overlap between healthy and schizophrenia brain*, these findings are of greater research interest than clinical use (i.e. findings are not diagnostic):

Enlargement of lateral ventricles - most consistent finding!!!; enlargement is present from disease onset and is nonprogressive.

Decreased medial temporal brain volume (i.e. smaller hippocampus.)

Cell architecture abnormalities in prefrontal cortex.

Decreased size of thalamus.

LABORATORY STUDIES

- only to exclude treatable causes. see p. Psy9 >>

SCHIZOPHRENIA SUBTYPES

Paranoid type

- A. Preoccupation with one or more **delusions** or frequent **auditory hallucinations**
- B. *Does not have* prominent disorganized speech, disorganized behavior, flat or inappropriate affect, or catatonic behavior (i.e. **preservation of cognition and affect** → *most prone to suicide* in despair based on realistic recognition of effect of their disorder).

Disorganized type

- A. All of following are prominent:
 1. Disorganized speech
 2. Disorganized behavior
 3. Flat or inappropriate affect
- B. Does not meet criteria for catatonic type.

Catatonic type - clinical picture is dominated by at least two of following:

- A. Motoric immobility (catalepsy or stupor).
- B. Excessive motor activity (apparently purposeless and not influenced by external stimuli)
- C. Extreme negativism or mutism.
- D. Peculiarities of voluntary movement such as posturing, stereotyped movements, prominent mannerisms, or prominent grimacing.
- E. Echolalia or echopraxia.

Undifferentiated type - criteria are not met for paranoid, catatonic or disorganized types.

Residual type

- A. Criterion A for schizophrenia is no longer met, and criteria for other subtypes of schizophrenia are not met.
- B. Evidence of disturbance (evidenced by negative symptoms or two or more criterion A symptoms) is present in attenuated form.

ALTERNATIVE CLASSIFICATION:

Deficit subtype - **prominent negative symptoms** unaccounted for by other factors (e.g. depression, anxiety, understimulating environment, drug adverse effects).

Nondeficit subtype - may have delusions, hallucinations, and thought disorders but are relatively **free of negative symptoms**.

COURSE

- may be highly variable!

- symptoms may change and become less severe over course of illness.
- most of deterioration occurs in first 5-10 years and is usually followed by decades of relative stability (although return to baseline is unusual).

Pre-onset

- unexceptional childhood → personality change, decrease in academic, social, and interpersonal functioning during mid-to-late adolescence (about 1 year passes between onset of these vague symptoms and first visit to psychiatrist).
- in retrospect, family members may describe patient as physically clumsy and emotionally aloof child.

Onset

- **peak time of onset** is late **adolescence** + **early adulthood**.

- average age at onset:
18 yr (15-24) – men
25 yr (25-34) – women.
- patients with **early onset** tend to have more disorganized features and worse prognosis for recovery and function preservation.

Precipitating events

- stressors activate predisposition to development of schizophrenia.

Schizophrenia occurs in people with **neurodevelopmental vulnerabilities** - onset, remission, and recurrence are result of interactions between these enduring vulnerabilities and **environmental stressors**.

1. **Psychosocial stressors** (cultures experiencing social / economic stress are associated with high rates of schizophrenia).
2. **Traumatic events**.
3. **Drug / alcohol abuse** (amphetamines, cocaine, hallucinogens, phencyclidine, anticholinergics, alcohol may precipitate psychotic symptoms); some patients use substances as self-medication (e.g. nicotine is frequently heavily used by patients to alleviate negative symptoms by stimulating dopaminergic neurons in frontal lobes*).
*smoking briefly "normalizes" some average evoked potential abnormalities associated with schizophrenia.

Clinical course

1. **Initial presentation** – variable:

- a. **Abrupt** (may develop in period as short as 1-2 days) - confusion, agitation, affective involvement, hallucinations, and delusions, following identifiable stressor; relatively few of these patients develop schizophrenia with chronic course required for DSM-IV diagnosis (most meet criteria for **brief reactive psychosis** or **schizophreniform disorder**, which has less than 6-month course).
- b. **Trema** (German for "stage fright") - anxious, irritable, and depressed feelings that may last few days ÷ month or longer; these feelings may be reaction to perceptions that something is going wrong; trema may progress to frank psychosis, or resolve as if discrete episode.
- c. **Insidious prodromal phase** (bad prognosis!!!).

2. **Acute phase** - worsening positive symptoms (delusions, hallucinations, catatonia or agitation) and possible worsening of negative symptoms.

3. **Stabilization phase** (may last ≥ 6 months or more) - gradually decreasing severity of symptoms (usually positive symptoms).

4. **Stable phase** (usually after 5 yrs of clinical disease; can last months ÷ years) - little variation in symptom severity; some patients appear **asymptomatic**; most patients recover some social function but continue to experience some symptoms (esp. negative symptoms).

5. **Deterioration from previous level of functioning** (key feature of schizophrenia!!!)

- patients often do not return to their previous level of functioning.
- some recent studies challenge assumption that this deterioration is uniform and lifelong (but some evidence suggests that severity of illness may lessen in later life, particularly among women).

Patterns of long-term courses - almost any combinations of these elements:

Onset - acute / insidious.

Course - single continuous episode / episodic / episodic evolves to continuous.

Outcome - eventual severe impairment / complete recovery.

- $\approx 25\%$ cases are insidious onset, continuous course, eventual severe impairment.

Patterns of recovery:

SOCIAL recovery (economic and residential independence with little disruption in social relationships)
- more common than complete remission of symptoms (as many patients still suffer from negative symptoms).

COMPLETE recovery (complete remission of psychotic symptoms and return to previous levels of social and occupational functioning).

Hospitalization rates - measure of recovery failures.

DIFFERENTIAL DIAGNOSIS

- **careful family histories** and **longitudinal observations** may be required to differentiate some conditions from schizophrenia!

Organic mental disorders (psychotic symptoms attributable to medical condition) → see p. Psy9 >>

N.B. in organic mental syndromes, **visual hallucinations** are more common, and auditory hallucinations are less common!

Mood disorders

- depression with severe melancholic features may cause negative symptoms (e.g. catatonic syndrome).
- mood-congruent delusions / hallucinations are common in severe mood disorders.

Personality disorders - paranoid personality disorder, schizoid personality disorder, schizotypal personality disorder, borderline personality disorder.

Religious and cultural subgroups - diagnosticians from one culture may confuse beliefs and behavior patterns associated with another culture with symptoms of schizophrenia.

TREATMENT

Schizophrenia is **not curable!**

- every attempt should be made to **reintegrate patients into community**.

HOSPITALIZATION now focuses on **acute issues**, with only minority of patients in long-term hospitalization.

- current trend is increasing reliance on **community-based** (vs. **hospital**) treatment.
- indications for hospitalization:
 - 1) first episode of psychosis
 - 2) suicidal / homicidal ideation
 - 3) command hallucinations of threatening nature
 - 4) extreme fear
 - 5) significant confusion
 - 6) unusual presentations in chronic schizophrenia
 - hospitalization is not necessarily indicated for exacerbation of psychotic symptoms if adequate community alternatives are available.
- therapeutic environment of inpatient ward is known as **"therapeutic milieu"**.

GROUP THERAPY

- mainstay of treatment in both inpatient and outpatient settings.
- best used in conjunction with other forms of therapy (particularly medications).
- produces improvements in *social integration*.
- some physicians believe that unstructured, confrontational group techniques may exacerbate psychotic symptomatology.

INDIVIDUAL PSYCHOTHERAPY

- **supportive and adaptive techniques** (oriented to helping patients adapt to details of daily life) are far more effective than **insight-oriented techniques** (focus on patients' inner experiences).
- cognitive and behavioral therapies may reduce deficit symptoms in schizophrenia.
- attempts to establish **close / intense therapeutic relationship** may exacerbate symptoms in patients who are highly suspicious or who feel overwhelmed by interpersonal relationships.

FAMILY THERAPY

- effects of familial "high expressed emotion" (hostile overinvolvement and intrusiveness) on outcome of persons with schizophrenia who return home have generated interest.
- studies have found that **family therapy / interventions may prevent relapse!**
- family members should be referred to *National Alliance on Mental Illness (NAMI)*.

COMMUNITY TREATMENT

- majority of patients receive most of treatment in community.
- **CASE MANAGER** is clinician who is most involved in case of particular patient, maintaining contact on frequent basis and checking for signs of relapse, noncompliance, and adverse effects.
- **psychosocial rehabilitation** is significant part of treatment programs.

SELF-HELP PROGRAMS

- some patients receive majority of treatment and support from **consumer-operated self-help organizations** (specially trained persons with mental illness, who in turn, become providers of services to persons with schizophrenia) - psychosocial rehabilitation, vocational training, housing assistance, and financial management services.
- **National Alliance for Mentally Ill (NAMI)** has brought much attention to need for more research into effective treatments for severe and persistent mental illnesses.
 - NAMI is also **major voice** of parents, siblings, and children who care for persons with illnesses such as schizophrenia.
 - NAMI offers valuable **educational programs** to help dispel stigma associated with schizophrenia and help families better understand symptoms of schizophrenia.

NEUROLEPTICS

- only efficacious treatment for schizophrenia!
- not all patients respond (if treated early, patients tend to respond more quickly and fully); complete behavior normalization is seldom achieved.
- not curative and do not eliminate fundamental thinking disorder (but permit patient to function in supportive environment).
- evaluate patient for movement disorders before exposure to antipsychotic agents!

Choice of proper agent is more of art than science, and as both physician and patient gain experience, job becomes easier:

Traditional neuroleptics are most effective in treating **POSITIVE symptoms**;

- less effective with chronic or well-organized delusions.
- little effect on **NEGATIVE symptoms** (apathy, anhedonia, amotivation).

Newer neuroleptics opened new era in treatment of schizophrenia - are effective in resistant cases, and target both **POSITIVE and NEGATIVE symptoms**.

RISPERIDONE should be included among first-line antipsychotics.

CLOZAPINE should be reserved for refractory severely schizophrenic patients.

Route of administration

- many patients have trouble adhering to **ORALLY administered regimen**.
- **PARENTERAL route** is necessary for patients who are too agitated or incapacitated to comply with treatment.
- **DEPOT formulations** – for patients:
 - a) who prefer not to have to take medication on daily basis.
 - b) with history of dangerous behavior and established noncompliance.

Acute psychosis

- **equivalent of 200-400 mg CHLORPROMAZINE** in divided doses (e.g. **HALOPERIDOL** – drug of choice for acute psychosis) - significant effects are reached in 3-10 days (some patients may require ≥ 30 days to respond).
- **massive doses** of 1000-2000 mg are sometimes used, but controlled studies indicate that this approach is no more effective than standard dosing (but small subset of patients apparently respond only to very high doses).
- because all neuroleptics have time delay for onset of efficacy, **additional psychotropic agents** are sometimes added during early days of treatment (e.g. **ALPRAZOLAM**).

Stabilization phase

- once patients have begun to respond to treatment, dosage is titrated toward maintenance level - to balance symptom control and incapacitating side effects (e.g. sedation, orthostatic hypotension).

Maintenance phase

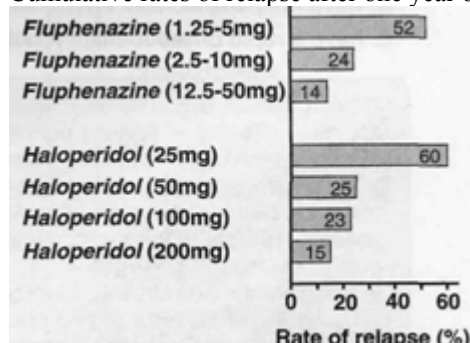
- patients who have had ≥ 2 schizophrenic episodes should receive maintenance for **at least 5 years** (some experts prefer indefinite therapy).

80% patients relapse within 1 year if antipsychotic medications are stopped, while only 20-30% relapse if treated!

- patients prone to **violent outbursts / self-destructive behavior** must be treated with **higher doses** (higher level of side effects, but minimized risk of harm).

- in general, higher doses are more effective in preventing relapse:

Cumulative rates of relapse after one year of maintenance therapy:



Nonresponse

- relapse in patient whose schizophrenia was once under control.
- use alternative drug (esp. in another chemical class).
- blood levels should be obtained (noncompliance can be identified).

ELECTROCONVULSIVE THERAPY (ECT)

- was only effective treatment option available until modern medications were developed.
- ECT is most effective in affective symptoms and catatonia.
- disadvantages - risks of anesthesia, negative public perception of ECT.
- indications:
 - clearly refractory patients (ECT should be considered after 3-4 drug trials).
 - life-threatening circumstances (severe catatonia, extreme suicidal ideation).
 - disabling massive doses of neuroleptics (patients can be maintained on standard doses of neuroleptics after ECT).

PROGNOSIS

Poor prognostic factors:

- early onset (so prognosis is worse for men)
 - family history of schizophrenia
 - disorganized** or **deficit** subtypes (prominent negative symptoms)
 - poor cognitive performance on neuropsychological testing
 - poor premorbid functioning
 - abnormalities on neuroimaging.
- paranoid** or **nondeficit** subtypes have best prognosis for recovery!

MORTALITY

Risk of death in *young* schizophrenics is several times higher* than in general population; as schizophrenic becomes *older*, risk of mortality approaches that of general population.

***suicide** (10% lifetime risk!), **homicide**, **medical illnesses** due to unhealthy lifestyles / decreased health care (e.g. cardiovascular, infectious, cancer associated with smoking).

In general, **lifespan is shortened by ≈ 10 yrs.**

QUALITY OF LIFE

- patients with chronic schizophrenia tend to have *small social networks* (3-5 individuals vs. 20-30 individuals for normal people).
- despite normal or high intelligence, many schizophrenics are *unable to complete educational plans* after onset of illness.
- significant *difficulties finding employment* (schizophrenics often have jobs that require less skill than their education and intelligence suggest).
- marriage rates are lower* (esp. for schizophrenic men).
- most schizophrenics are **no more violent than average persons!!!** (most patients are afraid of others rather than threatening to others, except for small subset of persons with history of violent actions when experiencing psychosis).
- 5-8% schizophrenics are *homeless*; many more live in substandard housing.
- 20-70% patients have comorbid **substance abuse** problem.

PEDIATRIC ASPECTS

- schizophrenia in prepubertal children is extremely rare.
- childhood schizophrenia forms continuum with adult form.
- preoccupation with gory or grotesque fantasies.
- hallucinations usually not prominent (visual hallucinations are more common).
- delusions are less common.
- poor attention span.

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