Phenomenology

The concept is a loss of touch with reality--loss of the ability to properly evaluate reality. This happens as a result of a loss of "normal thought: a disorder of cognition, or **Thought Disorder**. Thought disorders can be divided into different types. Most commonly they are divided into disorders of "process" or of "content".

		Schizophrenia
General		Poor grooming and hygiene. Poor eye contact.
Emotional	Mood	Anxious, angry or apathetic.
	Affect	Blunted, constricted, inappropriate
Thought	Process	Tangential, Circumstantial, loosening of associations.
	Content	Delusions, Hallucination.
Cognition		May be subtle deficits, ex., difficulty with abstractions.

Disorders of thought process involve a disturbance in the way one formulates thought: the process by which we come up with our thoughts. Thought disorders are inferred from speech, and often referred to as "disorganized speech." Historically, thought disorders included associative loosening, illogical thinking, over inclusive thinking, and loss of ability to engage in abstract thinking. Associative loosening includes circumstantial thought and tangential thought. Other types of formal thought disorder have been identified, including perseveration, distractibility, clanging, neologisms, echolalia, and blocking. With the possible exception of clanging in mania, none appears to be specific to a particular disorder.

Disorders of Thought Content include hallucinations and delusions. Hallucinations are perceptions without external stimuli. They are most commonly auditory, but may be any type. Auditory hallucinations are commonly voices, mumbled or distinct. Visual hallucinations can be simple or complex, in or outside field of vision (ex. "in head") and are usually normal color. Olfactory and gustatory are usually together--unpleasant taste and smell. Tactile or haptic hallucinations include any sensation--electrical, or the feeling of bugs on skin (formication). These are common across all cultures and backgrounds; however, culture may influence content.

Delusions are fixed, false beliefs, not amendable by logic or experience. There are a variety of types. Delusions are most commonly persecutory, but may be somatic, grandiose, religious or nihilistic. They are influenced by culture, and none is specific to any one disorder (such as schizophrenia).

Among other disorders of cognition is **lack of insight.** Truly psychotic persons have a

breakdown in this ability to rationally critique their own thoughts. This may best distinguish psychotic disorders (like Schizophrenia) from "normal" hallucinations and delusions. Other cognitive symptoms are usually normal (for example, orientation and memory). However, IQ usually is less than normal population for their age; it does not tend to decline over time.

Other symptoms associated with psychosis **include motor disturbances**, **disorders of behavior, disorders of mood and affect**, **and neurological/other signs and symptoms**.

Motor disturbances include disorders of mobility, activity and volition. **Catatonic stupor** is a state in which patients are immobile, mute, yet conscious. They exhibit waxy flexibility, or assumption of bizarre postures as most dramatic example. **Catatonic excitement** is uncontrolled and aimless motor activity. It is important to differentiate from substance-induced movement disorders, such as extrapyramidal symptoms and tardive dyskinesia.

Other disorders of movement include:

Stereotypy: repeated but non-goal-directed movement such as rocking.
Mannerisms: normal goal-directed activities that appear to have social significance but are either odd in appearance or out of context, such as repeatedly running one's hand through one's hair, r grimacing.

Mitgehen: moving a limb in response to slight pressure on it despite being told to resist the pressure.

Echopraxia: imitating the movements of another person.

Disorders of behavior may involve deterioration of social functioning-- social withdrawal, self neglect, neglect of environment (deterioration of housing, etc.), or socially inappropriate behaviors (talking to themselves in public, obscene language, exposing self). Substance abuse is another disorder of behavior. Patients may abuse cigarettes, alcohol or other substances; substance abuse is associated with poor treatment compliance, and may be a form of "self-medication" for negative symptoms or medication effects.

Disorders of mood and affect include **affective flattening**, which is a reduced intensity of emotional expression and response that leaves patients indifferent and apathetic. Typically, one sees unchanging facial expression, decreased spontaneous movements, poverty of expressive gestures, poor eye contact, lack of vocal inflections, and slowed speech. Anhedonia, or the inability to experience pleasure, is also common, as is emotional emptiness. Patients may also exhibit inappropriate affect. Depression may occur in as many as 60% of schizophrenics. It is difficult to diagnose, as it overlaps with (negative) symptoms of schizophrenia and medication side effects.

Neurological and other Signs/Symptoms include "soft signs" (nonlocalizing neurological signs). Neurological soft signs occur in a substantial portion of patients,

and include abnormalities in stereognosis, graphesthesia, balance, and proprioception. They may reflect defects in the integration of proprioceptive and other sensory information. Disorders of smooth pursuit eye movement are also a common sign. A disorder of the visual tracking of smoothly moving targets has consistently been observed in schizophrenic individuals and their relatives. They may represent a biological marker for schizophrenia. Sleep disturbance is another common symptom associated with schizophrenia.

It is important to differentiate **positive symptoms** of schizophrenia from **negative symptoms**. Positive symptoms are disorders of commission, including things patients do or think. Examples are hallucinations, delusions, marked positive formal thought disorder (manifested by marked incoherence, derailment, tangentiality, or illogicality), and bizarre or disorganized behavior. Negative symptoms are disorders of omission: things patients don't do. Negative symptoms include alogia (i.e., marked poverty of speech, or poverty of content of speech), affective flattening, anhedonia or asociality (i.e., inability to experience pleasure, few social contacts), avolition or apathy (i.e., anergia, lack of persistence at work or school), and attentional impairment. The relevance of these symptoms is unclear. Perhaps they represent independent subtypes of schizophrenia? Probably not. Different stages of disease? Maybe--positive symptoms tend to occur early on, negative symptoms later. Most patients have a mix of symptoms.

Epidemiology

There is an overall 0.7% incidence of "Nonaffective Psychosis" in the National Comorbidity Study. This study included schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder and atypical psychosis.

Schizophrenia has about 1% lifetime prevalence in ECA studies. There is a lower incidence (chronic disorder): 1/10,000/year. Incidence is equal across gender, but men may get it earlier. It most commonly starts in late adolescence/early adulthood. It rarely occurs in children. Women are more likely to get late onset. Generally, this version tends to have better psychosocial functioning. Schizophrenia occurs throughout the world, regardless of site or culture.

Schizophreniform Disorder has a lifetime prevalence of 0.2%, with 1-year prevalence of 0.1%. Otherwise, it is similar in epidemiology to Schizophrenia.

Schizoaffective Disorder is probably less common than Schizophrenia. There is little data about the community prevalence of Delusional Disorders. However, lifetime prevalence appears to be 0.03%. Clinical studies show delusional disorder to be 1-2% of

inpatient psychiatric admissions.

Brief Psychotic Disorder and **Shared Psychotic Disorder** also have little information and are probably rare. Shared Psychotic Disorder may go unrecognized in clinical settings; it is also probably more common in women.

Psychotic Disorder Due to a General Medical Condition, and Substance-Induced Psychotic Disorder are both probably common, particularly in clinical settings.

Pathology

Neurotransmitter Theories: The Dopamine Theory

Stated briefly the dopamine theory suggests that psychosis is caused by increased dopamine in the brain. There exists quite a lot of evidence for this theory. All available medications used to treat psychosis are dopamine blockers. A number of dopamine agonists (ex. L-Dopa) can cause psychosis as well. However, there are also problems with this theory. Studies measuring dopamine metabolites in cerebrospinal fluid are inconclusive. Also, the theory does not account for time lag: most of the dopamine blockers start blocking dopamine immediately, yet it takes about 2 weeks for psychosis to resolve. Even if the theory is true, it probably represents a final common pathway, and doesn't tell us enough about individual causes of psychosis. Dopamine blockers used to treat Schizophrenia are equally effective in treating, say, an LSD-induced psychosis. Refinements of neurotransmitter theories have come to pinpoint specific receptors (D-2), and other receptors such as norepinephrine, glutamate and serotonin.

Anatomic insights.

Are psychotic disorders caused by structural abnormalities, (either congenital or degenerative)? Studies of schizophrenics consistently show widened ventricles on neuroimaging. This has been shown even early in their disease. Certain other areas of the brain are decreased in size, for example the anteromedial temporal lobe.

Histopathological insights

Abnormalities of cytoarchitecture have been found in the parahippocampal gyrus of schizophrenics, indicating an abnormal alignment of neurons. A reduced neuronal density has also been found in the prefrontal region, thalamus and cingulate gyrus, along with an absence of gliosis, normally associated with degeneration.

Smooth pursuit eye movements are abnormal in 50-85% of schizophrenic patients. It is also abnormal in 45% of their relatives, even if they don't have schizophrenia. However, this phenomenon is nonspecific. It occurs in other disorders such as mood disorders and

This suggests a possible developmental abnormality.

Neurophysiological insights

Generalized problems, including cognitive insufficiency, have been observed in schizophrenics, as well as deficits in attention, alerting, memory, learning and shifting sets. **Hypofrontality**, a phenomenon in which patients cannot activate prefrontal cortex, has also been observed. Thus, prefrontal area can be normal in schizophrenics when viewed at rest, but when given a task that requires that area (Ex. The Wisconsin Card Sort) normal patients would light up that area on a SPECT or PET. Schizophrenics cannot.

Genetic Insights

Concordance rates for relatives of schizophrenics are remarkably high.

50% monozygotic twins.
40% 2 parents
12-15% dizygotic twins
12% 1 parent
8% non-twin siblings

These rates suggest that the disorder is inherited (strong concordance), but with incomplete penetrance, or that it is multifactorial.

Psychosocial Theories

It has been noted that schizophrenics often have low socioeconomic status. Social theories developed about the possible effects of environmental stressors on development. Far more likely is the "downward drift" theory, in which schizophrenics cannot hold a job or function well in society, thus they "drift" down to a lower status. Few people believe that schizophrenia and other psychotic disorders are not a biological disorder. Psychological factors, however, may mitigate the presentation (time of onset, degree of social impairment).

The Diagnoses

Criteria for Schizophrenia (See DSM-IV (or textbook) for specific criteria

1. Patients have to have been psychotic at some time. This is referred to as the "A" Criteria of Schizophrenia. 2. Additionally, two or more (1 if the delusions or hallucinations are pretty bad) are required:

delusions
hallucinations
disorganized speech
disorganized behavior/catatonia
negative symptoms

3. symptoms must persist for 1 month (less if treated).
4. Finally, during the the overall duration of the disorder must show some signs of disturbance (psychotic episode + prodromal or residual symptoms) for at least 6 months.

- **DSM-IV**: five subtypes of schizophrenia: *paranoid, disorganized* (i.e., hebephrenic), *catatonic, undifferentiated, and residual.*
- **ICD-10** includes the *simple, latent, and schizoaffective* subtypes as well
- Strongest data exists for *paranoid/nonparanoid*

Subtypes of Schizophrenia

The purpose of subtyping is to improve prediction of likely effective treatment and/or course of illness.

The types are listed as follows:

Paranoid subtype

a preoccupation with one or more delusions or frequent auditory hallucinations; disorganized speech/behavior, catatonic behavior, and flat or inappropriate affect are not prominent.

Disorganized subtype

characterized by disorganized speech and behavior, and flat or inappropriate affect; it does not meet the criteria for catatonic schizophrenia.

Catatonic subtype

dominated by at least two of the following: motoric immobility as evidenced by catalepsy or stupor, excessive motor activity, extreme negativism or mutism, peculiarities of voluntary movement (e.g., stereotypies, mannerisms, grimacing) and echolalia or echopraxia.

Note that the signs and symptoms of catatonic subtype can be found in other psychiatric disorders as well (including mood and organic mental disorders), and in a variety of other conditions such as viral encephalitis, frontal lobe tumors, metabolic derangements (i.e., acute intermittent porphyria), and toxic reactions. A patient displaying catatonic features requires careful evaluation and differential diagnosis.

Undifferentiated subtype

a residual category for patients meeting criteria for schizophrenia but not meeting criteria for the paranoid, disorganized, or catatonic subtypes.

The residual subtype: as described in DSM-IV is used for patients who no longer have prominent psychotic symptoms but who once met criteria for schizophrenia and have continuing evidence of illness.

Schizophreniform disorder

is like Schizophrenia except the duration is between 1 and 6 months (prodrome + episode + residual). If the duration is less than 1 month it is Brief Psychotic Disorder. Impaired psychosocial functioning is not required for the diagnosis; probably about 2/3 go on to become Schizophrenics.

Schizoaffective Disorder

has symptoms of both Schizophrenia and of a Mood Episode:. It fulfills symptoms of "Criterion A" of Schizophrenia. For diagnosis, at some point, psychotic symptoms have to be independent of mood (for at least 2 weeks). Symptoms of a Mood Episode may include either manic, depressed or mixed symptoms. These have to occur for a "substantial" amount of time; otherwise patient might be a depressed schizophrenic.

Delusional Disorder

is a disorder in which patients present with persistent delusions. Delusions are nonbizarre, thus differentiating this from schizophrenia. Hallucinations are not prominent. Generally, psychosocial functioning is okay, except for direct impact of delusion (ex. Might not go on bus, because thinks people talking about them).

Brief Psychotic Disorder

is different in that the psychotic symptoms last for less than a month and there is full remission by one month.

Shared Psychotic Disorder

is also called *Folie à Deux* and has two components. The inducer or primary case is a person already has some delusional disorder. Also, a second person, in close relationship with the inducer, comes to share the delusion. This person is usually in a dependent relationship with the inducer. This person rarely seeks treatment; rather, shared psychotic disorder comes to attention when the inducer is treated. Treatment is to separate this person from the inducer.

Psychotic Disorder Due to a General Medical Condition

includes hallucinations or delusions that are directly secondary to a medical disorder. One must differentiate this from Delirium, in which delusions or hallucinations can occur, but are part of the delirium. In Psychotic Disorder Due to a General Medical Condition, the psychosis occurs in a clear sensorium.

Substance-Induced Psychotic Disorder

has the same story as Psychotic Disorder Due to a General Condition, including the Delirium rule out.

Psychotic Disorder Not Otherwise Specified

is a term usually used for cases of inadequate information or disorders that don't meet criteria for one of the "official" psychotic disorders.

Differential Diagnoses

MEDICAL CONDITIONS

There is a long list of medical conditions that can cause psychotic symptoms. Some would justify a diagnosis of Psychotic Disorder Due to a General Medical Condition, but you wouldn't want to make the diagnosis of, say Schizophrenia, without ruling one of these diagnoses out. The most common of these is **delirium.** Delirium is an acute confusional state, with multiple possible etiologies that can cause delusions and hallucinations. Usually delusional hallucinations are poorly formed, and not very elaborate, and they occur in a setting of "clouding of consciousness." **Dementia** is another disorder to rule out. Disorders such as Alzheimer's can cause delusions and hallucinations. Typical are persecutory delusions: after losing wallet, might accuse loved one of stealing it. These also tend to be poorly formed, not elaborate, and they wouldn't justify a second diagnosis of a psychotic disorder.

Neurological Disorders must be ruled out as well. These may include *Temporal Lobe Epilepsy, tumor, stoke, and brain trauma*.

General Medical disorders to consider may *include endocrine and metabolic disorders (like Porphyria), vitamin deficiency, infections, autoimmune disorders (like Systemic Lupus Erythematosus) or toxins (like heavy metal poisoning).*

Medications and drugs that can cause psychotic symptoms may include *stimulants (amphetamines, cocaine) hallucinogens (PCP), anticholinergic medications, Alcohol Withdrawal (Delirium Tremens), and barbiturate withdrawal.*

Other Psychiatric Illnesses mistaken for psychosis include the following: *Major Depression with psychotic features* (which only occurs during depressive episodes), *Panic Disorder* (Patients may report they feel they are "going crazy"), *Depersonalization Disorder, and Obsessive-Compulsive Disorder.* In OCD, obsessions may reach point where they seem like delusions. However, classically speaking, they are seen as being ego-dystonic, meaning that the patient has good insight into obsessions as being abnormal and intrusive. *Personality Disorders*, especially Cluster B (Borderline Personality Disorder, for example), can show elements of psychosis. Finally, one must consider factitious disorder and malingering as

Subtypes of delusional disorder include the following:

- Erotomanic type: believes someone else in love with the person. The other person may be famous or otherwise unobtainable.
- Grandiose: great but unrecognized talent or insight.
- Jealous: spouse/lover is unfaithful. This is often based on small bits of misinterpreted "evidence."
- Persecutory type: the most common. The patient feels conspired against or cheated and often seeks legal/government action.
- Somatic type: the delusion centers around bodily function or sensation. For example, emitting foul odor, being infested with parasites, or feeling that parts of body not functioning or that parts

possibilities. Fortunately, these disorder are difficult to fake.

Comorbidity

Comorbidity is very common. In one study of new onset psychosis, about 50% of patients had some other medical or psychiatric disorder. The most common of these **are substance abuse** and **mood disorders**.

Substance Abuse is more common in the general population and is associated with poorer outcome. Most often it is alcohol abuse.

Mood disorders are also common; 60% of Schizophrenics are reported to have depressive symptoms. But depression is difficult to diagnose, as it can be comorbid with Schizophrenia, be Schizoaffective, or can be the primary disorder (Major Depression with Psychotic Features) depending on one's assessment of its relative predominance.

Medical disorders are also more common in psychotic individuals than in the general population (17% in one study). These patients tend to be older. The effect on outcome depends; in first episode cases, it may predict better outcome. However, in chronic disorders, it is probably associated with a poorer outcome.

Predictors of good outcome include:
acute onset
short duration of active phase
good premorbid functioning

Course and Prognosis

There are four possible outcomes:

Complete resolution of psychosis, with or without treatment. Complete resolution is typical of brief reactive psychosis, and medical/substance related causes of psychosis. It can also be associated with mood disorders with psychotic features.

Repeated recurrences with full recovery every time. These are more typical of Mood disorders with psychotic features (ex. Bipolar Disorder).

Repeated recurrences in which recovery is incomplete so that a persistent defect state develops. These are typical of Delusional Disorder, which tends to have a chronic, unremitting course. Also typical of schizophrenia.

Progressive deterioration. Progressive deterioration is typical of schizophrenia.

Predictors of Poor Outcome include:
insidious onset
long duration (chronic)
personal and/or family history of psychiatric illness
obsessions or compulsions
assaultive behavior
poor premorbid functioning
poor psychosocial functioning

Schizophrenia has three stages of disease: prodromal phase, active

phase and residual phase. Prodromal phase may precedes the active phase of illness by many years. It is characterized by social withdrawal and other subtle changes in behavior and emotional responsiveness. Active phase has psychotic symptoms ("Criterion A"), which predominate.

Residual phase is similar to the prodromal phase, although affective flattening and role impairment may be worse. Psychotic symptoms may persist, but at a lower level of intensity, and they may not be as troublesome to the patient. Symptoms tend to change over time. The preponderance of positive symptoms occur early. Over time patients develop more negative or deficit symptoms.

One review suggested that after a first admission 1/4 had a good outcome (defined as no hospital readmission during follow-up), 1/4 had a bad outcome (defined as continuous hospitalization during follow-up, or moderate to severe intellectual or social impairment) and ½ had an intermediate outcome. Schizophrenia has a high mortality rate: perhaps 10% commit suicide.

Treatment

SOMATIC: ANTIPSYCHOTICS

Classic antipsychotics include the phenothiazines, butyrophenones and others. More modern "atypical" antipsychotics have largely supplanted these in many situations.

The Mechanism of Action of all known antipsychotics is thought to be antagonism of the dopamine receptor, particularly D_2, and perhaps D_4.

Antipsychotics are typically indicated and effective for acute psychosis, maintenance therapy for schizophrenia, and acute mania. More controversial is the use of antipsychotics for anxiety/insomnia, somatization, and personality disorders (borderline, schizotypal). Clinical approach for antipsychotics relies on drug potency and the use of low doses.

The main side effects and risks associated with antipsychotics include anticholinergic effects, extrapyramidal effects, tardive dyskinesia, neuroleptic malignant syndrome, among others. Specific drugs and their side effects are detailed in a table at the end of this chapter.

Extrapyramidal effects include:
- Parkinsonism, bradykinesia
- Dystonia
- Akathisia
- Rabbit syndrome

OTHER SOMATIC TREATMENTS

These include electroshock therapy and benzodiazepines. Electroshock therapy may

be useful for catatonia, but is otherwise of little use in schizophrenia. Benzodiazepines are used for controlling agitation associated with psychosis. They may be as useful as antipsychotics in the acute setting if your main goal is to calm a patient down. These are safer (particularly in younger patients) than antipsychotics, but are not for long term management.

PSYCHOSOCIAL TREATMENTS

Are rarely used as a primary therapy. Good data to suggest that psychosocial treatments can improve functioning, particularly social functioning. Therapy tends to be educational and supportive rather than "insight oriented." It is focused on the practical needs of the patient. Therapy with family is thought to be helpful, both in helping them to cope with an ill family member, as well as educating them in useful approaches to the patient. One study has been influential in showing that family therapy + medication is more effective than meds alone in preventing relapse.

HOSPITALIZATION.

In the past, long term institutionalization was the treatment for schizophrenia. Since the 1960's however, and the rise of the Community Mental Health Movement, great efforts have been made to keep chronic psychiatric patients in the community. Nowadays, most schizophrenics are hospitalized only acutely, for a specific problems (ex. exacerbation of their psychosis).

SPECIFIC TREATMENT CONCERNS WITH NON-SCHIZOPHRENIC PSYCHOSES.

As *Schizoaffective disorder* tends to be a hybrid of psychotic and mood disorders, the treatment is also a hybrid, with both antipsychotic and antidepressant drugs used. In the bipolar type, Lithium and the anticonvulsants appear to help. *Delusional disorder* is usually thought to be relatively non-responsive to medications. Little has been done to study this clinical impression. Medications may diminish the intensity of delusions, even if not altering the delusion itself. One form of somatic delusional disorder, *monohypochondriacal paranoia* is thought to be particularly amenable to the antipsychotic pimozide. *In Shared Psychotic Disorder,* the primary treatment is to separate the couple.

Drugs use to treat Psychosis					
	Class	Relative potency	Kinetics	Common Side effects	Serious side effects
Chlorpromazine (Thorazine)	Phenothiazine	100 mg	$t_{½}$ = 12 hours, liver metabolized, > 150 metabolites.	Orthostatic hypotension, high anticholinergic disorder effects, low to moderate extrpyramidal side effects (EP)	tardive dyskinesia, neuroleptic malignant syndrome
Thioridazine (Mellaril)		100 mg	little known, $t_{½}$ @ 10-30 hours, metabolized in liver		
Fluphenazine (Prolixin)		2 mg		high EPS, low anticholinergic	
Perphenazine (Trilafon)		8 mg			
Trifluoperazine (Stelazine)		5 mg			
Thiothixene (Navane)	Thioxanthine	4 mg			
Haloperidol (Haldol)	Butyrophenone	2 mg	probably no active metabolites.	Very high EPS, very low anticholinergic	
Clozapine (Clozaril)	Atypical Antipsychotic	50 mg	12 hours with large range	high anticholinergic, high sedation, hypotension, rare EPS. Rare but reported agranulocytosis	agranulocytosis (requires blood monitoring)
Quetiapine (Seroquel)				rare EPS and anticholinergic, moderate sedation and hypotension	tardive dyskinesia and neuroleptic malignant syndrome possible, but much rare than above agents.
Olanzapine (Zyprexa)		N/A		very low EPS and anticholinergic, moderate sedation	
Risperidone (Risperidal)				low EPS, very low anticholinergic, low sedation, moderate hypotension	