# Schizophrenia: An Overview

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Abstract

Schizophrenia is a severe and disabling mental illness that affects approximately 1% of the population. The illness is characterized by positive (hallucinations and delusions) and negative (avolition and flat affect) symptoms. Schizophrenia typically occurs during late adolescence or early adulthood and disrupts the life of the patient and their family. This paper will discuss a brief history, diagnosis and treatment of this very severe mental illness.

Schizophrenia: An Overview

## History

Schizophrenia has plagued the human race for centuries with events of psychosis documented in ancient Egyptian, Greek and Roman writings. While it is impossible to make a post morbid diagnosis of schizophrenia, it appears that schizophrenia has always played a role in human existence. Throughout the medical community it is accepted that schizophrenia is a complex disorder that is caused by a number of factors, to include a genetic predisposition to the illness as well as environmental insults. Schizophrenia is considered a major psychiatric brain disorder that can result in a chronic and disabling prognosis for the patient. The impact of the illness can be devastating especially to individuals that are delayed in getting diagnosis and treatment.

The earliest recorded case of schizophrenia involved a London man named James Tilly Matthews. He was born in 1770 and at the age of twenty he fled to France. Once in France Mr. Tilly became active in French politics, and in 1793 he was arrested and jailed on the suspicion of being a double agent for England. He was later released from prison because he was found to be mentally insane. After returning to London in 1797 he was committed to the Bethlam psychiatric hospital following an inappropriate scene at the House of Commons. In 1810 John Haslem, a resident at Bethlam hospital, wrote a book named Illustrations of Madness which was a detail account of Matthews delusions. Mr. Haslem's book documented what is considered the first historical account of a patient who was likely schizophrenic.

In the late 1800's Emil Kreapelin, a German physician, differentiated several mental illnesses. For example, he identified dementia praecox and distinguished this illness from manic-depressive disorder by identifying that these patients have an early onset, a change in

cognition, and that they continue to deteriorate over time. He also noticed that they would often suffer from hallucinations and delusions.

Then, in 1908, Eugene Bleuler, a Swiss psychiatrist, coined the term "schizophrenia," a disease of the mind effecting personality, cognition, and perception. Like Kreaplin, Bleuler believed that hallucinations and delusions were characteristic of this disease, but unlike Kreaplin, Bleuler did not believe that schizophrenia always had a deteriorating course of illness. He used the term "schizophrenia" to describe the division between thought, emotion and behavior that is frequently seen in schizophrenia. He is also responsible for coming up with the four A's of schizophrenia: association, affect, autism and ambivalence (B. J. Sadock, Kaplan, & Sadock, 2007). The four A's identify areas of deficits that are associated with schizophrenia and are still used as part of the definition today.

In the 1950's Kurt Schneider, a German psychiatrist, introduced first rank symptoms. Although first rank symptoms were not specific to schizophrenia, Schneider believed that patients with schizophrenia often presented with these types of hallucinations or delusions. The identified themes have since been coined "first rank symptoms," so named because these thought distortions can appear in other disorders but are often found in schizophrenia (e.g., (i) Audible Thought, (ii) Voice Arguing, (iii) Voice Commenting (iv) Thought Insertion, (v) Thought Withdrawal, (vi) Thought Broadcasting, (vii) "Made" Affect, (viii) Impulse, and (ix) Somatic Passivity (B. J. Sadock, Kaplan, & Sadock, 2007)). Audible Thought is when a patient hears his own thought with an echo. Voice Arguing is when the patient hears one or more voice(s), separate from his or her own voice, arguing and often the arguing is about the patient. Voice Commenting is when a voice distinct from the patient's own voice, is giving a running commentary (i.e. he is sitting down, he is walking). Thought Insertion is when a patient believes

that thoughts are literally being put into his or her brain. For example, a patient believes that aliens are inserting thoughts into the patient's brain though a transmitter in the patient's head. Thought withdrawal is similar to thought insertion, but differs in that the patient believes thoughts are literally being removed from their brain. Thought Broadcasting is when the patient believes that their thoughts are being broadcast to other people. A client that has "Made" Delusions believes that another person controls him or her and Made Affect refers to the belief that the person is being made to feel much like a puppeteer is controlling him or her. Made Impulse is the belief that the patient is not in control of his or her own movements or impulses. Somatic Passivity is when the patient believes that he or she is being made to feel a sensation by someone or something other than him or her self.

## Prevalence and Challenges

The diagnosis of schizophrenia has remained relatively stable throughout the course of time, occurring in approximately 1% of the world's population. Although approximately 1% of the world's population is affected by the illness, clinical evidence shows that schizophrenia is diagnosed more frequently in certain ethnic groups. For example, a greater percentage of African Americans and Asians are diagnosed with Schizophrenia as compared to Caucasians (Bresnahan et al., 2007; Goater et al., 1999). However, it is not known if this is due to decreased cultural sensitivity relative to the illness or if there is simply a higher rate of illness amongst those races. Studies also show that individuals in developing countries have a more acute course and better outcomes compared to individuals in industrialized nations (Jablensky et al., 1992; Jablensky & Sartorius, 2008). The World Health Organization consistently ranks schizophrenia as having one of the highest levels of global burden, as an estimated 2.5% of all health care costs are spent on schizophrenia. In 2002, it was estimated that the United States of America spent

62.7 billion dollars on direct and indirect costs related to the treatment of schizophrenia (E. Q. Wu et al., 2005).

Schizophrenia can occur in both genders, however, several reports suggest that schizophrenia occurs in a higher percentage of the male population (1.4%) then the female population (1.0%) and that men have a poorer prognosis than women (J. McGrath, Saha, Chant, & Welham, 2008). Most individuals are diagnosed with Schizophrenia during their late adolescence, early twenties or early thirty's. However, some rare cases have been diagnosed later in an individual's life and others in early childhood. Generally the median age for a male's diagnoses is 15 to 25 years of age, whereas the median age for a female's diagnoses is 25 to 35 years of age.

People with schizophrenia have a dramatically shortened life expectancy, specifically, it is estimated that people with schizophrenia live 15 to 25 years less than the average person (Laursen, Munk-Olsen, & Vestergaard, 2012; Raedler, 2010). The shortened life expectancy is attributed to an array of issues including a higher risk of suicide, homelessness, inadequate access to healthcare, resistance to treatment, effects of antipsychotic medication and unhealthy lifestyle choices.

As previously mentioned, the rate of suicide is 5% higher amongst the schizophrenic community as compared to the general population (Qin, 2011). Additionally, schizophrenic patients account for 10% of completed suicides (Cohen, Abdallah, & Diwan, 2010). With regard to homelessness, legislation passed during the 1970's and 1980's resulted in the deinstitutionalization of psychiatric patients, to include schizophrenic patients, many of whom found themselves without a home. To date, many mentally ill patients are still homeless or residing temporarily in community shelters as their inappropriate or abnormal behavior prevents

them from establishing or maintaining functional relationships with those individuals who can provide a home to them. Some studies estimate 11% of the homeless population has schizophrenia (Foster, Gable, & Buckley, 2012).

Another factor contributing to a schizophrenic individual's shortened life expectancy is that he or she most likely has a difficult time navigating the health care system (Laursen, Munk-Olsen, & Vestergaard, 2012). Locating care, having the financial means to pay for care and then consistently participating in the care can be overwhelming for an individual that struggles through even the most basic daily tasks. Even if a mentally ill individual is able to navigate through the health system, he or she may distrust medical care providers or resist medical interventions. Some research shows that patients who have schizophrenia and cardiovascular disease have fewer invasive cardiac procedures then patients without schizophrenia (Laursen, Munk-Olsen, & Vestergaard, 2012). If a schizophrenic individual is able to locate a care provider and obtain medication for treatment, the metabolic side effects associated with medications used to treat their mental illness can also contribute to the patient's shortened life expectancy.

Shorter life spans of people with schizophrenia have also been associated with metabolic diseases, cardiovascular disease and diabetes. For example, some evidence suggests there is a link between diabetes and schizophrenia. That is, an individual with schizophrenia is more likely to develop diabetes than an individual without schizophrenia (Hsu, Chien, Lin, Chou, & Chou, 2011). Much debate still exists as to the whether biological reasons are the main contributor to the onset of diabetes or if side effects from high levels of antipsychotic medication used to treat schizophrenia are the main contributor to the onset of diabetes.

As a healthcare provider it is important to educate the patient and his or her family about the treatment for schizophrenia, as well as the potential negative side effects resulting from the treatment. Advising patients and their family members regarding the challenges that are associated with schizophrenia, while at the same time offering risk reduction methods that can be used to decrease the incidence or severity of such problems, can provide patients with the tools necessary to overcome difficulties associated with schizophrenia. It is also important to give the patient a clear understanding of the risks associated with the disease and ensure that the diagnosis of schizophrenia is appropriate

## Diagnosis

The criteria used to diagnosis schizophrenia have changed over time; however, consensus models have worked to make the diagnosis of this disorder more uniform. Although clinicians may disagree on discrete nuances of the disorder, several symptoms that are staples of this disorder have been used to determine an appropriate diagnosis for over a century. Currently the most appropriate diagnosis is made following a thorough interview with patients and his or her family members. As technology continues to advance in the field of medicine, it may become possible to confirm a mental health diagnosis with laboratory tests.

Currently, there is a blood test that states it can identify markers for schizophrenia but it costs approximately $2500. Insurance does not usually cover the cost associated with this test as the Food and Drug Administration has not approve the test, nor is it considered 100% reliable for diagnostic purposes (Tomasik, Schwarz, Guest, & Bahn, 2012). Historically, the best screening and diagnostic tool used to identify schizophrenia is the interview that takes place between the patient and the mental health care professional. Ideally the patient and his or her family will be involved in this process, as it is very important to have a good family history. The clinician must

remember that some symptoms of schizophrenia can resemble other mental health disorders; therefore, it is important to rule out all other medical and psychiatric disorders prior to diagnosing schizophrenia.

Differential diagnoses to consider when evaluating other possible disorders include schizoaffective disorder and schizophreniform disorder. It is important to differentiate these two disorders from schizophrenia to ensure the patient is getting the best treatment. It is also important for the clinician to differentiate schizophrenia from mood disorder with psychotic features and to ensure that symptoms are not side effects of substance use or abuse, or related to a general medical condition. Patients with autism spectrum disorder may also be diagnosed with schizophrenia, but only if hallucinations are present for at least one month.

During the prodromal phase of schizophrenia, the phase before the disease is clearly evident, a patient may present with odd beliefs and/or behaviors. They may also become more withdrawn from friends, family and social functions and an obvious dysfunction in several areas of the patient's life will be noted for an extended period of time. Although not as evident during the prodromal period and the residual phase as compared to the active period, a patient may also begin to have difficulty with logical and linear thought. Family members will often start noticing a change during the prodromal phase due to of the presence of the negative symptoms, but often times the symptoms are similar to or confused with those found in individuals suffering from depression.

**Diagnostic Criteria**

In order for a patient to be considered schizophrenic, he or she must have a marked decline in social and occupational functioning, at least two or more of the characteristic symptoms must be present for at least 6 months and there must be evidence of at least one month

of active phase symptoms. With respect to the decline in social and occupational functioning, following the initial disturbance the patient must have a significant deterioration in function either at home, work or if a child, at school. As schizophrenia involves a collection of cognitive and emotional dysfunction presenting in multiple behaviors, no one behavior can be classified as schizophrenic and diagnosis is based on the recognition of a constellation of signs and symptoms (American Psychiatric Association & American Psychiatric Association. Task Force on DSM-IV, 2000). There must also be a history of difficulty for at least 6 months and if there are characteristic symptoms present they can be less severe then during the active phase. Characteristic symptoms include delusions, hallucinations, disorganized speech and grossly disorganized or catatonic behavior.

Symptoms are generally described as either positive or negative symptoms. Positive symptoms are thought of as an addition to normal function and negative symptoms are thought of as a decline from normal function. Positive symptoms include disturbances with delusions, hallucinations, disorganized speech, and grossly disorganized or catatonic behavior. Positive behaviors fall into two different categories, either psychotic or disorganized. Psychotic behaviors involve the presence of hallucinations or delusions and disorganized behavior involves problems with speech and thought processes. These subcategories of positive symptoms are thought to be associated with dysfunction in different areas of the brain. Negative symptoms are identified by a decline in the emotional expression of a patient from what was previously demonstrated. Negative symptoms include deficits in the fluency and productivity of though and speech, as well as difficulty with initiating goal directed behaviors (American Psychiatric Association & American Psychiatric Association. Task Force on DSM-IV, 2000).

**Positive and Negative Symptoms**

When a patient presents with symptoms, the symptoms can provide clues about the patient's prognosis. Although positive symptoms can appear more psychotic than negative symptoms, they can indicate a better prognosis then a patient that presents with negative symptoms.

Delusions, a positive symptom, are described as a strong and inaccurate belief held by an individual even when evidence is presented to the contrary. Persecutory delusions are the most common and an example of a persecutory delusion is when a patient believes someone or something is going to or wants to cause the patient harm. Treatment providers should be cautious when dealing with patients that are experiencing these types of delusions, because they can cause the patient to be fearful for his or her life and become aggressive or violent. Referential delusions are also quite common and an example of a referential delusion would be when a patient erroneously attaches excessive meaning to seemingly insignificant interactions. Bizarre delusions are often characteristic of schizophrenia and discerning between "bizarre and non-bizarre" delusions can prove challenging; however, bizarre delusions are generally implausible. Currently, delusions that fit the criteria for Schneider's first rank symptoms are enough to satisfy the first criteria for the diagnosis of schizophrenia. It is recommended however that the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders no longer make an exception for Schneider's first rank symptoms. The American Psychiatric Association believes that the reliability of diagnosis based on Schneider's first rank symptoms is considered to be poor. (American Psychiatric Association, 2012)

Hallucinations, another positive symptom, can originate in any of the five senses. Auditory hallucinations are the most common and they are separate from the person's own

thoughts. Often times auditory hallucinations present in schizophrenia have a particular pattern such as thought echo, voice commenting, or arguing.

Disorganization in speech is also a positive symptom and occurs when a patient is unable to produce logical coherent thoughts and/or speech. Some patients may have difficulty with linear thought as well and they will move from topic to topic with little connection between the topics. Disorganization in speech can be extremely disabling and in extreme cases it effectively eliminates a patient's ability to have meaningful conversation. Disorganization not only effects speech, it can also effect a patient's behavior and thoughts. Disorganized behaviors can make it extremely difficult for a patient to complete every day tasks such as bathing, dressing and preparing meals. Disorganized thoughts can affect a patient's ability to interact with others. At times a patient may appear disheveled or he or she may dress inappropriately. Or, a patient may be emotionally labile, quickly shifting from one extreme mood to another without provocation. A patient with catatonia may remain fixed in one position for several hours at a time thus creating an additional risk for potential malnutrition due to their lack of taking in food or water while stationary.

Negative symptoms are seen as a decrease in normal behavior beginning at the onset of the illness. Affective flattening, an example of a negative behavior, can be explained as a decrease in expressiveness. Generally, a, patient presenting with affective flattening will no longer appear as interested in activities or events that he or she was interested in at one time. Avolition, another negative symptom, is described as the inability of a patient to produce goal directed behavior. It may appear as if the patient has little interest in doing anything, similar to a presentation of a depression, except that depression is associated with a deep feeling of hopelessness or loss. The next negative symptom I plan to discuss is alogia and it is described as

a marked decrease in speech. A patient that presents with alogia may only use one-word answers, he or she may not ask follow up questions, or he or she may appear as if his or her fluency and production of speech is restricted.

As I previously mentioned, patients that present with negative and disorganized symptoms are often associated with poorer outcomes as compared to patients that present with hallucinations and delusions. This is because negative symptoms and disorganization can have a greater impact on a patient's ability to manage day-to-day activities. Negative symptoms must be carefully evaluated and they must represent a significant change in a person's behavior. They cannot be related to medication and cannot be symptomatic of depression. In differentiating negative symptoms from depressive symptoms, the key may be in how a patient's emotion is attached to the symptoms. Depression is often associated with emotional pain, whereas negative symptoms are associated with a lack of emotion.

Schizophrenia has several sub-types and these classifications are fluid and representative of a patient's current and active presentation. The sub-types include (i) Catatonic type, (ii) Disorganized type, (iii) Paranoid type, (iv) Undifferentiated type and (v) Residual type. Although Catatonic type is rare, if any catatonic symptoms such as muscle rigidity, mutism or waxy flexibility appear to be present in a patient, he or she would be classified as catatonic type. In the absence of Catatonic type, Disorganized type is assigned when a disorganization of thought or speech is obvious in a patient. Paranoid type is assigned to a patient when there is an absence of catatonic or disorganized behaviors, and when there is a preoccupation with a delusion. A patient can often be hostile, aggressive or suspicious when presenting with the paranoid subtype because he or she is fearful for their life. Undifferentiated type is characterized when a patient meets the criteria for characteristic symptoms of schizophrenia but does not fit the

criteria for the catatonic, disorganized or paranoid sub-types. The diagnosis for residual type is given in the absence of prominent active symptoms but evidence of active disturbance. While it is important to understand sub-types for current diagnostic purposes and to assess historical information, it is also valuable to know that the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders is recommending that all sub-types be removed from the diagnosis of schizophrenia. The rationale behind the decision for the removal of the sub-types is that the sub classification does not represent a clear clinical picture of schizophrenia and most of the sub-types are rarely diagnosed.

## Biological Basis

Scientists are still working to gain a better understanding of potential causes of schizophrenia, specifically, they hope to determine whether the disease is attributed to neurodevelopmental issues or neurodegenerative issues. It is a fact that the brain in an individual suffering from schizophrenia is different than the brain in an individual not suffering from the disease. There are several biological changes that occur within the brain of a schizophrenic, to include (i) the prefrontal cortex, (ii) the limbic system, (iii) the basal ganglia and (iv) the cerebral ventricles. The most consistent finding is decreased volume in the frontal lobes, hippocampus, thalamus and enlarged cerebral ventricles.

A decreased size of the frontal lobe and temporal lobe has been documented though imaging studies of schizophrenic patients (Akhtar, Naqvi, Hussain, Ali, & Ahmad, 2010; Cobia, Smith, Wang, & Csernansky, 2012). A decrease in frontal lobe and temporal lobes may explain the problems with attention, executive and cognitive functioning, as well as several negative symptoms such as adhedonia, avolition and effective flattening. Additionally, studies have

shown there to be a decrease in the size of the limbic system, especially related to the amygdala and hippocampus (Sadock & Sadock, 2007).

The limbic system is compromised of the hippocampus, amygdala and fornix and plays a role in emotional regulation and memory. Structural and functional changes in this area can cause dysfunction in a schizophrenic patient's ability to appropriately regulate emotions, as well as cause a decline in cognitive function. Dysfunction in the language and memory centers within the amygdala and hippocampus are thought to be responsible for the development of hallucination and delusions (Heckers, 2001). Due to the role the limbic systems plays in associating information, dysfunction in this area may contribute to disorganized speech, which is a symptom of schizophrenia (Williams, Avery, Woolard, & Heckers, 2012).

The basal ganglia is responsible for the initiation and control of muscle activity. This may be why a schizophrenic patient has trouble with muscle activity, such as seen in catatonic patients. Alterations are also evident in the cerebral ventricles. Imaging studies consistently show significant changes in several regions of the brain, such as cerebral ventricles (Mitelman et al., 2010). The pathological implications of this finding are not well understood, but it is one of the most consistent findings in postmortem and imaging studies done on patient with schizophrenia. Enlarged ventricles are also seen in patients with other mental health disorders, so having enlarged ventricles alone does not cause schizophrenia. Scientists find creating and replicating suitable studies to help determine the exact causes for changes in the brain associated with schizophrenia to be very challenging, but they hope to learn more about the disease through continued research efforts.

## Biological Theories

As research for schizophrenia continues, it is becoming more apparent that multiple neurotransmitters play a role in schizophrenia. An accepted belief is that schizophrenia is a disease that disrupts the neurotransmitters in the brain and limbic system, which then cause the symptoms of the disease. Several theories have been hypothesized regarding the cause of schizophrenia.

The first credible theory was the dopamine hypothesis of schizophrenia, which identified the hyperactivity of dopamine in the brain. This theory was postulated for two reasons. The first reason was that when patients increased their dopaminergic activity with drugs like phencyclidine (PCP) and amphetamines, they would exhibit symptoms of delusions and hallucinations much like patients with schizophrenia. The second reason was that when schizophrenic patients would take medication that blocked or decreased dopamine, they would show a decrease in symptoms. Altering the role of dopamine remains a key mechanism for pharmacologic management of positive symptoms of schizophrenia; however, the complete blockage of dopamine can lead to severe side effects.

Dysregulation of several neurotransmitters in the brain is still a major focus of research and it is very important in the pharmacologic management of schizophrenia. For example, the role Serotonin (5-HT), *y*-aminobuteric acid (GABA), and Glutamate play in schizophrenia is becoming clear. A disruption in distribution of Serotonin, which regulates mood, sleep, learning and memory, has been associated with many mental health disorders, such as bipolar disorder, depression, anxiety, and schizophrenia. Manipulation of the serotonin receptors, by changing the amount of serotonin available to the postsynaptic neuron, has showed relief of symptoms in all of these disorders.

In schizophrenic patients, treatment with atypical antipsychotic agents showed an improvement in both the positive and the negative symptoms. Many atypical antipsychotic medications on the market decrease the activity of dopamine as well as serotonin in the brain. GABA is an inhibitory neurotransmitter in the brain and some studies show that patients with schizophrenia have a decrease in GABA (Rowland et al., 2012). As GABA has a direct effect on the inhibition of dopamine, it stands to reason that in a brain with overactive dopamine the mechanism that inhibits it would be faulty. The role of glutamate in psychosis has stemmed from the effects of PCP and Ketamine, which block glutamate and cause symptoms similar to the positive symptoms of schizophrenia (Moghaddam & Krystal, 2012). Glutamate, is an excitatory neurotransmitter in the brain, and plays an important role in prefrontal cortical functioning and behavior, including memory and learning. Mounting research is indicating that dysregulation of glutamate could play a key role in the development of schizophrenia.

The hyper-dopamine and hypo-glutamate hypothesis suggests that excess dopamine is caused by a decrease in glutamate. Glutamate acts directly or indirectly on the expression of dopamine. Therefore, a dysfunction in glutamate, which in turn creates a dysfunctional dopamine system, can cause positive and negative symptoms related to schizophrenia (Steele, Moore, Swan, Grant, & Keltner, 2012). Due to the important and sensitive role that glutamate plays in the brain, researchers continue to explore the development of medications to help manipulate glutamate levels in the brain as well as the potential side effects of said medications. Currently, there is a great deal of research underway to evaluate which neurotransmitters have the most significant impact on schizophrenia and in time this research may provide the basis for new pharmacological treatment. The dysfunction of neurotransmitters is a symptom of schizophrenia, however, in order for the patient to present with symptoms there must be a

biological underpinning for the disorder. Research is also evaluating the role of genetics in schizophrenia.

## Risk Factors

Clinicians continually work to determine what factors contribute to an individual's likelihood for developing schizophrenia. Although there is not concrete information that helps clinicians determine exactly why certain people are at risk for developing Schizophrenia, many great theories have emerged over time that help clinicians better understand why the disorder will express itself in some patients and not others. The general consensus is that a patient must have both a genetic risk and an environmental risk for full expression of the disorder to take place.

### Genetic Risk Factors

There is strong evidence that schizophrenia has a genetic component. However, several monozygotic twin studies have illustrated that in addition to the strong genetic component there are other factors that must be present for schizophrenia to exist. The general belief is that there is interplay between genetic and environmental factors that lead to the development of schizophrenia. The diathesis stress theory is the most widely recognized theory related to the development of schizophrenia, and the theory states that an individual will develop schizophrenia based on the interaction of several factors, including genetics, environment, neurobiology and stress.

The strongest genetic risk factor involves a first or second degree relative with a history of schizophrenia or schizoid personality type. The general population has about a 1% prevalence of having schizophrenia, whereas a child who has one parent with schizophrenia has a 12% risk of having schizophrenia. If a child has two parents with schizophrenia, the percent chance of

being inflicted with the disease increases to 40%. In twin studies, monozygotic twins (twins formed from the same fertilized egg who share 100% of their DNA) had a 50% concordance rate, as compared to dizygotic twins (twins from separate fertilized egg that do not share DNA) that had a concordance rate of 12% (B. J. Sadock, Kaplan, & Sadock, 2007). Therefore, if schizophrenia were purely genetic, the expected concordance rate would be 100% between monozygotic twins.

There are several genes (DISC-1, GRM 3, COMT, NRG 1, RGS 4 and G 72) currently being studied to determine what, if any, significance they have in the development of schizophrenia (B. J. Sadock, Kaplan, & Sadock, 2007). Research also suggests that if an individual is genetically predisposed to schizophrenia and later in life succumbs to events that fully express certain genes, he or she will likely become schizophrenic. Other individuals that have the same genetic predisposition to the illness, but are exposed to different environments, may never fully express the genes. These individuals may have no apparent dysfunction, or they could be identified as being on the schizophrenia spectrum but not be disabled by the disease.

**Environmental Risk Factors**

There are also several environmental risk factors associated with schizophrenia. Research has found that paternal age, maternal stress and immigration all appear to have a positive correlation with an increased risk in schizophrenia.

Specifically, several studies have shown that despite the lack of personal family history, advanced paternal age at the time of conception presents an increased risk that the offspring will have schizophrenia. The belief is that there may be a malfunction during spermatogenesis that leaves the offspring more vulnerable to schizophrenia (Frans et al., 2011; Goriely & Wilkie, 2012; Naserbakht, Ahmadkhaniha, Mokri, & Smith, 2011).

Other studies have shown that mothers who were under extreme stress during pregnancy, especially in the 1st trimester, had an increased incident of having a child who later developed schizophrenia. There is also evidence showing that women who were exposed to influenza during their first trimester had schizophrenic children at higher rates than those who were not exposed to influenza. The belief is that exposure to influenza early in pregnancy cause a disruption in the neurodevelopment of the fetus (Matheson, Shepherd, Laurens, & Carr, 2011).

Complications during pregnancy and delivery have also been investigated as a possible risk factor for Schizophrenia. Specifically, some evidence suggests that obstetrical complications such as hemorrhage, preterm labor, and fetal hypoxia may increase risk for schizophrenia (Forsyth et al., 2012). Although the evidence is not overwhelming and more research needs to be done, the belief is that early trauma to the brain increases the risk for schizophrenia. It is also well documented that there were higher than average rates of schizophrenia in people that were conceived during a famine. The hypothesis in all of the studies is that maternal stressors interfere with neurodevelopment in the early stages of pregnancy, thus putting the child at an increased risk for schizophrenia later in life (Li et al., 2009).

Last, but not least, immigration has been associated with increasing the risk for schizophrenia. Specifically, there is a great deal of evidence linking 1st and 2nd generation immigrants to above average rates of schizophrenia when compared to the general population (Ampadu, 2011; Bourque, van der Ven, Fusar-Poli, & Malla, 2012; Weiser et al., 2008). This is especially true when the immigrants are moving to an area where their culture is perceived negatively. It is not fully understood if mental illness may have precipitated the move to another

area or if the stress of moving to a hostile nation hastened the development of schizophrenia. It is my opinion that more research should be done to investigate this linkage.

## Treatment

Schizophrenia has mystified clinicians for centuries and there is still much debate regarding the best or most effective treatment for these patients. Over the years a variety of treatments have been used to treat the disease, including lobotomies and electroshock treatment. Unfortunately none of these treatments proved to be very effective and several made the patients worse. Based on the most current medical information available today, clinicians believe the best outcomes are produced when a patient is treated with antipsychotic medication, psychosocial therapy and community interventions.

### Pharmacological Treatment

Antipsychotic medications are the first line drug of choice used to treat schizophrenia, as there benefit has been well established in treating the positive symptoms of schizophrenia. Newer atypical antipsychotic medications can help with the negative symptoms of schizophrenia, although there effectiveness at treating negative symptoms is less extensive than the treatment of positive symptoms. Antipsychotics should be used with caution as they can have serious side effects on the patient. For this reason, clinicians should always use the lowest possible dose needed for stabilization and maintenance. Before starting treatment with antipsychotic medication, it is vital to have a baseline of your patient's medical health. Such baseline diagnostic tests should include a blood pressure, evaluation of any movement disorders, blood work (i.e. blood panel, electrolyte panel, fasting glucose, lipid panel, liver, renal, thyroid test) and an electrocardiogram. As antipsychotic medications can increase the risk of several disorders such as, movement disorders, diabetes, dyslipidemia, elevated prolactin levels and

prolonged QT waves, having a baseline understanding of a patient's medical condition will allow the clinician to manage and treat the patient holistically.

Current treatment recommendations advise clinicians to start a patient on one antipsychotic medication and then evaluate the effects. The patient should experience significant improvement within the first two weeks of treatment and then experience the full benefit of the medication in four to six weeks. If after four to six weeks of treatment with medication the patient requires additional medications or a higher dosage, the clinician can then safely make the appropriate adjustments. At six weeks it may be appropriate to augment the therapy by adding a mood stabilizer, anxiolytic or antidepressant medication if the need arises. Although it is not generally recommended, some clinicians use more than one antipsychotic at a time. That being said, some studies are showing that in treatment resistant patients adding clozapine to a regimen may be beneficial.

There are two different classes of antipsychotics, first generation and second generation or "atypical". The first-generation antipsychotics (FGA) first appeared in the 1950s' with the introduction of Thorazine (Chlorpromazine). These medications are extremely effective at calming psychiatric patients, however, they can cause various movement disorders. Second-generation (SGA), or atypical antipsychotics became available in the United States in the 1990's and are believed to be less likely to cause movement disorders and a better alternative for treating negative symptoms of schizophrenia as compared to first generation medications. One negative aspect of second-generation antipsychotics is that they appear to have an increased risk for metabolic side effects. Additionally, evidence supporting the claim that second generation antipsychotics do not cause movement disorders is debatable, however, it does appear that they are less likely to cause movement disorders when given at higher doses than first generation

antipsychotics. As antipsychotics are known for their negative side effects, scientific studies support the importance of finding the lowest effective dose.

One major difference between the FGA and the SGA is the mechanism of action. Specifically, the FGA bind mainly to $Dopamine_2$ receptors in the brain, blocking its action. The SGA bind to more Dopamine receptors as well as to Serotonin receptors. Initial administration of medication should be titrated up as quickly as the patient can tolerate. A patient undergoing treatment may feel tired initially, which is due to the medication anticholinergic sedating effects, but this side effect should decrease within two weeks of initial administration.

The cost of medication necessary for treatment can range from $50 - $550 per month for a single patient. In 2002, of the 22.7 billion dollars spent on direct health care expense related to schizophrenia, 5 billion was spent on medications (E. Q. Wu et al., 2005). Indefinite pharmacological treatment is required for almost every patient that suffers from schizophrenia since it is a life-long disorder and a sudden discontinuation of medication can initiate a relapse and subsequent neurodegenerative events. The prevention of recurrent psychotic episodes, as well as treatment of negative symptoms and cognitive deficits, is essential for a patient's quality of life. For this reason and others, an increased emphasis is being placed on the importance of regular pharmacological treatment in patients with schizophrenia.

During a patient's stabilization, the focus of treatment is on decreasing active symptoms or psychosis and minimizing side effects in patients. Many new approaches to caring for patients during the maintenance phase not only involve preventing relapse and managing side effects; they involve improving the patient's quality of life. The desired outcome is one that includes the patient's ability to establish and maintain healthy relationships, be free of psychotic episodes and experience relief from the impact of negative symptoms and mood instability.

Maintenance and relapse prevention that involves the use of any antipsychotic drugs is only successful if the drugs are taken as prescribed. Unfortunately patients with Schizophrenia often have difficulty with adherence to treatment because of poor judgment and limited insight. It is also understandable that schizophrenic patients are at times reluctant to take antipsychotic drugs because of the side effects that they experience, such as extrapyramidal symptoms, weight gain, and sedation. The amount of side effects experienced by a patient during the maintenance phase may be a predictor of adherence during therapy.

Managing prescribed drugs side effects effectively during the maintenance phase is essential to medication adherence since clinicians have limited resources related to medication compliance in the outpatient setting. Psychomotor side effects can hinder patients from taking ideal drug doses and side effects such as akathisia, which is an involuntary motor restlessness, can be particularly troubling to schizophrenia patients and decrease adherence. In Parkinsonism, the patient may present with shuffling gat, resting tremors, or psychomotor slowing. Fortunately the symptoms can be treated with the anticholinergic agent Cogentin. Tardive Dyskinesia (TD) is an involuntary muscle movement that appears after long-term antipsychotic medication use. Symptoms may include lip smacking, facial grimacing, jaw movement and movement in the extremities. Patients should be evaluated at each visit for development of TD, as TD can become permanent. If TD begins, the antipsychotic should be weaned down, stopped and the patient should be switched to another drug such as Cloziril or Seroquel that have a much lower risk of causing TD.

Several studies have shown that schizophrenic patients who experience such side effects have a worse outcome of treatment as compared to patients that do not experience side effects (Englisch & Zink, 2012). Side effects have the potential to undermine maintenance

antipsychotic drug therapy and therefore the clinician should be very diligent in watching for and treating such problems. Patients who experience serious side effects with typical antipsychotic drugs may have better results with atypical antipsychotic drugs, such as clozapine, risperidone and olanzapine, which studies suggest have a lower risk of causing extrapyramidal symptoms (Haddad, Das, Keyhani, & Chaudhry, 2012).

Psychomotor side effects are not the only side effects of concern during maintenance therapy. There are several other metabolic side effects of concern, such as orthostatic hypotension that generally occurs in the first few days of treatment. Antipsychotic drugs can also cause elevations in plasma prolactin concentrations. First generation antipsychotics, Risperdal and Invega have a tendency to cause this more than others and patients experiencing galactorrhea, sexual dysfunction or gynomastia should have their prolactin levels evaluated. If a patient's levels are found to be elevated, than changing to an alternate medication, or adding aripiprizole, which lowers prolactin, is recommended.

Another side effect of antipsychotic medications includes weight gain and fatigue. During long-term maintenance therapy many patients can experience weight gain in excess of 10% of their usual body weight. A gain in weight can predispose a patient to dyslipidemia, hypertension, diabetes and heart disease (Caemmerer, Correll, & Maayan, 2012; Hsu, Chien, Lin, Chou, & Chou, 2011; Hsu, Chien, Lin, Chou, & Chou, 2012). The sedative effects the antipsychotic medications have on schizophrenic patients can also increase the risk for weight gain because the patient will shy away from activities that will decrease their weight, as well as other hygienic, physical or social activities that may contribute to overall good health. Encouraging a healthy diet, exercise and weight loss can help to fend off these additional complications (Kreyenbuhl, Buchanan, Dickerson, Dixon, & Schizophrenia Patient Outcomes

Research Team (PORT), 2010). Patients that are obese or are concerned about weight gain may benefit form aripiprazole and ziprasidone, as they have a lower risk of weight gain in their side effect profile.

There is growing evidence that atypical antipsychotic drugs have superior efficacy for treatment of negative symptoms in both the acute and maintenance treatment settings. For example, Clozapine treatment has been associated with long-term benefits in patients' quality of life (Fakra & Azorin, 2012). Specifically, one study following schizophrenic patients treated with clozapine for six months showed improvements in social functioning, including work ability and interpersonal relationships (Fakra & Azorin, 2012). Although medication therapy is essential to the prevention of relapse and improving cognitive function of patients, it is not the only tool available for helping patients with the illness. Several psychosocial approaches have been shown to also help improve the quality of life for patients when combined with pharmacologic therapy.

**Psychosocial Treatment**

While psychosocial approaches have limited value for acutely psychotic patients, they may be useful for patients during the maintenance phase. When psychosocial treatments such as family therapy, social skills training and cognitive behavioral therapy are incorporated into a patient's treatment regimen, the likelihood of the patient's complying with treatment improves and thus their quality of life can improve as well. Psychosocial treatments can also alter the environmental stressors related to relapse, thus improving compliance with medication administration and the patient's quality of life.

The relationship between environmental stresses and a poor outcome in schizophrenia has been a topic of discussion for many years. After acute stabilization, many patients are often

discharged and sent back home to their families. Therefore, it is important that family members understand both the need for the treatment plan as well as the difficulties and problems associated with the illness. High levels of stress in the patient's family or "expressed emotion" (EE) have been linked to higher rates of relapse in patients (Amaresha & Venkatasubramanian, 2012). Behavioral interventions aimed at decreasing high levels of expressed emotion were found to be more effective than the general educational programs for patients and their families. Education and training, to include coping strategies and problem-solving skills, may help families deal more effectively with the patient. The goal of family therapy, which includes decreasing stress, increasing knowledge about the disease and learning effective coping strategies, has proven to be very effective in decreasing the rate of relapse in patients.

Psychosocial approaches to treatment may also be useful in enhancing the quality of life in schizophrenic patients. Social skills training techniques designed to help a patient complete everyday tasks can lead to feelings of independence, thus improving the patient's quality of life. Social skills training programs may also assist patients with improving social functioning by better managing stressors in their everyday life and increasing their social network. Social skills training may include vocational counseling, job training, problem solving, money management skills, use of public transportation, and social skills training. The focus of these programs is to help patients learn to interact successfully within the community. Social skills training programs can improve the symptoms and social functioning of a schizophrenic patient long after treatment is complete (Kreyenbuhl, Buchanan, Dickerson, Dixon, & Schizophrenia Patient Outcomes Research Team (PORT), 2010).

Cognitive behavioral therapy (CBT), which combines social skills training and behavioral management, focuses on correcting one behavior at a time. A patient that continues

to have a degree of psychosis, despite effective medication treatment, may benefit from CBT (Dixon et al., 2010; Jones, Hacker, Cormac, Meaden, & Irving, 2012). The focus of CBT treatment with schizophrenic patients is often related to decreasing the intensity of their delusions. Medication treatment can help to decrease the development of new delusions; however, strongly held delusions that were present prior to the initiation of medication therapy show little improvement with medication alone. The goal of the therapist conducting CBT is to gradually challenge the delusional belief and offer alternative interpretations, while at the same time providing the patient with behavioral techniques designed to help the patient cope with the stress related to the belief. Psychosocial approaches to treatment such as therapy, social skills training and CBT are extremely effective in dealing with some of the residual deficits that effect the patient. The combination of psychosocial interventions and community-based programs can offer the patients and their family valuable skills necessary to improving a patient's independence and occupational satisfaction.

**Community Based Treatment**

It is important to consider the role a community plays in effectively caring for patients with mental illness such as schizophrenia. Assertive community treatment and supportive employment can increase independence, improve social functioning, and increase job sustainability. Although there is a large body of evidence supporting the importance of community interventions, there is an argument about whether or not the programs are cost effective. Community interventions may be expensive, but they can provide an environment to support and holistically treat the patient and promote the patient's success in the community.

Assertive Community Treatment, or ACT, is community-based treatment that offers support to patients with severe chronic mental illness. The key principles of ACT are: (i) a

community based management system, (ii) a low patient to staff ratio, (iii) a mental health team approach and (iv) direct support with employment, relationships, residential independence, finances, health and well being. ACT is considered a "medically monitored non-residential service" that provides a consistently less restrictive environment for patients who suffer from frequent relapse and hospitalizations. Assertive Community Treatment is the standard model used to illustrate comprehensive care for patients with mental illness (Dixon et al., 2010). Unfortunately, despite the relative superiority of ACT compared to other social treatments, it is implemented relatively infrequently as communities continue to have a difficult time justifying the cost effectiveness of the program. In the future, in order to fully consider the true cost effectiveness of ACT, it will be important to include all cost related to severe mental illness including the fact that patients with schizophrenia have a reduction in life expectancy.

Evidenced Based Supported Employment gives people with mental illness an opportunity to work in a career field they are interested in, be paid competitively and take care of their mental health needs (Dixon et al., 2010). Supported employment is collaboration among employers, patients and a mental health care team. Several decades ago mentally ill patients were often advised to seek vocational or factory work. With supported employment patients have often found meaningful employment within their community. Today, with the assistance of a vocational counselor and a mental health care team, a patient can work with an employer to customize a job that meets the needs of the patient and the employer. If the employer is concerned about the employee's mental health, he or she can contact the mental health care team for assistance. This type of supported employment has allowed many mentally ill patients to experience meaningful work, increased independence and an improved quality of life (Dixon et al., 2010).

## Conclusion

Schizophrenia has been a part of all societies and regularly impacts approximately 1% of the world's population. The costs associated with treating schizophrenia are extremely high and without a clear understanding of how to stop the disease, it is estimated that the costs will continue to increase. Research is continuing to explore risk factors for the disease as well as dysfunctions in brain in an effort to both better understand and treat the disease. Currently medication treatment involving antipsychotics drugs is a substantial part of therapy. Coupled with psychosocial treatment, clinicians work to improve a patient's function in family and society. Community partnerships such as Assertive Community Treatment care models and supported employment appear to offer a patient more independence and an increased quality of life.

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