>Statement of Objectives

After reading this lesson you will be able to:

1. Understand the definition and prevalence of schizophrenia.
2. Explain the pathophysiology of this illness
3. Compare some pharmacological options and their role in the treatment of schizophrenia.
4. Identify potential causes of non-compliance and assist patients in overcoming these barriers
5. Understand the potential outcomes of pharmacotherapy and the prognosis of schizophrenia.

>Instructions

1. After carefully reading this lesson, study each question and select the one answer you believe to be correct. Circle the appropriate letter on the attached reply card.
2. Complete the card and mail, or fax to (416) 764-3937.
3. Your reply card will be marked and you will be advised of your results in a letter from Rogers Publishing.
4. To pass this lesson, a grade of 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies). (Note: some provinces require individual pharmacists to notify them.)

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SCHIZOPHRENIA: A REVIEW OF THIS COMPLEX DISORDER AND THE DIFFICULTIES ENDURED BY NON-ADHERENCE TO THERAPY

Artemis Diamantouros, B.Sc.Phm., M.Ed.

CASE PRESENTATION

Jim grew up in a middle-class family, was a good student and had many friends. At 17, he had his first girlfriend and got his first part-time job. His marks at school were strong. He was on the school hockey and baseball teams. As he prepared for university and the future, it became apparent that Jim just didn't have the interest to pursue his goals. His parents began to realize that something was wrong and decided to take him to see the doctor who recommended a referral to a psychiatrist.

The psychiatrist determined that Jim was experiencing psychotic symptoms. Jim spoke elaborately about the voices he was hearing and the people who were following him. The doctor told Jim and his parents that Jim was having a psychotic episode and that it could be part of an illness known as schizophrenia. The doctor recommended treatment with an antipsychotic medication.

Jim began treatment, albeit unwillingly. He didn't believe that he was ill. The medication made him feel sleepy, sluggish and gain weight. Before long, he stopped taking it. His symptoms returned and he eventually lost his job and began smoking and drinking.

Jim had a number of episodes and he had to be hospitalized because he wasn't able to care for himself. His parents tried to be supportive, but Jim began to integrate them into his delusions and could no longer trust them. Soon Jim was living in a group home, spending periods of time in hospital and on the streets. At the age of 32, Jim's diagnosis was clear, but he could not accept that he had schizophrenia. As schizophrenia took over Jim's life, he slowly lost the ability to care for himself and live independently. His mood began to drop, his memory was affected and the only way he could function in society was by taking his medication. However, he wasn't willing or able to take it. Jim's psychotic symptoms became less active but schizophrenia had led him to be alone in the world and it had taken over his life.

PREVALENCE

Jim's story is a common one. Schizophrenia affects 1 in 100 people and spares no class, race, sex or socioeconomic status.[1,2] Compared to other chronic illnesses, schizophrenia is twice as prevalent as Alzheimer's disease and approximately 60 times as prevalent as insulin-dependent diabetes, yet schizophrenia receives considerably less funding for research.[3]

Schizophrenia is a chronic, debilitating illness affecting both the mental and physical well-being of those whom it afflicts. Schizophrenia is also associated with high direct and indirect costs. It is estimated that the direct costs of schizophrenia, including hospitalizations, medical visits and medications are approximately $2.3 billion dollars a year in Canada.[4] Indirect costs of schizophrenia

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total approximately $2 billion annually and include social support, housing and lost work.[4]

RISK FACTORS

Although men and women are equally at risk for developing schizophrenia, differences exist with respect to the onset of the illness. While men often have their first psychotic break between the ages of 15 and 25, women usually present with symptoms between the ages of 25 and 35.[5]

The only identifiable risk factor with evidence to support its relationship to the development of schizophrenia is a positive family history. The risk is greatest among first-degree relatives of patients who suffer from schizophrenia. An identical twin of a person with schizophrenia has a 48% chance of developing the illness, whereas if a sibling has the illness, the risk is reduced to approximately 9%.[6] Having a first-degree relative with schizophrenia raises the risk to 9%, whereas having two first-degree relatives or an identical twin with schizophrenia raises the risk to 48%.[6] More recent research has also focused on the first "risk gene" found in the general population. This research, done at the University of Toronto, has identified that a variant of the Nogo gene may be responsible for causing an increased predisposition to the illness.[7] This finding may be useful in focusing research and development of medications whose target is outside the dopamine system and perhaps the gene.

WHAT IS SCHIZOPHRENIA?

Schizophrenia has been described in a number of ways including: "A complex medical disorder that affects speech, emotions, behaviour, and the way people think"; "A split between emotions and thoughts"; or "A disconnect between what's real and what's not real." No matter how it is defined, it is important to recognize that schizophrenia is not a disorder of multiple or split personalities but rather a disorder of thinking and perception.

Symptoms of schizophrenia are classified in four clusters: positive, negative, cognitive and mood symptoms. The positive symptoms are those with which schizophrenia is most commonly associated and include delusions (thoughts or beliefs that are not based on reality), hallucinations (overstimulation or pseudostimulation of the senses) and disorganized thoughts. These are the most obvious symptoms of schizophrenia and the most likely to respond to treatment. The negative symptoms of schizophrenia are those most likely to contribute to the social isolation seen with schizophrenia. These symptoms include affective flattening (lack of emotional expression), alogia (poverty of speech), anhedonia (loss of interest) and avolition (lack of motivation). The negative symptoms of schizophrenia, along with the cognitive symptoms (loss of attention, memory and executive functions), are the most debilitating. A predominance of these symptoms is associated with a poor prognosis. The final group of symptoms, often underdiagnosed in schizophrenia, involve mood. Dysthymia, hopelessness and suicidality are often untreated in those with schizophrenia. A combination of all these symptoms affects a person with schizophrenia in all aspects of life – work, interpersonal relationships, academic functioning and personal care.

The diagnosis of schizophrenia is made with caution and requires a longitudinal perspective. It is important to rule out psychotic symptoms as part of another illness such as mania or depression with psychotic features or schizoaffective disorder. It is also prudent to rule out drug-induced psychosis. Drugs and substances which can cause psychosis include cocaine, anticholinergics, cannabis and amphetamines. Before a diagnosis of schizophrenia, a number of factors are considered and based on the diagnostic criteria outlined in the DSM-IV$_{TR}$.[2]

The course of schizophrenia can be divided into three phases. The prodromal phase is recognized through a retrospective look at the person's functioning and is characterized as the beginning of deterioration of everyday function; the stage at which symptoms have not yet appeared. The deterioration of everyday function manifests as symptoms or behaviours such as social withdrdawal, loss of interest in school, friends and work, and deterioration of personal hygiene. This is followed by the active phase of the illness, also referred to as full-blown schizophrenia, where the patient experiences a waxing and waning vulnerability to psychosis. Finally, the residual phase is the point at which the patient's symptoms subside with age, as if the brain has "run out of steam."

Prognosis for a patient with schizophrenia is dependent on a number of factors. Despite adequate treatment, it is important to recognize that symptoms can persist. Approximately 40% of patients will continue to experience mild or moderate symptoms; 25% will experience a mild or moderate remission; and 25% will continue to have chronic or severe symptoms. In addition, 40% of patients will attempt suicide with 10% being successful.[8-10] Risk factors for suicide include high premorbid achievement and aspirations, young age, high IQ, command auditory hallucinations, akathisia (restlessness), recent discharge from hospi-

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REVIEWERS

All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

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tal, non-adherence to treatment and awareness of loss of functioning.[11,12]

Variables identified as leading to better outcomes in schizophrenia include good premorbid functioning, absence of a family history of schizophrenia, later age of onset, a greater number of positive (rather than negative) symptoms, high IQ, a stable family environment and being married.[11,12] Early intervention, the patient's responsiveness and adherence to treatment all contribute to a better prognosis for schizophrenia.[11,12]

WHAT CAUSES SCHIZOPHRENIA?

SCHIZOPHRENIA IS CAUSED BY A COMBINATION of biological, sociocultural and environmental influences. A number of biological theories have been proposed to explain the pathophysiology of schizophrenia. It has been found that patients with schizophrenia have abnormal blood flow within the brain, smaller temporal and frontal lobes and less gray matter.[12] Other theories have explored the possibility that an event during brain development may destroy significant amounts of neurons in the limbic system. Still others suggest that schizophrenia may result from prenatal exposure to certain viruses that come out of dormancy in the late teens or adulthood.[11,12]

The most commonly proposed biological theories of schizophrenia involve neurotransmitters, specifically dopamine. The traditional neurotransmitter theory, the dopamine hypothesis, proposed that dopamine neurons fire too often, transmitting the message that there is an increase in dopaminergic activity leading to transmission of too many messages which confuse the brain and lead to symptoms of the illness, specifically the positive symptoms.[11,12] This was then complemented by the hypofrontality theory which introduced the notion that dopamine transmission may be reduced or dysfunctional in the mesocortical area leading to negative and cognitive symptoms of the illness.[12] The most recent of the neurotransmitter theories attempts to amalgamate the previous theories and is known as the dysregulation theory which proposes that there is defective regulation of mechanisms responsible for neurotransmitter synthesis, release, reuptake, metabolism and receptor activity.[11,12]

TREATMENT OPTIONS FOR SCHIZOPHRENIA

NON-PHARMACOLOGICAL TREATMENT OPTIONS for the treatment of schizophrenia include case management, vocational training, family therapy and support groups. These options are integral in the treatment of schizophrenia but are considered adjunctive as they have not demonstrated efficacy in the treatment and prevention of psychotic symptoms.

There are two general categories of antipsychotics: conventional and second-generation agents.

Conventional antipsychotics or neuroleptics were designed based on the dopamine hypothesis and are non-specific selective dopamine blockers. The pharmacology of these agents can be understood by considering the role of dopamine in the different tracts or areas of the brain. Conventional antipsychotics block dopamine with varying potency to exert their beneficial effect (see Table 1). By blocking dopamine in the mesolimbic pathway, conventional antipsychotics are effective in treating the positive symptoms of the illness.[11,12] The side effects of the conventional antipsychotics are related to the blockade of dopamine in other regions of the brain. These agents block dopamine in the nigrostriatal pathway where dopamine is responsible for movement and cause extrapyramidal side effects including parkinsonism, acute and tardive dystonias and tardive dyskinesias. In the mesocortical pathway, dopamine blockade could potentially lead to worsening of cognitive symptoms; blocking dopamine in the tuberoinfundibular pathway can lead to hyperprolactinemia and thermal dysregulation.[11,12]

Despite these side effects, conventional antipsychotics still play an important role in therapy. Conventional or traditional antipsychotics are less expensive than newer medications and offer the advantage of a variety of dosage forms including rapid-acting and long-acting injections, oral tablets and oral solutions. These dosage forms give conventional antipsychotics a role in the treatment of patients who are acutely agitated or who are non-compliant with their medications.

The unattractive side effect profile of conventional antipsychotics, along with their lack of efficacy in the treatment of the negative, cognitive and mood symptoms of schizophrenia, prompted the need for new medications with a more selective receptor profile.

As a class, ***second-generation antipsychotics*** offer the advantage of dopamine blockade that is more specific to the mesocortical and mesolimbic pathways of the brain. As well, these agents are associated with a low ratio of D2:5HT2 blockade and have very low D2 blockade leading to minimal or no EPS.[13,14] Second-generation antipsychotics are now first-line therapy in the treatment of schizophrenia. If a patient does not respond to one atypical second-generation antipsychotic, another one can be tried because they are all structurally different. Second-generation antipsychotics are as effective as conventional antipsychotics in the treatment of positive symptoms and may offer a clinical advantage in the treatment of negative, mood and cognitive symptoms with new evidence emerging to suggest that some of these agents may even possess antidepressant properties.[15-17] The onset of action of these agents is approximately 4 to 6 weeks, but beneficial effects have been seen up to one year after treatment is initiated.[13,15] Despite their similarities as a class, differences do exist among second-generation agents and are worth exploring.

Clozapine was the first of the atypical antipsychotics. Originally produced in the 1960s, it was pulled from the market due to reports of agranulocytosis in the 1970s. The risk of agranulocytosis has been found to be between 0.5 and 2%. Clozapine was re-released with strict monitoring under the Clozaril Support and Assistance (CSAN) program.[18] Clozapine is the only second-generation agent to show efficacy in treatment-refractory schizophrenia as well as reduction in the risk of suicide in schizophrenia. However, its use is limited because of monitoring restrictions.[19-22] Compliance with clozapine therapy cannot be overemphasized. Evidence suggests that the risk of early relapse after stopping clozapine is significantly greater than with any other antipsychotic.[23,24] Because of the bothersome side effects (e.g. sedation, weight gain, hypersalivation) that patients experience on clozapine therapy, non-compliance is a high risk. Therefore, pharmacists can play a crucial role in

helping patients understand clozapine-related adverse effects and the importance of compliance.

Risperidone was introduced in the early 1990s. Risperidone is unique among the second-generation agents because of its dose-related D2 potency. At doses greater than 6 mg/day, risperidone tends to be associated with an increased risk for extrapyramidal side effects and hyperprolactinemia due to greater D2 receptor occupancy.[25] For these reasons, recommended doses of risperidone are lower than initially recommended. Risperidone has demonstrated efficacy in the treatment of a number of symptom clusters of schizophrenia. It has been shown to be effective in treating both positive and negative symptoms and there is more recent evidence suggesting that risperidone may also improve cognitive symptoms and have beneficial effect on mood symptoms.[26-28]

Olanzapine was designed to be structurally and pharmacologically similar to clozapine without the risk of agranulocytosis. It is a very effective antipsychotic but has been unable to achieve the efficacy in treatment-resistant schizophrenia for which clozapine is known. Olanzapine has been shown to be as effective as haloperidol in the treatment of positive symptoms.[29] Some trials suggest greater improvement in negative and cognitive symptoms associated with schizophrenia.[30] Contrary to the initial marketing of risperidone, initial dosing of olanzapine was suggested at 5 or 7.5 mg per day. Clinical experience and further investigation have demonstrated that olanzapine's antipsychotic effect is optimal at doses of 10 to 20 mg per day. The anticholinergic effects of olanzapine limit its use in the elderly and lower doses are recommended in this population.[31] For the elderly, dosing should be 2.5 to 5 mg. To help monitor compliance, olanzapine has also recently been released as a quick-dissolve tablet (Zydis® formulation) which dissolves on the tongue within 15 seconds.

Quetiapine is the fourth of the second-generation agents released to market shortly after olanzapine. Quetiapine has a greater affinity for 5HT2 receptors with a very low D2 receptor affinity.[32] As a result, quetiapine has a low risk for EPS. The specific role of quetiapine among the second-generation agents is difficult to determine because of the lack of long-term data and studies in subpopulations. Quetiapine doses were initially recommended at approximately 200 mg/day but more recent recommendations suggest that the antipsychotic effect is seen at doses of 600 to 900 mg/day. At these doses, the risk for orthostatic hypotension should be considered especially when a rapid titration schedule is initiated. Pharmacists can play an important role in identifying and preventing this drug-related problem. Quetiapine appears to be effective for the treatment of positive symptoms and has comparable efficacy to haloperidol.[33] The efficacy of quetiapine in the treatment of negative symptoms was demonstrated only with high doses (>360 mg/day) and there is no data with quetiapine in treatment-resistant schizophrenia.[34] As quetiapine is

TABLE 1 Pharmacological Options for the Treatment of Schizophrenia

TYPICAL ANTIPSYCHOTICS[11,12,61]

Potency	Examples of Medications	Usual Dose	Common Side Effects
High Potency	Haloperidol Trifluoperazine Fluphenazine	2-20 mg/day 10-80 mg/day 5-80 mg/day	High risk for EPS (tremors, rigidity, acute dystonia, etc.), prolactin elevation
Mild Potency	Perphenazine	10-64 mg/day	EPS side effects (akathisia, parkinsonism), drowsiness, some weight gain
Low Potency	Chlorpromazine	100-800 mg/day	Sedation, weight gain, orthostatic hypotension, prolactin elevation

COMMONLY USED DEPOT ANTIPSYCHOTICS[11,12,61]

Drug Name	Usual Dose Range	Usual Duration of Action
Flupenthixol Decanoate (Fluanxol®)	20 to 100 mg	2 to 4 weeks
Fluphenazine Decanoate (Modecate®)	12.5 to 100 mg	4 weeks
Haloperidol Decanoate (Haldol LA®)	50 to 300 mg	4 weeks
Zuclopenthixol Decanoate (Clopixol Depot®)	150 to 300 mg	2 to 4 weeks

SECOND-GENERATION ANTIPSYCHOTICS[16-34,61]

Drug	Usual Dose	Common Side Effects
Clozapine	Start at 25 to 50 mg/day and increase to a target dose of 150 to 450 mg/d (max 900 mg) BID to TID (to minimize side effects)	Sedation, weight gain, constipation, orthostatic hypotension, enuresis, hypersalivation seizures (risk is low and dose-related)
Risperidone	Start at 1 mg twice daily with a target dose of 4 to 6 mg/d OD to BID dosing	Nausea, headache, anxiety or agitation; dose-related EPS and prolactin elevation
Olanzapine	10 to 20 mg/d; 2.5 to 5mg in the elderly. Once daily (at bedtime)	Sedation, weight gain, dizziness
Quetiapine	Start at approximately 50 mg BID with a target dose of 300 to 800mg/day BID dosing	Dizziness, somnolence, dry mouth and postural hypotension

used in more patients at the higher therapeutic doses, its clinical efficacy in schizophrenia will be easier to evaluate. Currently, quetiapine is a good choice in patients with Parkinson's disease or in patients at high risk of EPS or TD (for example, the elderly) and for patients who do not tolerate or respond to other antipsychotics.[32]

New antipsychotics currently awaiting approval include ziprasidone and aripiprazole. In addition, medications such as benzodiazepines, antidepressants, anticonvulsants and lithium have been used as augmenting agents.[60]

NEW AGENTS, NEW SIDE EFFECTS

SECOND-GENERATION ANTIPSYCHOTICS HAVE provided tremendous benefit for patients by reducing the risk of relapse and hospitalization rates. In addition, these agents have led to improved quality of life, long-term course and reduction of cognitive impairment and functional deterioration. Second-generation agents are not, however, without their limitations. Many patients find the side effects of second-generation agents, such as weight gain, very troublesome and are non-compliant with their therapy. Weight gain and appetite increase were reported in 50 to 75% of patients treated with clozapine.[35-37]

Olanzapine is also associated with approximately 25% incidence of increase in appetite.[30] The risk of weight gain is higher in patients with lower BMI (<19) and most of the weight gain occurs in the first 38 weeks of treatment and then plateaus.[38,39] Significant weight gain (>20 kg) with olanzapine occurs in approximately 8% of patients and this rate increases to 40% in patients who experience weight gain of 10 to 20 kg.[38,39] The incidence of weight gain is lower with the other second-generation agents. A 7% increase in body weight is seen in approximately 25% of patients treated with quetiapine[40] and patients treated with risperidone experience low to moderate weight gain.[41] There is a high variability with respect to weight gain between individual patients and there still exists a lack of long-term data. The exact cause of weight gain has not yet been determined but is believed to be multifactorial involving blockade of H1 and 5HT2 or potential action on the hypothalamus.[41] Pharmacological intervention for the treatment of weight gain has not been thoroughly investigated. However, one small study has suggested a role for nizatidine in the treatment of weight gain.[46] Other agents currently being investigated for the prevention and treatment of weight gain include amantadine and topiramate. The results of this research will be important in the treatment of this bothersome and potentially hazardous side effect. It is important to educate patients about preventing weight gain. Monitoring waist circumference and BMI is recommended at baseline and then at regular intervals such as 1, 3 and 6 months.

Despite recent attention paid to the association between second-generation antipsychotics and diabetes, there is a lack of long-term studies investigating this association. Most available data is from poorly designed studies, case reports and industry databases.[43-47] When this data is compiled, the results are conflicting and it is difficult to draw any concrete conclusions. What appears to be clear is that there is reported hyperglycemia, glucose intolerance, new-onset or worsening of pre-existing diabetes with all of the second-generation antipsychotics. When evaluating the risk, it appears that there is a greater risk with clozapine, followed by olanzapine, then quetiapine and risperidone.[43-47] It is also important to consider that the diagnosis of schizophrenia is associated with a higher risk for diabetes and the Canadian Diabetes Association is considering adding schizophrenia to its list of risk factors for the development of diabetes. In light of this evidence, it is helpful to monitor at least fasting blood glucose at baseline and then every 6 months to allow for early detection and treatment.

Although the incidence of "conventional" side effects is lower with the newer agents, the risk of EPS and related effects still needs to be considered with some of the second-generation agents (not all). Elevated prolactin, in particular, is a side effect of concern because of the medical consequences in both men and women. Hyperprolactinemia can lead to hypogonadic states, galactorrhea, amenorrhea, sexual dysfunction, osteoporosis and mood, cognitive and behavioural problems. All of these side effects can lead to non-compliance and patients often do not feel comfortable openly discussing the exact cause of the non-compliance.[11] Of the second-generation agents, clozapine and quetiapine are considered to be prolactin-sparing drugs and olanzapine has been associated with dose-dependent elevation of prolactin.[48] Risperidone, however, has demonstrated persistent dose-dependent elevations in prolactin in up to 10% of women treated with the medication in some studies.[49,50] For this reason, it is important to monitor patients for any sign of prolactin elevation (e.g. amenorrhea in women, sexual dysfunction in men) and treat the patient appropriately.

COMPLIANCE AND SCHIZOPHRENIA

MEDICATION COMPLIANCE IS AN IMPORTANT part of the success of any illness treatment program. Compliance is of particular importance in psychiatric illness where it has been shown that as many as 50% of patients do not take their medications as directed. In schizophrenia, this percentage rises as high as 60 to 75%.[51,52]

Compliance was traditionally defined as "following the instructions of the health-care provider." This definition neglects the involvement of the patient in decision-making and the need to respect patient autonomy. A more suitable definition may be "the extent to which a person's behaviour coincides with medical advice regarding medication, lifestyle changes and referrals/return visits." Compliance may also be referred to as treatment adherence or cooperation. However it is defined, compliance is important for maximum therapeutic success, especially in an illness such as schizophrenia where pharmacotherapy is the only treatment that has demonstrated efficacy in treating psychotic symptoms and preventing future episodes.

A number of factors affect compliance in schizophrenia – insufficient understanding of potential therapeutic effects, lack of insight into the illness and side effects of antipsychotic medications.[53-55] In addition, it is important to take into account poor therapeutic alliance, social instability and an inappropriate health belief model, such as "one only takes medicine if one feels ill" on patient's compliance.[53-55] Insight is vital. Patients who do not perceive themselves as being ill are also likely to be non-compliant. Many patients with schizophrenia say they feel the need to take medications when symptoms are present (for example, hallucinations or

delusions) but do not feel the need to take the medication when these symptoms are gone.[56] Those who suffer from paranoid schizophrenia may feel that they are being "poisoned", therefore, non-compliance can lead to exacerbation of symptoms. Conversely, exacerbation of symptoms can also trigger non-compliance.[57] In some cases, non-compliance is an extension of the illness itself and may involve avolition or anhedonia, leading to a lack of interest in self-care and trouble with daily functions such as taking medication.

The high risk of substance abuse among patients with schizophrenia, its impact on the illness and compliance should not be underestimated. Up to 50% of patients with schizophrenia suffer from comorbid substance abuse.[62] Although it is not believed that schizophrenia is caused by illicit substances, they can act as a trigger for the initial episode of psychosis and can adversely affect the course of the illness as well as counteract the effect of the medication used for treatment. The most common substance used by people with schizophrenia is nicotine. Smoking rates among these patients are 2 to 3 times that of the general population. Many patients smoke to help relieve the symptoms of their illness. Although nicotine is not known to exacerbate psychotic symptoms, it can affect the clearance of some antipsychotic medications.[61] As well, smoking increases the health risks posed by some of the potential side effects of antipsychotic medications such as weight gain. Other substances such as marijuana, PCP, amphetamines and alcohol have an impact on the illness itself as well as compliance with treatment.

When considering factors that may impact compliance, it is important to remember that patients often misunderstand the physician or pharmacist's instructions about how to take the medication. A clear prescription label together with patient counselling can be vital. Have the patient repeat the information at the end of the session to ensure that they have understood your intended meaning.[58] Patients' forgetfulness with respect to taking medication can be tackled a number of ways. Try to ensure that the patient is on the simplest available regimen.[59] Recommend that the patient try to match medication doses to their daily regimen, for example, take once-daily medications after brushing their teeth every night or after meals. Packaging strategies can be used to help patients remember to take their medications. Pill boxes or dosettes are available in a variety of shapes and sizes and can be used to organize multiple medications making it easier to retrieve medications and serving as a reminder of whether the medication has been taken at a particular time. Many pharmacies are also able to provide blister-pack programs to patients. These are practical and useful for schizophrenic patients, especially if they are delivered on a weekly basis. Working with patients to identify what might work best for them is important in gaining an understanding of what might be causing their non-compliance.

Educating patients about side effects and their management can also help patients benefit optimally from the medication. Side effects should not be trivialized as this can have a strong impact on the pharmacist-patient relationship. Empathy is key in gaining their trust and strengthening this relationship.

Finally, it is important to consider the role of depot neuroleptics in the treatment of patients who are unable to take oral medications because of trouble with compliance. Currently, a number of conventional antipsychotics are available in depot formulations (see Table 1) and risperidone and olanzapine are in phase 3 clinical trials with their respective depots as well.

ROLE OF THE PHARMACIST

PHARMACISTS PLAY AN IMPORTANT ROLE IN THE care of patients suffering from schizophrenia. A trusting, therapeutic relationship with the pharmacist is an important component. Pharmacists can be a vital source of patient education and counselling around the diagnosis of schizophrenia. They can discuss the role and value of medication for patients, families, other health-care professionals and caregivers. Initial discussion with patients about side effects and management, as well as follow-up to assess tolerance to medication and the emergence of any new side effects are vital for optimal patient care. Community pharmacists often see patients more often than any other health-care professional. They play an important role in identifying early relapse and possibly saving the patient from the need for readmission to hospital. Some prodromal symptoms include poor sleep, poor hygiene, irritability, confusion and suspiciousness. Alerting the health-care team to these symptoms can help ensure that the patient receives appropriate treatment to prevent further deterioration. Strategies to overcome non-compliance should also be addressed with any patients who appear to be at risk or who are non-responsive to their treatment.

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QUESTIONS

1. The prevalence of schizophrenia is:
a) 1 in 1,000
b) 1 in 100
c) 1 in 10,000
d) 1 in 1,500

2. Risk factors for schizophrenia include:
a) Substance abuse
b) Family history of schizophrenia
c) Male gender
d) A and B

3. All of the following are considered negative symptoms of schizophrenia EXCEPT:
a) Anhedonia
b) Loss of executive function
c) Affective flattening
d) Alogia

4. Conventional antipsychotics block dopamine non-specifically; by blocking dopamine in the tuberoinfundibular region, they have the potential to cause:
a) Tremors and rigidity
b) Acute dystonia
c) Thermal dysregulation
d) Tardive dyskinesia

5. J.C. is an 18-year-old male who was admitted to the hospital after having his first psychotic break. J.C.'s parents had noticed that he was acting strangely for the last few months. His grades in school had dropped; he wasn't interested in hanging out with his friends any more; and he had been fired from his part-time job. Most of J.C.'s time was spent alone in the basement staring blankly at the TV. When it appeared that J.C. was responding to external stimuli, his parents brought him to the emergency department worried that something was wrong with their son.

J.C.'s social withdrawal, as well as his loss of academic and occupational functioning is most consistent with:
a) Prodromal phase of schizophrenia
b) Depression
c) Acute phase of schizophrenia
d) Residual phase of schizophrenia

6. As part of the initial screening for this patient, it would be important to include:
a) Complete blood count and electrolytes
b) Urine drug screen
c) Urine culture
d) Thyroid function tests

7. The most appropriate choice of medication treatment for J.C. would be:
a) Clozapine
b) Olanzapine
c) Perphenazine
d) Chlorpromazine

8. Second-generation antipsychotics as a class offer the following advantage:
a) High D2 blockade
b) Dopamine blockade specific to the nigrostriatal and mesocortical areas
c) Low ratio of D2:5HT2 blockade
d) Rapid dissociation from the serotonin receptor

9. The efficacy of second-generation antipsychotics as compared to conventional antipsychotics can be summarized as:
a) Equally effective for positive symptoms and negative symptoms, less effective for cognitive symptoms and mood symptoms.
b) Equally effective for positive, negative, cognitive and mood symptoms.
c) Equally effective for positive symptoms, more effective for mood and cognitive symptoms and less effective for negative symptoms.
d) Equally effective for positive symptoms, more effective for negative, cognitive and mood symptoms.

10. Clozapine was the first of the second-generation antipsychotics. It was pulled from market because of the risk of agranulocytosis which can occur with an incidence of:
a) 4%
b) 1%
c) 5%
d) 3%

11. Risperidone at doses greater than _____ loses its "atypicality" and begins to show some of the side effects of the conventional antipsychotics.
a) 4 mg
b) 10 mg
c) 6 mg
d) 8 mg

12. For the treatment of schizophrenia, an average dose of olanzapine would be:
a) 7.5 mg/day
b) 30 mg/day
c) 10 mg/day
d) 5 mg/day

13. Which of the following second-generation agents is most likely to cause prolactin elevation?
a) Risperidone
b) Olanzapine
c) Quetiapine
d) Clozapine

14. The propensity of second-generation agents to cause weight gain can be ordered as follows:
a) Clozapine>Risperidone>Quetiapine>Olanzapine
b) Olanzapine>Clozapine>Risperidone>Quetiapine
c) Risperidone>Quetiapine>Olanzapine>Clozapine
d) Clozapine>Olanzapine>Quetiapine>Risperidone

15. If a patient fails to respond to an adequate trial of risperidone, the next choice for treatment is:
a) Clozapine
b) Haloperidol
c) Modecate
d) Olanzapine

16. Despite adequate trials of and compliance with appropriate pharmacotherapy, what percentage of patients will continue to have severe or chronic symptoms?
a) 10%
b) 25%
c) 35%
d)40%

17. All of the following are considered variables that lead to a better prognosis in schizophrenia EXCEPT:
a) Stable family environment
b) Positive family history of schizophrenia
c) High IQ
d) Later age of onset

18. Adjunctive medications in the treatment of schizophrenia include all of the following EXCEPT:
a) Antidepressants
b) Antioxidants
c) Anticonvulsants
d) Benzodiazepines

19. Intentional non-compliance includes:
a) Stopping medication because of side effects
b) Forgetting to take medication
c) Not being able to afford medication
d) Not understanding the directions of how to take medication

20. The rate of non-compliance in schizophrenia is:
a) 25%
b) 60%
c) 15%
d) 85%

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Feedback on this CE lesson

1. Do you now feel better able to provide pharmaceutical care to patients with schizophrenia? ❑ Yes ❑ No
2. Was the information in this lesson relevant to your practice? ❑ Yes ❑ No
3. Will you be able to incorporate the information from this lesson into your practice? ❑ Yes ❑ No
4. Was the information in this lesson... ❑ Too basic ❑ Appropriate ❑ Too Difficult
5. Do you feel this lesson met its stated learning objectives? ❑ Yes ❑ No
6. What topic would you like to see covered in a future issue? _____

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