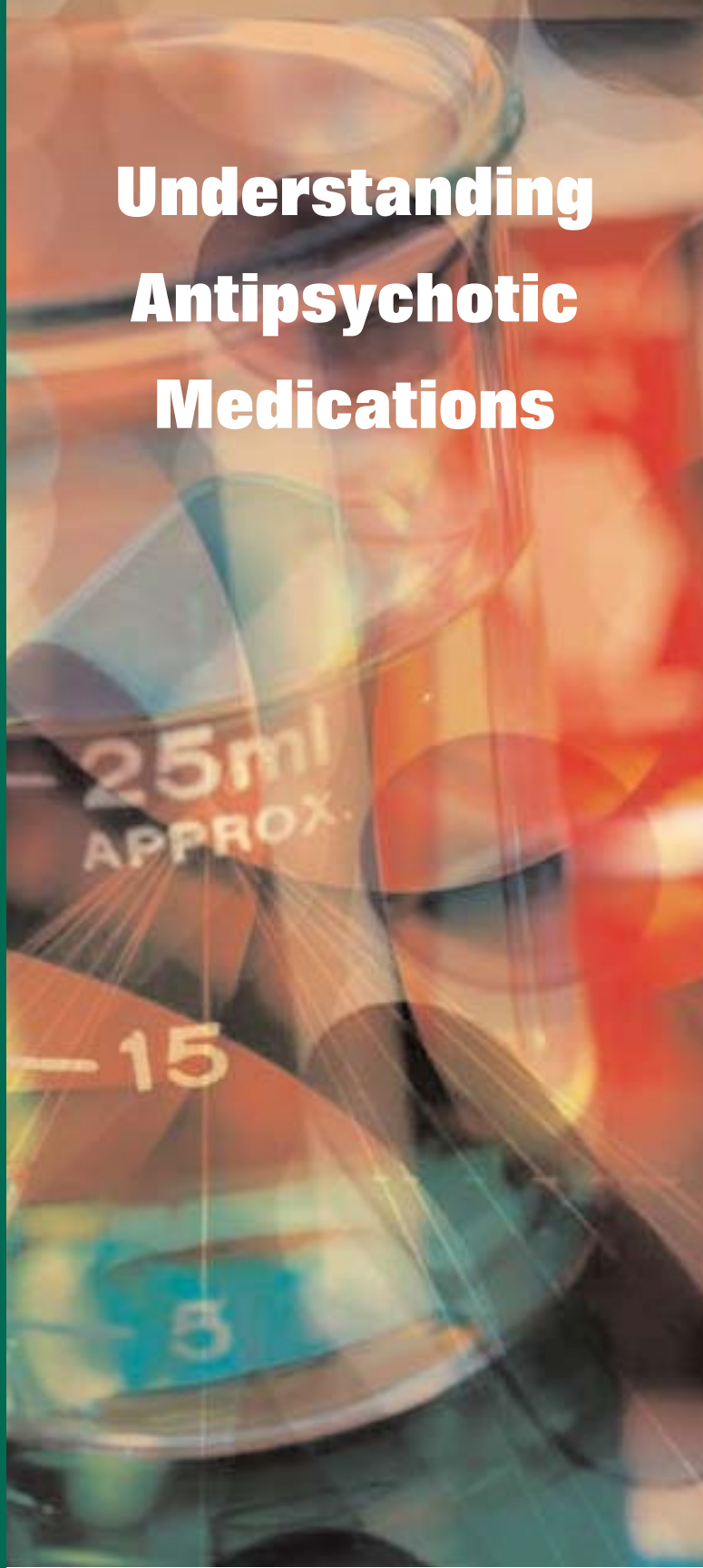
Understanding Antipsychotic Medications



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Antipsychotic Medications

Antipsychotic medications (also called neuroleptics) are mainly used in the treatment of severe psychiatric or neurobiological disorders. These medications first became available in the mid-1950s, and were used to treat people with severe psychiatric disorders that feature psychotic symptoms, such as schizophrenia spectrum disorders, delusional (paranoid) disorders, and other disorders with psychotic features, including psychotic depression. Psychotic symptoms often are characterized as losing touch with reality, and may include hallucinations, delusions, disorganized thinking or markedly disorganized behavior. Currently, antipsychotics are also used to treat some forms of dementia (including dementia associated with Alzheimer's Disease) and bipolar disorder (formerly known as manic-depression) with or without psychotic features.

Additionally, the newer antipsychotics appear to be helpful in the treatment of conduct disorder, personality disorders, autism, and childhood and adolescent psychosis. Researchers are exploring the use of antipsychotics with aggression, agitation, Attention Deficit Hyperactivity Disorder (ADHD), Posttraumatic Stress Disorder (PTSD), Borderline Personality Disorder (BPD), and behavioral disturbances associated with learning disabilities.

Talk with Your Doctor

Different antipsychotic medications—both traditional and atypical drugs—have different side effects. Additionally, an antipsychotic may be prescribed in conjunction with another medication/s and needs to be monitored closely. The team of clinicians involved with a person and his/her long-term care has an obligation to discuss the treatment plan and side effects associated with a medication with the individual. Because each person is different, it is important to understand each side effect so the individual and the care team can determine which antipsychotic medication is best. The adverse consequences of antipsychotic therapy must be considered in the overall rehabilitation, reintegration and recovery of those living with a severe psychiatric disorder. Active involvement in the treatment plan is a vital part of this process. Research and medicine now provide those living with neurobiological disorders with more treatment options than ever before. It is not advisable to discontinue treatment without consulting a doctor.

Because each person with a neurobiological disorder has a unique set of symptoms, no single medication works best for all individuals. A few people continue to have symptoms even when they take medications; however, even then symptoms may be less severe. Increasing the dose of the medication may interrupt a relapse. For many people, antipsychotic medications can decrease the risk that symptoms will return or reduce the severity of symptoms if a person has a relapse. Understanding the importance of medication and other options available is important for patients, family members and friends.

How Can Relapses Be Prevented?

The best way to prevent relapse is to take the prescribed medication. It is important to understand why a person might stop taking his/her medication. Unpleasant side effects are difficult to endure, especially when symptoms have decreased. Therefore, it is very important to find the most effective medication and proper dosage to control symptoms while minimizing side effects. Convenience is also important, as some medications need to be taken many times a day versus once a day. If medication compliance is a problem, it may be possible for an individual to receive monthly injections of long-lasting medication, which is referred to as depot medication.

Can Medications be Stopped?

Most people with a severe psychiatric disorder may need special medical care and medication for the rest of their lives. Antipsychotic medications do not cure these disorders--they only control the symptoms of the individual disease. If a person stops taking antipsychotic medication, he/she may experience a relapse. If a person taking an antipsychotic medication as an adjunct to another medication plans to discontinue use (such as is sometimes the case with bipolar disorder in which an antipsychotic may be used during a manic episode until a mood-stabilizing medication begins to work) it is important to do so in conjunction with a physician.

Side Effects

Antipsychotic medications are thought to work by changing the balance or activity of chemicals that transmit messages in the brain. There are two major types: **traditional antipsychotics** and **newer**, or **atypical antipsychotics**. The atypical antipsychotics seem to be somewhat more effective in addressing symptoms such as agitation, depression, lack of motivation, and energy level. The primary differences between the two groups are the side effects each group may cause, and the symptoms they tend to address.

—Anticholinergic Effects—

Drugs that block the action of the neurotransmitter acetylcholine have anticholinergic effects. Most of these drugs aren't designed to block acetylcholine; therefore, their anticholinergic effects are considered side effects. The most common include dry mouth, blurred vision, constipation, dizziness or an inability to urinate or loss of bladder control.

Sedation

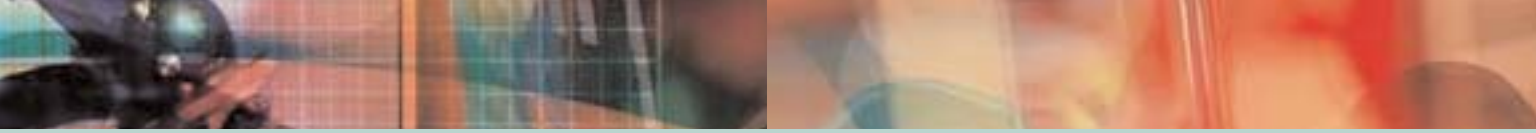
Sedation (drowsiness) is the single most common side effect of antipsychotic medications. Sedation occurs to some extent with all antipsychotics, but is usually experienced with low-potency agents. (If a drug is low potency, more of it is needed to relieve symptoms.) It can have therapeutic benefits for patients who experience agitation, but can be problematic if it causes extreme daytime drowsiness. Lowering the daily dose, consolidating divided doses into one evening dose, or changing to a less sedating medication can be helpful in these cases. Sedation is most pronounced during the initial phases of treatment; most people develop some tolerance as they continue taking a medication.

Seizures

Brain cells communicate by means of electric signals. Occasionally, there is an abnormal electrical discharge from a group of cells, and the result is a seizure. Antipsychotic medications can lower a person's seizure threshold—higher doses of medication are associated with a greater risk. Seizure rates are below one percent for most antipsychotic medications when taken within usual dose ranges, although those with a history of seizures have an increased risk. Treatment with the atypical antipsychotic clozapine is associated with a significantly greater risk of seizure. Prescription anticonvulsant medications can help to control many seizure problems associated with the newer, atypical medications.

Weight Gain

Many commonly prescribed antipsychotics can cause weight gain. Studies indicate that the older antipsychotic, chlorpromazine, and the newer antipsychotics, olanzapine and clozapine, are the



agents most likely to cause weight gain. Nutritional counseling, appropriate diet, and exercise can help patients to keep weight gain to a minimum. It is advisable to consult with a physician before starting a new exercise or diet regimen.

Elevation of Prolactin

Most, but not all, antipsychotic drugs increase the secretion of the hormone prolactin. In women, elevated prolactin levels may be associated with milk production, amenorrhea (suppression or absence of menses) and may affect interest in and enjoyment of sex, but do not occur in all women. Men may also have diminished interest in sex and may experience impotence if prolactin levels are raised. However, increases in prolactin levels related to antipsychotic medications are much smaller in men than in women. Additionally, high prolactin levels may cause osteoporosis (a condition of brittle bones which sometimes leads to fractures).

—Extrapyramidal Symptoms—

The neurological side effects of antipsychotic medications are often considered the most troublesome. Although all antipsychotic agents may cause nervous-system side effects, each differs in severity. Extrapyramidal symptoms (EPS) are perhaps the most serious of the neurological side effects and can develop within weeks of starting treatment with older antipsychotic medications. These side effects can be so unpleasant that they diminish the chances of compliance or continuation with medication, thereby increasing the chances for the illness to recur. EPS can be either chronic or acute. Chronic symptoms can occur after months or years of antipsychotic use, are not dose-dependent (related to the size of the dose of medication given) and may persist after medication is stopped. These symptoms include:

- ***Tardive dyskinesia*** (involuntary movements)
- ***Parkinsonism*** (tremors and rigidity)
- ***Akathisia*** (body restlessness)

Acute symptoms generally occur within the first few days or weeks of treatment, are dose-dependent and reversible upon dose reduction or discontinuation. These symptoms include:

- ***Acute dystonia*** (muscle contractions/twitching)
- ***Neuroleptic malignant syndrome*** (muscle rigidity, fever, rapid heart rate and difficulty breathing)

Although EPS are always an issue to be aware of for anyone taking an antipsychotic medication, studies suggest nearly two-thirds of all people taking older medications will experience EPS. Research also suggests that newer antipsychotics generally offer a milder EPS side-effect profile than the older medications.

Tardive Dyskinesia (involuntary movements)

One of the most common, potentially severe neurological side effects is tardive dyskinesia (TD) which is characterized by involuntary movements, most often affecting the mouth, lips, and tongue, and sometimes the trunk or other parts of the body. This chronic, potentially debilitating and irreversible movement disorder affects approximately 300,000 individuals treated with antipsychotic medications in the United States annually.

While the specific causes of TD are still unknown, antipsychotic medications are widely believed to be the primary factor in the development of the disorder. The majority of individuals who develop TD have mild symptoms, but approximately 10 percent develop moderate or severe symptoms. Studies show the newer, atypical medications are 5-10 times

less likely to cause TD than the older, typical antipsychotics. Additionally, schizophrenia may be associated with a risk of spontaneous TD. More research, however, is needed to fully understand the relationship between TD and antipsychotic medications.

A person may be more vulnerable to TD if he/she is older (particularly post-menopausal women), diagnosed with an affective disorder (particularly major depressive disorder), if there is a concurrent general medical disease or if high doses of antipsychotic medications are being taken. TD is usually managed or minimized by reducing the amount of the dose or by changing medications, as determined by a person's doctor. Because TD is a chronic disorder, in some cases, symptoms can persist following discontinuation of medication. Regular evaluations are critical in the management of TD.

Parkinsonism (tremors and rigidity)

Some individuals taking antipsychotics will experience symptoms that are characteristic of Parkinson's disease, including rigidity, tremors, temporary paralysis (akinesia) and extreme slowness of movement, including speech (bradykinesia). Up to 20 percent of those treated with antipsychotics experience these symptoms, which arise in the first few days or weeks of medication administration. It should be mentioned that akinesia and bradykinesia are features of medication-induced parkinsonism that have been noted alone or with other EPS in almost one-half of those treated with antipsychotics. Depressive symptoms can also be present in over 50 percent of persons with akinesia.

Generally, the symptoms of parkinsonism improve rather than worsen with a dose increase. This may be a result of an increase in the medication's effect on certain nerve cells and its ability to inhibit nerve impulses at higher doses. Medication-induced parkinsonism usually resolves after the medication is discontinued, although some cases of persisting symptoms have been reported.

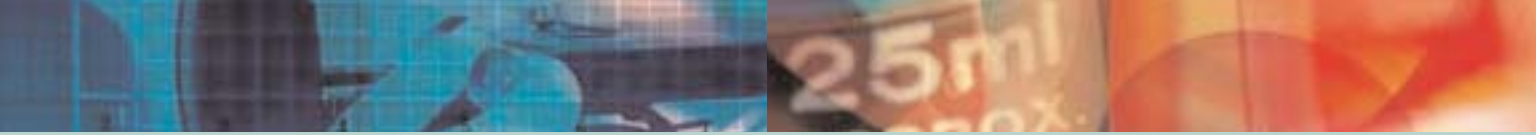
Akathisia (body restlessness)

Akathisia is a chronic EPS characterized by restlessness of the body and occurs in 20 to 25 percent of those taking antipsychotic medications. Those experiencing akathisia suffer from an inner sensation of restlessness and an irresistible urge to move various parts of their bodies. The most common form of akathisia involves pacing and an inability to sit still. This side effect is often extremely distressing and can lead to noncompliance with medication.

Akathisia is less responsive to treatment than parkinsonism or dystonia. A first step that may improve symptoms can be a slow reduction of medication dose. Doctors often treat akathisia, particularly if another EPS is present, with other types of medications, although these medications have limited efficacy.

Acute dystonia (muscle contractions/twitching)

Acute dystonia is characterized by the spastic contraction of muscle groups. These often painful reactions occur in up to 10 percent of those taking antipsychotic medications. Risk factors include age (youth), gender (males), use of high-potency medications, high doses of medications and intramuscular administration of the drug. Up to 90 percent of all dystonic reactions occur within the first three days of treatment. Reactions can occur in various body regions, but most commonly affect the neck, eyes and torso. These reactions occur suddenly, are dramatic in appearance, and can cause great distress. Acute dystonia can be effectively and rapidly treated with medication.



Neuroleptic malignant syndrome (changes in breathing and heart rate)

Neuroleptic malignant syndrome, an acute EPS, is characterized by rigidity, elevated body temperature and autonomic instability (abnormalities in heart rate, blood pressure, breathing or digestion). This condition can be sudden and unpredictable in its onset, is frequently misdiagnosed, and can be fatal if untreated. Although the prevalence is uncertain, neuroleptic malignant syndrome may occur in as many as two percent of those taking antipsychotic medications. Neuroleptic malignant syndrome usually occurs early in the course of treatment, often within the first week after treatment is begun or the dose is increased. Risk factors include age (youth), gender (males), preexisting neurological disability, physical illness, dehydration, rapid escalation of dose, use of high-potency medications and use of intramuscular injections.

If you believe you are suffering from any of these side effects, please see your doctor.

Traditional Antipsychotics

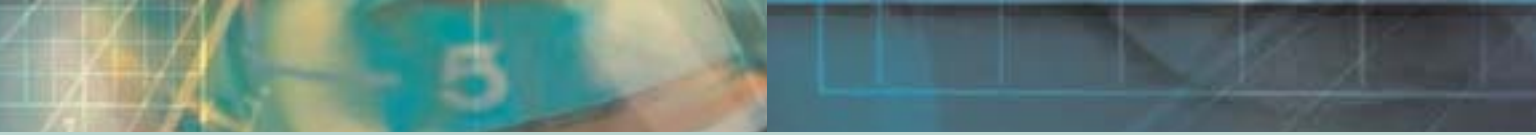
Traditional antipsychotic medications can control the psychotic symptoms of severe psychiatric disorders such as hallucinations, delusions, and disordered thinking very effectively. Researchers believe this may be explained by how these medications affect the brain chemical dopamine. Some believe that psychotic symptoms may be caused by too much dopamine in the brain, or by very sensitive dopamine receptors. One way of reversing the excess dopamine is to block the dopamine receptor, a protein on brain cells that signals the cell when dopamine is present. There are different subtypes of dopamine receptors that control normal brain functions, such as movement, emotions, behavior or appetite. Traditional antipsychotics seem to block a type of dopamine receptor called the type-2 receptor, which is important for emotions and behavior. However, because traditional antipsychotics are not selective (they block other types of receptors) they can interfere with normal functions. This explains many of the side effects observed in people taking these medications.

Traditional antipsychotics often do not improve symptoms such as depression and lack of motivation. This may be because brain chemicals other than dopamine control these symptoms. And though they have historically been used in the acute treatment of mania associated with bipolar disorder, there is limited evidence that they are effective during the maintenance phase (the period after an acute episode) of treatment. Most traditional antipsychotics appear to cause an elevation of prolactin, EPS, and anticholinergic effects. Some examples of traditional antipsychotics are **haloperidol (Haldol)** and **chlorpromazine (Thorazine).**

Atypical Antipsychotics

The newer atypical antipsychotics treat psychotic symptoms, and also address mania, agitation, depression, lack of motivation, and energy level. Generally these medications have milder side effects and are better tolerated than the older medicines. These medications block both dopamine and serotonin. They are more selective than traditional antipsychotics, working mainly on the part of the brain that causes psychotic symptoms but not the part that causes normal muscle movement.

Clozapine (Clozaril) is one of the newer antipsychotics. It is more selective for serotonin receptors, and has a lower effect on the dopamine type-2 receptors that are involved in brain functions such as movement. Therefore, clozapine is very effective in treating psychotic symptoms without causing



EPS, and does not appear to increase prolactin levels. It has also been useful in the treatment of bipolar disorder and other severe mood disorders. However, because it blocks many receptors in the brain in addition to dopamine and serotonin receptors, clozapine tends to cause other side effects, such as sedation and anticholinergic effects. In a small number of people, clozapine also causes significant weight gain, and can also lead to seizures or drooling. Clozapine has also been known to cause a significant reduction in the number of infection-fighting white cells in the blood (a condition called agranulocytosis). Because of this potentially dangerous complication, clozapine is typically reserved for individuals who have not responded to other types of antipsychotic medications, and requires that people taking this medication have blood tests once a week. It is not recommended as a first-line treatment, especially in the elderly.

Risperidone (Risperdal) is another newer antipsychotic. It is believed to block both dopamine and serotonin receptors and relieves psychotic, manic, and depressive symptoms. It is also used in treating dementia in the elderly (specifically psychotic features, agitation, and aggression). Like clozapine, risperidone is more selective for certain subtypes of receptors, and therefore has a reduced risk of EPS, anticholinergic effects, and sedation. It is safer than clozapine but tends to cause EPS at higher doses. It is therefore not recommended for elderly patients diagnosed with a certain type of dementia called dementia with Lewy bodies (DLB). Commonly experienced side effects may include anxiety, elevated prolactin levels and nausea.

Olanzapine (Zyprexa) is similar to clozapine. It is effective for psychotic, manic and depressive symptoms and has a low risk of EPS. Olanzapine is now used as a first-line pharmacological treatment for mania in bipolar disorder, either alone (in less severe cases) or in combination with the mood stabilizers lithium or valproate (which may also each be used alone as first-line treatments). Research indicates that an intramuscular injection of olanzapine helps treat agitation in schizophrenia, bipolar disorder, and dementia. Additionally, at lower doses it may manage agitation and psychotic features associated with dementia in the elderly. Olanzapine can cause some sedation, anticholinergic effects, and can cause weight gain. It has been associated with only a small or temporary rise in prolactin levels. Like clozapine, olanzapine blocks many receptors in the brain in addition to dopamine and serotonin.

Quetiapine (Seroquel) also blocks a variety of receptors but is more selective for serotonin receptors than dopamine receptors. It is more selective for receptors in the part of the brain responsible for psychotic symptoms and has minimal effect on muscle tone. Quetiapine is effective against psychotic, manic and depressive symptoms. Quetiapine appears to have a low risk of EPS and a low risk of elevating prolactin levels. Side effects may include dizziness, postural hypotension, dry mouth and dyspepsia. The incidence of somnolence (drowsiness) in clinical trials was 18% versus 11% for placebo. Somnolence may actually help elderly patients with dementia who exhibit disturbed sleep-wake cycles or evening agitation.

Ziprasidone (Geodon) is a dopamine and serotonin antagonist (a drug that binds to a receptor and produces an action) with the highest effect on serotonin receptors compared with dopamine receptors. The drug is also a moderate inhibitor of norepinephrine and serotonin reuptake, which increases these chemicals in the brain. These qualities are associated with a low risk of EPS and improvement in depressive symptoms. Research also indicates that ziprasidone may be helpful in treating acute mania associated with bipolar disorder. Ziprasidone does not seem to affect weight levels, but has been associated with abnormalities in the electrical properties

of the heart, which could cause cardiac arrhythmias. Research indicates that intramuscular injections of ziprasidone can control agitation in patients with schizophrenia and schizoaffective disorder.

Aripiprazole (Abilify) affects different subtypes of serotonin and dopamine receptors. The medication aims to reduce hyperactive dopamine neurons that mediate psychosis while at the same time enhancing underactive dopamine neurons that have an effect on depressive and cognitive symptoms. The most commonly reported side effects are anxiety, insomnia, nausea, and mild akathisia. Aripiprazole is associated with minimal weight change, minimal EPS and a modest difference in sedation compared to placebo.

What is the Outlook?

Advances in medications over the last several decades have improved the outlook significantly for people with neurobiological disorders. Currently, important breakthroughs are leading the way to a better understanding of the brain as scientists continue to search for the biological origins of brain disorders. Research is crucial in furthering these advances. Additionally, public education is imperative, as it serves to combat stigma and preconceived notions about these disorders. Through research and education, NARSAD continues to offer hope by providing insight into potential causes, improved treatments and eventual cures for the severe neurobiological disorders.

NARSAD is a national, not-for-profit organization whose primary objective is to raise funds for research to find the causes, cures, better treatments, and ways to prevent the severe mental illnesses.

Founded in 1985, NARSAD represents a unified commitment for the support of research by the members of the country's largest mental health organizations: National Alliance for the Mentally Ill, national Mental Health Association, National Depression and Manic Depressive Association, and the Schizophrenia Research Foundation.

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