Antiparkinson agents are used primarily in the treatment of Parkinson's disease, which is a neurologic disorder that is characterized by tremors, slow movement, a masklike face, rigidity, stooped posture, and drooling. In psychiatry, these agents are used to treat neuroleptic-induced movement disorders. Neuroleptics are older antipsychotic medications that induce neurologic side effects that frequently cause movement disorders known as extrapyramidal syndromes (EPS). Neuroleptic-induced EPS include parkinsonism, dystonia, and akathisia. Drug-induced parkinsonism, as the name implies, has symptoms that mimic primary Parkinson's disease. Dystonia is an adverse reaction induced by antipsychotic medications that is manifested by a sudden spasm of the tongue, jaw, neck, and muscles of the eye. Although not an allergic reaction, it can be very frightening for the patient. Dystonias may be treated and rapidly reversed with an injection of benzotropine or diphenhydramine. Akathisia, another form of EPS, is an inner-driven restlessness caused by antipsychotics. It is described as a feeling of nervousness, with the need to pace and the inability to sit still, muscular discomfort, and agitation.

The antiparkinson medications used for EPS include anticholinergic agents (benztropine, biperiden, procyclidine, and trihexyphenidyl); diphenhydramine, an antihistamine; and amantadine.

How do these medications work? Movement disorder, whether caused by Parkinson's disease or neuroleptic medications, may be exacerbated by excessive activity of the cholinergic system because dopamine, a neurotransmitter, is diminished in certain areas of the brain. Anticholinergic medications oppose the action of the cholinergic system (i.e., are anticholinergic), facilitating the balance between the cholinergic and dopaminergic systems. Diphenhydramine, although an antihistamine, may work by a similar mechanism because it also possesses anticholinergic activity. Amantadine, however, is not an anticholinergic drug and works in ways that are different from anticholinergic agents. Its effect may be achieved by its ability to increase dopamine levels. The advantage of amantadine is that it does not have the side effects of anticholinergic agents, a benefit for the patient who cannot tolerate anticholinergic side effects.

The commonly used antiparkinson medications are listed above by their generic and brand names. Amantadine, benztropine (oral), diphenhydramine, and trihexyphenidyl are available in generic preparations as well. Benztropine (Cogentin) and diphenhydramine (Benadryl) also come in injectable forms for intramuscular administration. Moreover, diphenhydramine has antihistamine activity with a sedative property, and the drug is prescribed commonly for allergies and insomnia.
HOW THESE MEDICATIONS ARE PRESCRIBED

Benztropine is the anticholinergic drug most commonly used for treating neuroleptic-induced parkinsonism and acute dystonia, although other anticholinergics are equally effective. Amantadine is effective for parkinsonism but usually not for acute dystonia. For akathisia, although a trial of an anticholinergic medication or amantadine is reasonable, these agents are generally not effective. A different treatment strategy is usually needed for treating akathisia.

For treatment and prevention of EPS, benztropine (0.5–2 mg two times a day), trihexyphenidyl (2–5 mg three times a day), diphenhydramine (25–50 mg three to four times a day), biperiden (2 mg one to three times a day), procyclidine (5 mg two to three times a day), or amantadine (100–200 mg two times a day) are usually effective. For treatment of an acute dystonic reaction, usually 1–2 mg of benztropine or 50 mg of diphenhydramine, administered in a single intramuscular injection, is effective for aborting the reaction.

Antiparkinson medications are commonly prescribed for prophylaxis (prevention) of EPS with the older, conventional antipsychotics, because these antipsychotics are associated with a high incidence of EPS. The newer, atypical antipsychotics (e.g., olanzapine) have a very low incidence of EPS, and antiparkinson medications may not be needed until EPS occur. The question whether prophylaxis is needed with antipsychotics, and for how long, continues to be debated. Many physicians favor prescribing an anticholinergic agent with conventional antipsychotics, especially with the high-potency agents such as haloperidol. They maintain that prevention of EPS, especially dystonia, is crucial for patients to adhere to their treatment.

PROPER USE OF YOUR MEDICATION

Storing Your Medication
- Keep your medication in a tamper-resistant vial and out of reach of children.
- Store your medication so as to keep it from excessive heat, moisture, and direct light.
- Keep your medication in its original prescription vial with the label intact to prevent others from taking the medication inadvertently.

Taking Your Medication
- Take your medication as instructed by your physician. Do not abruptly stop taking your medication without consulting with your physician. Abrupt discontinuation of anticholinergic agents may result in unpleasant withdrawal symptoms, including irritability, nausea and vomiting, headache, and insomnia. Although anticholinergics are not indicative of addiction, gradual tapering of dosage may be needed before discontinuation of these agents.
- If you miss a dose, take it as soon as possible. However, if it is near the time of your next dose, skip the dose you missed and go back to your regular dosing schedule, but do not double-up the dose.
- You may take your medication with or without food. If the medication upsets your stomach, take it at mealtime.

Use of Alcohol and Other Medications
Patients should refrain from consuming alcohol while taking antiparkinson medications. Some side effects, such as drowsiness and dizziness, may be exacerbated when these medications are combined with alcohol.

Certain medications, including over-the-counter medicines, may interact with the antiparkinson drugs. The drug interaction may lower the blood level of the affected drug and decrease the drug’s effectiveness; or, it may elevate the blood level of the affected drug and cause toxicity. Some medications (e.g., tricyclic antidepressants) have anticholinergic action and may exacerbate the side effects of antiparkinson agents. Inform your physician of all the prescription and over-the-counter medications you are taking. If you have questions about your medications, consult your physician or pharmacist.
POSSIBLE SIDE EFFECTS

In the area of the brain where anticholinergic action is desired, the patient derives therapeutic benefits, but in other areas of the body where such action is undesirable, side effects may occur. Since the cholinergic system is widely distributed throughout the body, anticholinergic agents may interfere with those body functions regulated by the cholinergic system. These side effects are known as anticholinergic side effects.

Patients should also be aware that other medications they take may have anticholinergic activity. For example, diphenhydramine (Benadryl), an antihistamine commonly used for allergies and sleep, also has anticholinergic activity.

Possible anticholinergic side effects are as follows:

- Drowsiness and sedation
- Feeling of “spaciness”
- Confusion and memory impairment (especially for the elderly)
- Blurred vision
- Decreased salivation and dry mouth
- Decreased sweating
- Decreased bronchial secretions (exacerbation of asthma and other lung diseases)
- Palpitations
- Constipation
- Delayed or retrograde (flowing backward) ejaculation
- Urinary hesitancy or retention

**Warning:** These medications may cause drowsiness and dizziness. Exercise caution when engaging in daily activities that require mental alertness, such as operating a motor vehicle. It is recommended that you do not engage in hazardous tasks until you are reasonably certain that your medication does not adversely affect your performance or impair your judgment.

POSSIBLE ADVERSE REACTIONS

- **Seizures.** Amantadine should be used with caution in patients with a history of seizure disorder. Seizures have been reported in patients who were taking amantadine.
- **Heatstroke.** Anticholinergic agents may diminish sweating and compromise the body’s ability to dissipate heat. With exposure to hot weather, patients may be susceptible to heatstroke. Elderly patients are especially susceptible. Patients taking large doses of anticholinergic medication and patients taking more than one medication with anticholinergic activity may also be susceptible to heatstroke.
- **Delirium.** Excessive anticholinergic activity, especially from overdosage, may result in a toxic brain reaction known as delirium. Delirium is diagnosed by the manifestation of symptoms that include impairment of consciousness with inability to focus or sustain attention, tremors, loss of coordination, restlessness, agitation, and inability to control urination. If left untreated, delirium may be fatal.

   Elderly patients have a higher risk for developing delirium. Other predisposing factors include patients with brain damage, diabetes, alcohol dependence, and malnutrition. In these patients, when a anticholinergic agent is used, lower dosages should be prescribed, especially when the medication is used in combination with other medications with anticholinergic activity.
PREGNANCY AND BREAST FEEDING

Diphenhydramine is classified in Category B of the U.S. Food and Drug Administration (FDA) Pregnancy Risk Categories, whereas amantadine, benztropine, biperiden, procyclidine, and trihexyphenidyl are in Category C. Diphenhydramine did not show any evidence of fetal risk in animal studies, whereas amantadine, benztropine, biperiden, procyclidine, and trihexyphenidyl showed positive evidence of fetal risk. However, there are no clinical studies with antiparkinson agents in pregnant women, and the data are insufficient, to determine the risk during pregnancy. Antiparkinson agents should be used during pregnancy only if the benefits outweigh the potential risk.

Small amounts of amantadine are excreted in breast milk, but it is not known if the other agents are. Women who take antiparkinson medications should not breastfeed.

If you have any questions about this handout, please consult your physician.