

## Primer for Prescription Medicines: The Medicines for Side Effects—Part One

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Psychotropic medicines—like all medicines—can potentially produce side effects. Most side effects are mild, but some can be serious, even life threatening. Most physicians define medication side effects as *undesirable* experiences or conditions produced by a medicine. An example might be drowsiness, caused by an antidepressant, in a patient who is already sleeping too much. The same effect in someone who is sleeping too little may not be called a side effect by this definition, especially if the drowsiness is at bedtime (although some would say this is still a side effect, but a “desirable” one). Some side effects manifest at a physiological distance from the target organ or system, e.g., nausea caused by SSRI antidepressants. Some side effects are related to dosage and can be improved by decreasing the amount of the offending medication, although this risks decreasing that medication’s effectiveness. Other side effects are related to a given class of medications and may occur regardless of dose. Some side effects, like tardive dyskinesia (a movement disorder) go unnoticed by the patient, at least in the early stages, although others who are around the patient will notice them. These can be monitored by various screening tools for extrapyramidal syndrome. Others, such as agranulocytosis (a decrease in certain white blood cells that are important to the body’s immune response), are never noticed directly by the patient, so patients must be screened for them periodically via blood tests. Certainly, not all side effects can be treated by additional medication. Sometimes one must stop the offending medication, lower its dose, or change the accompanying medications (if any), which can affect the body’s breakdown or storage of the side-effect-producing medicine by raising the relative blood level. However, some medicines causing side effects work well and are too vital to stop. In such cases, one may add

another medicine to decrease the side effect or the distress it causes.

Of the side effects for which adding another medicine may help, let’s begin with the extrapyramidal side effects, sometimes called “EPS.” EPS was a bigger problem when only typicals like chlorpromazine (Thorazine) or haloperidol (Haldol) were available for psychosis. But EPS can occur even with some newer atypical antipsychotics; this is especially true when they are used at the higher end of their therapeutic range. EPS may also occur with some antidepressants, and there are case reports of effects like EPS with the SSRIs. Of course, any discussion of brain mechanisms is subject to change with new data, but most studies to date have pointed to dopamine receptor blockade in a brain area called the substantia nigra and its surrounding neural pathways as the likely cause of, or at least a contributor to, EPS.

EPS can be subdivided into dystonias, pseudo-parkinsonism, and akathisia. The dystonias are severe muscle spasms that usually put some part of the body into an abnormal position. Oculogyric crisis, for example, deviates the eyes, and torticollis positions the head oddly through neck spasm. Pseudo-parkinsonism is named for its mimicry of Parkinson’s disease symptoms—tremor at rest, impaired gait, mask-like facial expression, drooling, and other more subtle symptoms. Finally, there is akathisia, which is a subjective feeling of restlessness and an inability to sit still. Each of these conditions can be caused by other factors, but when a patient is taking a medicine known to cause them, one should at least consider the possibility that a side effect is occurring. EPS may be treated using anticholinergic medicines, such as benztropine (Cogentin) or trihexyphenidyl (Artane), both in the oral dose range of 1 to 2 mg taken 1 to 3 or more times a day; an injectible antihistamine like diphenhydramine (Benadryl), which is usually given at 25 to 50 mg intramuscularly; or a medicine such as amantadine (Symmetrel), for which the actual mechanism is not yet known, although it may increase levels of dopamine. Amantadine’s usual oral dose is 100 mg once or twice a day. For akathisia, it is also possible to get relief by adding a beta-blocker, for example propranolol (Inderal), generally starting at an oral dosage range of 10 to 20 mg taken 2 to 4 times per day. A benzodiazepine such as alprazolam (Ativan), beginning with 1 or 2 mg twice a day or so, also may be used, although it can be habituating (patients may require higher doses over

time and could have withdrawal symptoms if the medicine is discontinued abruptly). Even benztropine and diphenhydramine, which are routinely used for EPS and are not addicting, may still be abused (intentionally taken in too high a dose, or too often, or both) by some patients because of the “effects” they cause (described as a “buzz” by some patients, or sedation, respectively).

Medicines used for side effects may have side effects of their own. Some common side effects for anticholinergics are dry mouth, constipation, and urinary hesitancy, whereas amantadine may produce nausea, dizziness, and insomnia. They can also worsen psychosis, which is often the primary condition being treated. Diphenhydramine can cause dry mouth and nose, among other side effects. The beta-blockers can cause blood pressure or heart rate to drop, yielding possible dizziness or falls. The benzodiazepines, diphenhydramine, and others also bring risks for over-sedation.

Another side effect sometimes treated using anticholinergics such as benztropine is sialorrhea, the excessive salivation that may occur with clozapine (Clozaril), but sialorrhea is not a form of EPS. A routine side effect of the anticholinergics—dry mouth—can treat another medication’s side effect, excessive salivation.

(NOTE: All medication dosage ranges cited in this article are generally those recommended for young to middle-aged, otherwise healthy, adults. Lower doses and slow titration upward as needed would be necessary for children, older adults, or anyone who has liver, kidney, or certain other diseases in addition to the psychiatric disorder for which they are being treated.)

## References

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