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MEDICAL MEMO

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What Is an Antipsychotic?

What are they used for?

Antipsychotic medications were invented to treat psychosis. Psychosis means "out of touch with reality" and typically includes hallucinations, delusions, and severe often bizarre or very paranoid thinking disorders. Generally people experiencing psychosis have schizophrenia, psychotic depression, or bipolar disorder (manic depression), but may have drug or medicine toxicity or withdrawal, may be reacting to a catastrophe (brief reactive psychosis) or may have a brain injury or disorder like dementia or delirium, or have certain other severe health conditions. Antipsychotics were discovered in the 1950's and were first used to treat forms of schizophrenia, psychotic depression, and bipolar disorder. They are often very helpful.

Over the last 40 to 50 years we have learned antipsychotics, like other medicines, may help some other conditions as well. Used alone or in combination with other treatments, antipsychotics are effective for nausea and vomiting (e.g. Compazine), are good sedatives, help sleep, calm agitation and irritability, help impulsive aggression, anger, rage, and temper, treat Tourette's syndrome, suppress tics, help the behavioral problems associated with head injuries, and may help autism and related conditions, etc. Antipsychotics are sometimes used as boosters to make other medicines more effective in obsessive compulsive disorder, some depressions, and other conditions where thinking, compulsive behavior, or impulsive behaviors are problems.

Atypicals are often very helpful medicines in treating behavioral and neuro-psychiatric complications of Alzheimer's disease and other dementias. At least Zyprexa and Risperdal of the newer "atypical" antipsychotics also work as mood stabilizers and may treat or help treat even non psychotic Major Depressions.

The "atypicals" are Clozaril (clozapine), Risperdal (risperidone), Zyprexa (olanzapine), Seroquel (quetiapine), Geodon (Ziprasidone), and Abilify (ariprazole). Clozaril is used least despite excellent benefits because it has some quite troublesome side effects. Abilify, the newest, is actually a "third generation" antipsychotic known as a "dopamine system stabilizer" which means it focuses its dopamine blocking more loosely and primarily on the targeted thought disorder sites in the brain and not on the movement sites thereby lessening those side effects.

There are two main groups of antipsychotics - typical and atypical.

Atypical means not typical. All antipsychotics decrease action of the neurotransmitter dopamine in the brain. Atypical antipsychotics (called "atypicals" for short) also partly decrease the action of serotonin. This double, or dual, action gives atypicals their broader benefit and changes their side effect patterns, generally for the better.

My medicine chart on Antipsychotics, page 1, gives useful information about the typical antipsychotic group including names, doses, common side effects, pros, and cautions. Some common and useful typicals include Haldol, Thorazine, Moban (the least likely to increase weight), Orap (pimozide - often the best for tics and Tourette's) and several others.

The updated medicine chart Antipsychotics, page 2 provides the same categories of important information about the atypical antipsychotic group. Atypicals are newer, still under patent, and are much more expensive than the typicals, but are usually preferred due to their broader benefits and substantially reduced rate of short and long term "extrapyramidal" side effects. Another advantage of the atypicals, unlike typicals, is they help not only the obvious schizophrenia symptoms of hallucinations, delusions, and severe thought disorder but also better reduce so called "negative" symptoms of apathy, poor motivation, and alienation from society and also help mood. Unfortunately, some atypicals (Zyprexa, Risperdal, and sometimes Seroquel) may cause weight gain, increase the risk of diabetes, may raise cholesterol and triglyceride levels, and may sedate patients.

The two main advantages of the atypicals over the typicals is the broader range of diagnoses and symptoms they treat and their greatly reduced, though not zero, risk of causing extrapyramidal symptom (EPS) side effects. Short term reversible EPS include parkinsonian symptoms (looks like but isn't Parkinson's disease), akathisia (internal restlessness), acute dystonic reactions (scary intense muscle tightness but often easily treated), and related effects. These short term reversible EPS side effects can be reduced or cured by changing the antipsychotic medicine dose, changing the antipsychotic medicine, stopping the antipsychotic, adding a medicine like Cogentin (benztropine), Artane, benadryl, amantadine or a beta blocker to counteract the EPS.

Tardive Dyskinesia (TD) is a possibly ireversible EPS movement disorder long term side effect. The primary risk is from long term (usually years, rarely , if ever, less than six months), high dose treatment with the older typical antipsychotics which are also known as neuroleptics. The risk of TD is essentially zero for low dose short term (weeks to months) use. The risk of TD with the old typical group is about 5% per year (this means about 5 of every 100 persons who takes an average dose of one of these medicines for a year will show some TD

at the end of that year). Risk increases with age (especially in women), dose, duration, and being nonwhite. The newer atypical antipsychotics have a much lower risk, estimated at roughly 0.1% to 0.5% per year (1 to 5 in 1000 will show TD after a year). Risperdal and Geodon are probably close to the 0.5% risk while Seroquel, Zyprexa, and Abilify are at the 0.1% level. Clozaril may even treat or reverse TD. Antidepressants, anti-anxiety meds, sleeping meds, mood stabilizers, and stimulants do not carry any TD risk at all. TD is a group of abnormal movements that typically start mildly with subtle involuntary snake like (choreo-athetoid) and/or chewing-like frequent movements of the tongue and mouth and may progress, especially with continued use of the medicine, to affect the arms, legs, and other parts of the body in severe cases.

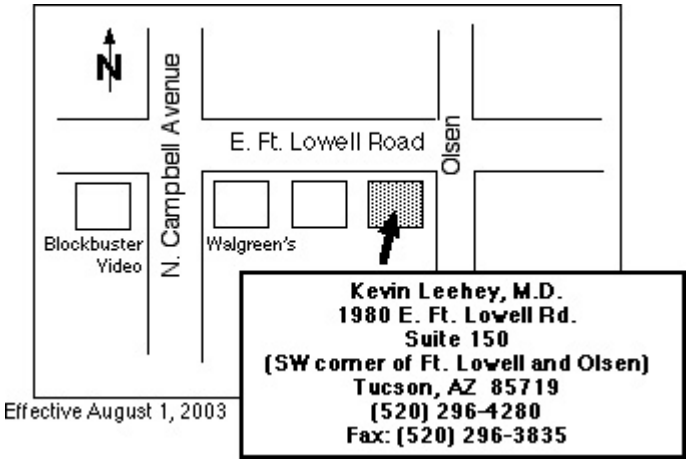
TD may be very mild to severe and disabling with the degree usually related to the dose and duration of antipsychotic medicine exposure. TD symptoms are not always caused by medication. Abnormal movements indistinguishable from TD occur in some people with other neurologic conditions, some people with schizophrenia, and even in some elderly persons, even without any treatment ever with an antipsychotic medicine. About 1/3 of TD cases believed to be caused by antipsychotic medication recover completely without any special treatment. Another 1/3 improve with time and treatment but not fully. The final 1/3 do not improve or recover and may progress. The best treatment for TD is using Clozaril or high dose vitamin E; other options exist but are less consistently helpful or are experimental.

Prevention of TD is the best treatment. My patients who take the antipsychotics become very used to the modified AIMS testing I do at a number of the follow-up visits. They are most aware of the finger tapping and tongue examination but are less aware of the way I watch them walk, sit, stand, and how I look for other subtle early signs of Tardive Dyskinesia. I am also watching and listening for signs of the fully reversible and fully treatable false parkinson's, acute dystonia, and akathisia.

Although not yet certain, it appears the chances of the allergic like uncommon neuroleptic malignant syndrome (NMS) is rare with atypicals. The greatly reduced risk of all EPS, especially TD and NMS, is my favorite advantage of the atypicals and makes the often impressive benefits and advantages of this family of medicines more available for more situations and more patients with far less risks than before. Risperdal and Zyprexa are the 2 most tried and true atypicals for both adults and kids. Seroquel is an alternative with more moderate sedation and weight gain. Geodon has the least sedation. Geodon and Abilify have the least or no weight gain. Risperdal and less so Geodon can increase the hormone prolactin which can lead to breast engorgement and discharge. Geodon has a tendency to mildly slow heart conduction but this is rarely a problem. No atypicals require regular

blood or other special testing and generally are easy to give. Once daily dosing is common, with Geodon and Seroquel more often given twice a day. All work rapidly, often the first day or in the first week. I have seen many situations where an atypical antipsychotic medicine, especially Risperdal or Zyprexa, has rapidly prevented or stopped a potentially dangerous situation that would have likely otherwise gone on to hospitalization, arrest, or serious harm. So which is best? As usual, that depends on matching the medicine to the patient, the target symptoms, what effects are wanted and what effects are not wanted. Abilify, with its low EPS and very low TD risk, its moderate sedation, no problematic prolactin or heart effects, little to no weight gain, and good benefit is becoming, although the newest, a top choice.

In summary, the new atypical antipsychotics are wonderful additions to our treatment options. They are often rapidly helpful in crisis situations where other lesser options have failed. I particularly like them for extreme impulsive aggression and rage. Low to moderate doses are usually enough. They are quite safe and easy to use. Although the risk of Tardive Dyskinesia makes them "big guns" the risk of TD is zero on a short term basis. They are also easier and safer to use than other "big guns" like Tegretol, Depakote, Lithium, and the older typical antipsychotics. It is important to remember that we don't often use antipsychotic medicine for aggression unless the situation is severe, other attempts have failed, and they won't be kept unless they are very helpful. Then we can decide how long to keep them at a more leisurely pace after things are calmer.



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