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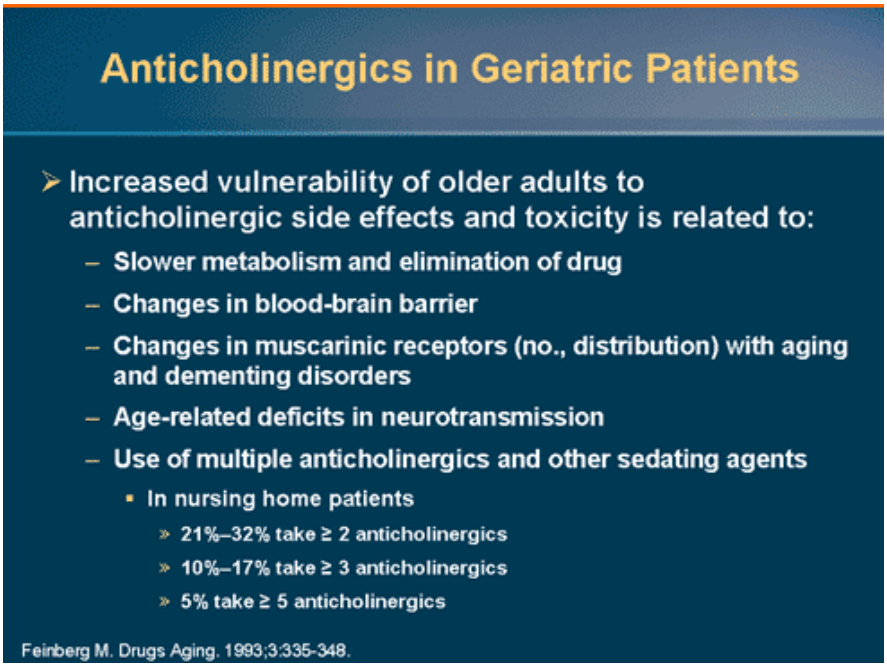
Cocktail of Popular Drugs May Cloud Brain

By RONI CARYN RABIN

Many people are unaware that dozens of painkillers, antihistamines and psychiatric medications — from drugstore staples to popular antidepressants — can adversely affect brain function, mostly in the elderly. Regular use of multiple medications that have this effect has been linked to cognitive impairment and memory loss.

Called anticholinergics, the drugs block the action of the neurotransmitter acetylcholine, sometimes as a direct action, but often as a side effect. Acetylcholine is a chemical messenger with a range of functions in the body, memory production and cognitive function among them.



The difficulty for patients is that the effect of anticholinergic drugs is cumulative. Doctors are not always aware of all of the medications their patients take, and they do not always think to review the anticholinergic properties of the ones they prescribe. It's a particular problem for older patients, who are more vulnerable to the effects of these drugs and who tend to take more medicines over all.

Now a spate of new research studies has focused on anticholinergic medicines.

After following more than 13,000 British men and women 65 or older for two years, researchers found that those taking more than one anticholinergic drug scored lower on tests of cognitive function than those who were not using any such drugs, and that the death rate for the heavy users during the course of the study was 68 percent higher.

That finding, reported last July in The Journal of the American Geriatrics Society, stunned the investigators.

“So far we can’t tell why they are dying, but it wasn’t because they were sicker or older,” said Dr. Malaz A. Boustani, director of the Wishard Healthy Aging Brain Center and a scientist at the Regenstrief Institute, both in Indianapolis, who was one of the paper’s authors. “We adjusted for age, gender, race, other medications they were taking, other diseases and social status. We adjusted for everything we could, and that signal did not go away.”

He added: “These are very, very common drugs. That’s the scary piece.”

Dr. Chris Fox, a senior lecturer at Norwich Medical School at the University of East Anglia in England and the paper’s lead author, said he and his colleagues suspected that anticholinergics take a toll on bodily organs and systems like the cardiovascular system, although there are no studies confirming this.

Anticholinergics have also been implicated in the delirium that intensive-care patients frequently develop in the hospital. “Clinicians don’t think of them nearly as often as they should as a potential cause of cognitive problems,” said Dr. Wesley Ely, a professor of medicine at Vanderbilt University who studies neuropsychological deficits that occur after intensive care hospitalization.

Of the 36 million Americans 65 and older, at least 20 percent take at least one anticholinergic medication. A study by Dr. Boustani of nearly 4,000 older adults in Indianapolis found that those who had been using three or more possibly anticholinergic drugs consistently for 90 days or longer were nearly three times as likely to receive a diagnosis of mild cognitive impairment as those who had not taken anticholinergics.

“If you were taking one of the drugs we know is definitely an anticholinergic for 60 days, you doubled the odds of developing mild cognitive impairment” compared with a patient taking no anticholinergic medicines, Dr. Boustani said.

No association was found between chronic use of anticholinergics and dementia, however, even though mild cognitive impairment often precedes dementia. Dr. Boustani said the reasons for this were not clear.

The aim of studies like these is to evaluate the magnitude of the effects of different drugs, to determine whether there are safe thresholds for their use and to learn whether the effect is transient and reversible. Still, there is already a consensus in the scientific community that anticholinergic compounds should be prescribed with caution, especially for the elderly.

“There’s not much doubt about this,” said Dr. William Thies, chief medical and scientific officer for the Alzheimer’s Association, adding that studies from large clinics that treat

people with memory disorders have shown that up to 25 percent of the patients who seek help have reversible disorders, including those caused by polypharmacy — taking a combination of medications, some of which may have anticholinergic activity.

Still, Dr. Thies said, “it would be unfair to suggest that this is the cause of a great deal of cognitive impairment in our society.”

Even so, why do physicians prescribe any medications with anticholinergic activity to elderly people, who may be using them regularly for many years? Not only are doctors often unaware of all the medicines their patients are taking, but the list of drugs with anticholinergic properties is a long one.

The heart drug digoxin, the blood thinner warfarin, the painkiller codeine and prednisone are considered mild anticholinergics. Those with the most severe effects include Paxil, Benadryl, a drug for overactive bladder called oxybutynin, and the schizophrenia drug clozapine.

“People are worried, but we’ve gotten pushback from some physicians who say, ‘Great, thank you, but what do we do? We’ve got to use these pills,’ ” Dr. Fox said.

So what’s a patient to do?

If you or an elderly relative take one or more drugs on a regular basis, ask your primary care physician to evaluate the cumulative anticholinergic burden of all them (as well as other potential interactions and side effects).

“The patient is critical in triggering that kind of discussion,” Dr. Thies said. “It may not be automatic, but if in fact the patient asks for it, it’s much more likely to be done.”

Remember to tell your physician about drugs prescribed by other specialists, as well as nonprescription or alternative medicines you take. He or she should be able to prescribe substitutes without anticholinergic effects. This review should be done once a year. Do not stop medications on your own without medical supervision.

Even before going to the doctor, do your own research. Use the Anticholinergic Burden scale, developed by scientists from the Regenstrief Institute, to assess your risk. The scale ranks drugs based on the strength of their anticholinergic activity, from zero if there is no effect to 3 for severe effect.

Keep in mind that many over-the-counter drugs, including allergy medications, antihistamines and Tylenol PM, have anticholinergic effects. “Don’t overreact to your cold,” Dr. Boustani advised. “Try Grandma’s remedy for a couple of days before you ramp up to Advil PM or Aleve PM.”

For people with an overactive bladder, he suggested, “try scheduled toileting or bladder exercises before jumping to medicine.”

There may be no adequate substitutes for some essential anticholinergic drugs. In that case, Dr. Fox said, “We’re saying, ‘O.K., but you can’t take one or two others that also have the effect.’ ”