

## Hospital Discharge Rife For Adverse Drug Events

*Have patients bring a list of their medications, match the drug with the condition, and get rid of the rest.*

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SEATTLE — Nursing home patients have a higher rate of adverse drug reactions than is sometimes seen in intensive care units, and many of these events occur right after the patient gets out of the hospital, where medication regimens generally get changed, Joseph T. Hanlon, Pharm.D., said at the annual meeting of the American Geriatrics Society.

Studies suggest that up to 50% of persons in a nursing home have some kind of adverse drug event every 6 months, and while many of those are relatively minor events, they can be serious. Older persons have a fourfold higher risk of hospitalization from an adverse drug reaction than younger people, said Dr. Hanlon, a professor of pharmacology and geriatric medicine at the University of Pittsburgh.

“Medication-related adverse patient events are really common and a major source of morbidity in older people,” he said.

Adverse drug reactions can and do occur at any time. But one study found that 20% of elderly persons had an adverse drug reaction in the first month after hospitalization, with most of those events caused by a prescription that was new to the patient.

Moreover, in his own study of 808 elderly patients discharged from 1 of 11 Veterans Affairs hospitals, Dr. Hanlon found that one-third of the patients had an adverse drug event, and most of those events occurred within 3 months of the

hospitalization. Forty percent of the events were preventable, his study concluded.

“The point is, going to the hospital is a bad thing,” Dr. Hanlon said. However, the research is not very clear on what can be done to reduce adverse drug events in the elderly, Dr. Hanlon said. Most trials have looked at using a geriatrics team or a pharmacist to review medications. One randomized, controlled study found that pharmacist review cut adverse drug events 32%. But most of the other studies have found that while that type of approach may improve the quality of prescribing, it has not shown a reduction in adverse events.

Clearly, the complexity of the drug regimens that elderly people are put on is partly to blame, and in the U.K., pharmacists review a patients’ medications every year in order to prune unnecessary or redundant medications, Dr. Hanlon said.

In Australia, the medical schools have started teaching medical students simple pharmacotherapy about of the most commonly used drugs and five basic things they need to know about each one.

“I haven’t heard much about us embracing that in the [United States], and I think that is an area that we need to move forward on,” he said.

Dr. Hanlon said when he talks to physicians, he recommends they take the simple step of having patients bring in a list of their medications for review, matching each of the drugs to their conditions, and getting rid of what is not needed.

That step can actually solve two-thirds of the medication problems, he said. ■

## Protein C Is Linked to Cognitive Impairment Following ICU Stay

SEATTLE — Low protein C levels appear to be associated with the cognitive impairment many patients have after a stay in the intensive care unit, according to a study of 46 patients conducted 3 months after they left the hospital.

“We believe low protein C levels in critically ill patients predict long-term cognitive impairment,” said Dr. E. Wesley Ely, of the department of medicine at Vanderbilt University, Nashville.

“The reason we think it is relevant is that there are different lines of intervention we could use for our elderly patients who do develop sepsis,” he said at the annual meeting of the American Geriatrics Society.

Protein C is a vitamin K-dependent plasma protein that, when activated by thrombin, inhibits the clotting cascade, and therefore is able to turn off coagulopathies like those seen in sepsis patients and others in the ICU.

The study found that 23 patients with long-term cognitive impairment, of 46 patients who had been mechanically ventilated in an ICU, had a mean protein C activity 28% lower than those patients who did not have cognitive impairment after their stay.

The patients came from a larger study of patients on mechanical ventilation during an ICU stay, during which the patients had plasma drawn. Dr. Timothy D. Girard, this study’s primary investigator, went to great lengths to find and perform cognitive tests on as many of those patients as possible 3 months later, even going so far as to track them down to trailer-home parks hundreds of miles away, Dr. Ely said.

The initial study enrolled 113 patients, of whom 77 survived to discharge. Another 11 patients died before 3 months.

Of the remaining 66 patients, half of whom had had sepsis, 46 were given a battery of tests.

“It’s about as high a follow-up as you are going to be able to get in a study like this,” he said.

The battery of neuropsychological tests administered to the patients took about an hour and a half to complete, and measured nine domains of cognitive function.

And the criteria for cognitive impairment used by the investigators was fairly stringent, to exclude deficits not clearly caused by the ICU experience, Dr. Ely said. The amount of impairment allowed in the study would have been readily apparent in the patients before their stay.

The investigation also involved assessing levels of D-dimer, plasminogen activator inhibitor-1, and von Willebrand factor, none of which differed between the two groups.

The difference in protein C was such that a decrease of 1 natural log equated to a 6-point drop in the neuropsychological score. And, a 6-point drop is “a big deal,” Dr. Ely said.

“With a 6-point drop, you are taking yourself down by nearly a standard deviation. This is a situation where people can have trouble finding their car in a parking lot or balancing a checkbook.”

The most striking and common deficits seen the study were in executive function and memory.

Previous cohort studies done at Vanderbilt have suggested that cognitive impairment following an ICU stay is quite common, occurring in between 50% and 66% of all elderly patients, Dr. Ely noted. ■

## ACE Inhibitors May Slow Mental Decline, Early Data Show

SEATTLE — Angiotensin-converting enzyme inhibitors that cross the blood-brain barrier slow mental decline by about 50% relative to the decline seen in patients on other antihypertensives, according to an observational study of 1,074 hypertensive subjects followed for a median of 6 years.

“If there is an indication for an ACE inhibitor, we might as well use one that crosses the blood-brain barrier,” Dr.

Kaycee M. Sink, principal investigator, said at the annual meeting of the American Geriatrics Society.

Hypertension itself is a risk factor for dementia, so it is important to know if an antihypertensive treatment has the ability to cut that risk, said Dr. Sink of the division of geriatrics at Wake Forest University, Winston-Salem, N.C.

Previous trials of treatment have had

mixed results. But in animal studies, the ACE inhibitors that cross the blood-brain barrier have been shown to halt cognitive decline at doses below what would be used to control blood pressure.

Those studies were the basis for the current investigation, Dr. Sink explained.

Her group looked at patients enrolled in the multicenter Cardiovascular Health Study, selecting out those patients who had hypertension and

took an antihypertensive, and those who did not have dementia at baseline. The mean age of the patients was 78 years.

The aim was to look at the incidence of dementia. There were 158 subjects diagnosed with dementia over the average 6 years of follow-up. But the only effect by type of antihypertensive the patient was exposed to was a slightly higher risk in those who took an ACE inhibitor that

did not cross the blood-brain barrier, with about an 18% higher risk than that seen in the subjects on other antihypertensives.

However, when the investigators looked at the subject scores on the Modified Mini-Mental State Exam, they did find a difference.

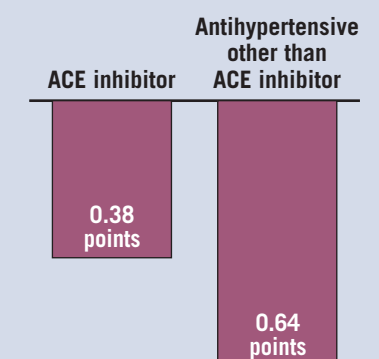
The group of patients on an antihypertensive other than an ACE inhibitor had a mean decline in exam scores of 0.64 points per year. Those on an ACE inhibitor had a mean decline of 0.38 points per year.

But the patients on an ACE inhibitor that crossed the blood-brain barrier accounted for almost all of that difference in decline. They had a mean decline of 0.32 points per year.

The ACE inhibitors that do not cross the blood-brain barrier are enalapril, benazepril, moexipril, and quinapril. The others are “centrally active,” Dr. Sink said.

It is thought that the centrally active ACE inhibitors might protect from de-

### Mean Annual Decline of Scores on the Modified Mini-Mental State Exam



Note: Based on a study of 1,074 hypertensive patients followed for a median of 6 years.  
Source: Dr. Sink

dementia and mental decline by decreasing oxidative stress and inflammation in the brain, she noted. ■