Identifying drug-related illness in the elderly

by Robert E Vestal

Since geriatric patients take more drugs than younger ones, it's not surprising they suffer more adverse effects. But how do you differentiate an adverse effect from another disorder that may mimic it?

Identifying adverse drug reactions in the elderly can pose a special challenge.

Multiple illness is the rule, rather than the exception, among geriatric patients, and with multiple illness come multiple medications and the possibility of confusing dosages and drug interactions.

Many geriatric patients see more than one doctor and may be taking two or more drugs of the same type or with similar side effects.

Antidepressants, antipsychotic agents, antihistimines, and nonprescription "cold" remedies and sedative preparations, for example, all have anticholingergic properties.

The effects, which may be additive, produce dry mouth, blurred vision, constipation, urinary retention, and neuropsychiatric symptoms.

Taken injudiciously, over-the-counter drugs by themselves may create problems; elderly people, more so than younger patients, are apt to rely on them as cure-alls for transient symptoms whose basis they don't understand.

Finally, we doctors may fail to diagnose drug-related illness in elderly patients, since the symptoms often mimic other disorders that we associate with the aging process — forgetfulness, weakness, confusion, tremor, anorexia, and anxiety. **(Table 1).**

Why are they vulnerable?

Though the potential for adverse drug reactions varies among aged individuals, certain age-related somatic and physiologic changes that affect drug distribution, hepatic metabolism, and renal excretion dictate that we rule out toxicity in symptomatic geriatric patients.

Drug distribution. Distribution, the process by which drugs are delivered to various sites in the body, depends on the proportions of body fat, total body water, and lean mass.

Again, there are variations; total body water, both in absolute terms and as a percentage of body weight, is usually reduced in elderly people, while body fat tends to increase.

The effect of these changes is to reduce the proportion of lean body mass per unit of total body weight. Such changes may affect blood levels of geriatric patients taking drugs regularly, especially obese and emaciated patients.

In the former, the capacity to store lipid-soluble drugs, such as barbiturates, increases and may result in a longer effect and greater risk of toxicity as drugs administered at the usual dosing intervals accumulate.

In emaciated patients, with reduced total body water, such water soluble drugs as antipyrine and ethanol can concentrate at toxic levels.

In addition, albumin levels are reduced in elderly persons. For drugs that are protein-bound, the reduced albumin results in an increase in the amount of free drug concentrate in the plasma and subsequent diffusion into body tissues where sites of action are located or into the liver and kidneys for elimination.

This is particularly true when renal failure results in low protein binding of a drug such as phenytoin. Even though the total plasma level may be in the low therapeutic range, a considerable amount of free drug may be available.

Increasing the dosage could result in an adverse reaction. **Table 2** lists therapeutic levels of drugs. Levels above this range can cause toxicity.

Hepatic metabolism. Liver mass represents 2,5 percent of body weight until middle age, when it becomes relatively and progressively smaller. Studies indicate that the decrease in size is accompanied by altered metabolic capacity for some drugs, which, in turn, results in a prolonged half-life and the possibility of drug accumulation and toxicity.

Renal excretion. Renal function decreases as much as 50 percent from ages 20 to 90, with an average

decline of about 35 percent. Thus, drugs that are eliminated by the kidneys, such as digoxin and the aminoglycosides, may reach toxic levels in the presence of reduced renal function.

Nutrition and environmental factors. In addition to age-related physiologic changes, the geriatric patient's nutritional status may affect drug metabolism. With some drugs, such as antipyrine and theophylline, a low-protein/high-carbohydrate diet is associated with a longer half-life. Because of socioeconomic circumstances, many elderly people have nutritionally poor diets. *Although overt protein malnutrition is relatively uncommon, look for signs of vitamin deficiency as an indication that the geriatric patient may have problems in drug metabolism.*

Take a drug history

Often, it is not physiologic or metabolic changes that account for toxic reactions in elderly patients, but simply the fact that they're taking too much of a drug or too many drugs. *Always review a geriatric patient's drug history when he comes in with a complaint. Think about possible adverse reactions and question the patient to determine if his symptoms coincide with a drug reaction.* While a printed form may do for younger patients, the elderly patient may need some memory jogging, so it's best to conduct the history on a face-to-face basis. The patient may forget the name of a drug — if, in fact, he ever knew it — but he'll be able to tell you about his "high-blood-pressure pills" or "those pills I bought at the chemist for my constipation."

It may be necessary to have a relative confirm the report. Find out what prescription drugs the patient is taking, what the dosage is, and how long he's been taking the drugs. If the patient or his relative cannot remember what drugs were prescribed by another physician, have your assistant phone the doctor's office.

Find out *when* the patient takes his medication. Is he following the prescribed regimen, or does he take his pills all at once? Ask about nonprescription medications.

Again, the patient may not be able to remember specific names, but

DRUG ILLNESS IN THE ELDERLY

TABLE 1

DRUG ALERT
These drug groups most frequently cause adverse effects in geriatric patients

Drug group	Presenting symptoms that suggest toxicity
CARDIOVASCULAR AND RESPIRATORY DRUGS	
Cardiac glycosides	Fatigue, weakness, anorexia, palpitations, visual complaints, psychic disturbances such as bad dreams, agitation, fainting, pseudohallucinations
Diuretics	Urinary retention or incontinence, joint pain suggestive of gout, weakness, fatigue, dizziness, fainting, skin rash
Antihypertensive agents	Headache, palpitations, nausea, dizziness or lightheadedness, nasal congestion, drowsiness, skin rash, dry mouth, fever, jaundice, depression
β-adrenoceptor blockers	Dyspnea due to heart failure or bronchospasm, hallucinations, nightmares, insomnia, fatigue, depression, fainting, dizziness
Antiarrgythmic drugs	Diarrhea, nausea, vomiting, anorexia, skin rash, joint pain, fever confusion
Anticoagulants	Bruising, bleeding, rash, rarely GI disturbances such as anorexia, nausea, vomiting, or diarrhea
Bronchodilators	Nausea, vomiting, palpitations, tremor, anxiety
DRUGS ACTING ON THE CENTRAL NERVOUS SYSTEM	
Analgesics	Drowsiness, confusion, delusions, hallucinations, nausea, vomiting
Sedative-hypnotic and anxiolytic agents	Restlessness to frank psychosis, drowsiness, confusion, ataxia, impairment of memory, reaction time, and auditory attention
Tricyclic antidepressants	Confusion, dryness of mouth, aggravation of glaucoma, urinary hesitancy and retention, dizziness, fainting
Anti-Parkinsonian drugs	Confusion, nightmares, increased forgetfulness, urinary hesitancy and retention, constipation. With levadopa, nausea, vomiting, depression or elation, impaired cognitive perception, paranoid or agitated behaviour, dizziness, fainting, dyskinesias
DRUGS ACTING ON THE ENDOCRINE SYSTEM	
Thyroid and antithyroid drugs	Tremor, weight loss, heat intolerance, palpitations, fever, skin rash
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	
Indomethacin	Nausea, vomiting, diarrhea, abdominal pain, headache, dizziness
Salicylates	Confusion, disorientation, tinnitus, drowsiness, nausea, vomiting, flushing, sweating, dizziness, dyspnea, palpitations, abdominal pain

through careful questioning you can learn whether he's in the habit of taking laxatives, unusual amounts of vitamins, aspirin or aspirin-containing drugs, or other over-the-counter agents, such as sleeping pills, antacids, or cold remedies that can interfere with the absorption of some drugs or exaggerate their effects. Cold remedies containing antihistimines, for example, have sedative qualities that may enhance the effects of tranquilizers. *Be sure to ask about drinking and smoking habits; chronic alcohol consumption and cigarette smoking can stimulate the metabolism of some drugs.*

The physical examination

While the diagnosis of drug-related illness depends on an accurate history and appropriate laboratory tests, the physical may give you some important clues. Check for postural hypertension. Examine the skin for rashes indicative of drug hypersensitivity.

In patients taking anticoagulants, look for hematomas or hemoarthroses, both of which signal an overabundance of free drug.

Confirmatory tests

Have patients with abdominal pain perform an occult-blood test to determine possible bleeding from aspirin or another nonsteroidal anti-inflammatory drug.

Prothrombin time more than two or two-and-one-half times control indicates a need to lower the dose of warfarin. A low serum potassium confirms diuretic-induced hypokalemia.

An ECG will tell you if digitalis use has caused arrythmias. Look for an increase in serum creatinine or a decrease in the 14-hr creatinine clearance test as an indication of nephrotoxicity from aminoglycosides.

Finally, plasma levels of some of the drugs listed in Table 2 will also help you confirm suspected drug toxicity. □

TABLE 2

TOXICITY ALERT
Plasma levels above these may cause drug-related illness

Although response to a given plasma level differs with individual patients, the frequency of adverse effects increases sharply at levels above the therapeutic range listed below. These ranges may vary slightly among laboratories.

Drug	Effective plasma levels
Digoxin	0.8-2.4 ng/ml
Digitoxin	12-25 ng/ml
Quinidine	3-7 μg/ml
Procainamide	4-8 μg/ml
Lidocaine	1.5-5 μg/ml
Theophylline	8-20 μg/ml
Phenytoin	10-20 μg/ml
Carbamazepine	8-12 μg/ml
Lithium	0.5-1.3 μg/ml
Amitriptyline	120-250 ng/ml[1]
Nortriptyline	50-150 ng/ml
Imipramine	150-250 ng/ml[2]
Desipramine	150-250 ng/ml
Gentamicin	5-10 μg/ml[3]
Tobramycin	5-10 μg/ml[3]
Amikacin	15-25 μg/ml[4]
Salicylate	20-100 μg/ml (antipyretic, analgesic)
	100-250 μg/ml (anti-inflammatory)

[1]Usually measured as amitriptyline + nortriptyline (an active metabolite)
[2]Usually measured as imipramine + desipramine (an active metabolite)
[3]Toxic level, peak > 12 μg/ml or trough > 2 μg/ml
[4]Toxic level, peak > 35 μg/ml or trough > 5 μg/ml