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Polypharmacy has become the exception rather than the rule among elderly patients accessing the emergency department. Typically, such co-morbid conditions as heart disease, diabetes, and hypertension co-exist, requiring patients to take multiple medications, many of them associated with a predictable incidence of adverse side effects.

Drug-related adverse patient events are an important cause of admission to the hospital and, as a result, emergency physicians must be skilled in detecting adverse drug reactions, drug interactions, and interactions between prescribed medications and over-the-counter drugs such as non-steroidal anti-inflammatory drugs (NSAIDs).

Part II of this two-part series on polypharmacy outlines a systematic approach to emergency evaluation of the older patient taking multiple medications. Drug-related side effects associated with antihypertensive agents, cardiovascular drugs, and NSAIDs are discussed in detail, and approaches to managing life-threatening events are presented.

—The Editor

Polypharmacy in the Elderly: Clinical Challenges in Emergency Practice

Part II: High-Risk Drugs, Diagnosis, and the Role of the Emergency Physician

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High-Risk Drugs

Many studies have found that only a limited number of drugs are responsible for the majority of adverse drug events (ADEs) and clinically relevant drug interactions.[1,2] An even smaller number of medications is responsible for the most serious drug-related complications. These medications include anticoagulants, antihypertensives, carbamazepine, digoxin, narcotic analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), and theophylline.[3,4] Many of these medications have narrow therapeutic-to-toxic ratios and require meticulous monitoring.[5] These drugs should serve as "red flags" to clinicians when they are noted in patients' medication lists. *(See Table 1.)*

Warfarin. Drug interactions with warfarin can result in devastating consequences. Warfarin toxicity is responsible for many cases of serious drug-related morbidity and mortality, and is associated with a high incidence of hospitalizations and a high risk of fatal bleeding. Intracranial hemorrhage, the most feared complication of excessive anticoagulation, occurs in 2% of patients on long-term anticoagulant therapy.[6] Warfarin's effect is potentiated when a sec-

ond drug inhibits its metabolism and causes drug accumulation. The effect on prothrombin time usually appears within 2-3 days, but does not peak until days 7-10.[5] The anticoagulant effect also can be potentiated by the addition of drugs or herbs with synergistic effects. Although the list of drugs that interact with warfarin is extremely long, drugs that are particularly troublesome include antibiotics, acetaminophen, aspirin, and NSAIDs.[7,8] *(See Table 2.)*

All antibiotics can potentiate warfarin's effect by inhibiting intestinal flora that produce vitamin K; however, antibiotics of particular concern include ciprofloxacin, clarithromycin, erythromycin, metronidazole, and trimethoprim-sulfamethoxazole. These drugs are P450 inhibitors that will decrease warfarin's metabolism. They should be avoided whenever possible with warfarin use.[9] If these drugs must be used, close monitoring of prothrombin time and International Normalized Ratio (INR) is essential.

Acetaminophen is a widely used over-the-counter medication whose potential to cause serious drug interaction with warfarin use generally is under-recognized by the public and clinicians. There is a highly significant dose-response relationship between acetaminophen and warfarin that is independent of other variables. This interaction is thought to result secondary to acetaminophen's effect on the P450 system and its hypothrombinemic response. Study patients taking more than 1.3 g (four regular-strength 325 mg tablets) per day for longer than one week have a tenfold increased risk of having an INR greater than 6.0 when compared to controls.[10]

Aspirin is another widely used over-the-counter medication that increases the risk of bleeding when coadministered with warfarin. Aspirin causes this interaction by platelet function inhibition, gastric mucosal damage, and hypothrombinemic response.[9] For patients in whom the benefits of combined warfarin-aspirin therapy outweigh the risk of bleeding, low-dose aspirin has been shown to be safer, yet effective.

NSAIDS also can potentiate the anticoagulant effects of warfarin by inhibiting platelet function, and potentially, displacing warfarin from its protein-bound state and inhibiting hepatic enzymes. Use of NSAIDs in the elderly is associated with a three- to fivefold increase in risk of peptic ulcer disease. Studies have shown that concurrent users of NSAIDs and oral anticoagulants had a nearly 13-fold increase in the risk of hemorrhagic peptic ulcer disease when compared with controls.[11] The newer cyclooxgenase-2 inhibitor agents probably are safer options, as they have not been shown to inhibit platelets or increase the incidence of gastric ulceration.[12,13]

Angiotensin Converting Enzyme (ACE) Inhibitors. The use of ACE inhibitors in the elderly has become widespread, owing to the significant clinical benefits that these drugs impart. Unfortunately, these agents also can cause several important, life-threatening, adverse effects.[14] ACE inhibitors have been shown to be responsible for the development of hyperkalemia in 9-38% of hospitalized patients. In addition, it has been shown that 10% of outpatients treated with ACE inhibitors develop hyperkalemia.[15] ACE inhibitors cause hyperkalemia by reducing aldosterone secretion, which impairs the secretion of potassium. ACE inhibitor-induced hyperkalemia can become hazardous when potassium-sparing diuretics such as spironolactone, amiloride, and triamterene or potassium supplements are used concurrently.[16] NSAIDs also can cause hyperkalemia by inhibiting renal prostaglandin synthesis, leading to decreased renin and aldosterone and impaired potassium excretion. Hyperkalemia has been seen most commonly with the use of indomethacin.[9]

Calcium Channel Blockers (CCBs). Used primarily for hypertension and tachyarrhythmia therapy, this class is virtually ubiquitous in the elderly population. Recently, indications have expanded, with CCBs used as therapy for angina, chronic pain, migraines, and esophageal spasm.[17] Polypharmacy concerns arise with the coadministration of beta-blockers and/or digoxin. Occasionally used for

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Table 1. High-Risk Drugs

- ACE inhibitors
- Benzodiazepines
- Calcium channel blockers
- Digitalis
- Lithium
- Nonsteroidal anti-inflammatory drugs
- Theophylline
- Anticoagulants
- Beta-blockers
- Carbamazepine
- Insulin
- Narcotics
- Serotonergic enhancing drugs

Table 2. Partial List of Medicinal Substances that Have Clinically Significant Interactions with Warfarin

ACETAMINOPHEN	
AMIODARONE	
ANTIBIOTICS	Ciprofloxacin, clarithromycin, erythromycin, metronidazole, trimethoprim-sulfamethoxazole
ANTIFUNGALS	Fluconazole, itraconazole, ketoconazole
BOTANICALS	Bromelains, danshen, dong quai, garlic, Ginkgo biloba
DISULFIRAM	
NONSTEROIDAL ANTI-INFLAMMATORY DRUGS	
SALICYLATES	

patients with recalcitrant hypertension, or in hypertensive patients with dysrhythmia, this combination has potential complications, such as symptomatic bradycardia, heart block, and profound hypotension, that can be disastrous.

More insidious are the potential drug interactions due to the class metabolism by the cytochrome P450 system, isozyme CYP3A4.[18] Both verapamil and diltiazem have been shown to inhibit hepatic metabolism of CYP clearance drugs.[19] In turn, serum concentrations of CCBs can be affected by the same means. Decreased CYP3A4 activity by erythromycin or other pharmaceuticals can lead to increased CCB concentrations and resultant hypotension and bradycardia. Conversely, increased activity by an enzyme inducer, such as rifampin, can result in significantly decreased concentrations and subsequent marked hypertension or tachydysrhythmia.[18] *(See Table 3.)*

Digoxin. A large number of elderly patients receive digitalis therapy. The risk of an adverse event caused by digoxin increases with age due to the physiologic changes associated with aging that affect pharmacokinetics. In fact, patients older than age 85 have double the risk of experiencing an adverse drug effect from digoxin as patients age 65-74.[20] Digoxin is a high-risk medication that must be monitored closely because it has a narrow margin between therapeutic and toxic doses. The kidneys excrete the majority of digoxin, thus, patients with renal insufficiency, congestive heart failure, and dehydration are at highest risk for ADEs. Clarithromycin, erythromycin, and tetracycline have been shown to increase digoxin level by altering the gut flora that is important in digoxin metabolism. The most important drugs causing interaction with digoxin, however, are the antiarrhythmics. Quinidine, for example, causes an increase in digoxin concentration in 90% of patients. This is caused by quinidine's ability to reduce significantly digoxin clearance and displace digoxin from its binding sites. Amiodarone also increases digoxin level by reducing its renal clearance. Within 24 hours after adding amiodarone, digoxin concentrations were seen to increase by 25-70% .[21] Verapamil, as well, increases serum digoxin concentrations as much as 70% by altering renal clearance.[22]

Serotonergic Drugs. Administration of two or more serotonergic enhancing drugs can produce a mild to life-threatening drug interaction known as serotonin syndrome. Seriously ill patients can progress rapidly to coma, seizures, and cardiac arrest. In a review of 100 cases of serotonin syndrome, 42% of patients required admission to an intensive care unit, and 25% required intubation and ventilatory support. An estimated 15-20 deaths have been attributed to serotonin syndrome. This syndrome is characterized by abnormalities in three areas: 1) central nervous system (CNS) abnormalities such as confusion, seizure, and coma; 2) autonomic nervous system dysfunction such as hyperthermia, diaphoresis, tachycardia, and hypertension; and 3) neuromuscular activity such as myoclonus, hyperreflexia, and muscle rigidity.[23] A common clinical scenario involves a patient taking a selective serotonin reuptake inhibitor (SSRI) (i.e., fluoxetine, sertraline, paroxetine, trazadone) or monoamine oxidase inhibitor (MAOI) (i.e., phenelzine, tranylcypromine), and a second serotonergic agent is added. Common inciting agents include St. John's wort, meperidine, dextromethorphan, amphetamines, and cocaine.

NSAIDs. These drugs commonly are prescribed for the elderly, yet most likely account for the greatest incidence of ADEs in the United States. In fact, it is estimated that if deaths from gastrointestinal effects of NSAIDs were tabulated separately in the National Vital Statistics reports, they would constitute the 15th most common cause of death in the United States.[12] The most common adverse effects of NSAIDs are gastrointestinal disease, such as dyspepsia, gastritis, and gastroduodenal ulcer. Proven risk factors for development of gastroduodenal ulcers include advanced age and concomitant use of corticosteroids, other NSAIDs, or anticoagulants. NSAIDs also can cause nephrotoxic effects that include renal failure and acute or chronic interstitial nephritis. These drugs interact with coumadin, digoxin, beta-blockers, ACE inhibitors, lithium, and thiazides.[24]

Diagnosis

The diagnosis of adverse drug effects should be considered for every elderly patient presenting to the emergency department (ED). These drug-related complications occur frequently in the elderly and are difficult to recognize. Symptoms often are vague, and clinical manifestations nonspecific. In addition, the clinical presentation of adverse drug reactions may mimic that of other common illnesses in the geriatric age group. Cognitive impair-

Table 3. Drugs and Their Interactions with Calcium Channel Blockers[8]

BETA-BLOCKERS
• Additive effect on chronotropy, inotropy, and conduction
• Hypotension, bradydysrhythmias
CARBAMAZEPINE
• Increased carbamazepine concentration (diltiazem, verapamil)
• Ataxia, altered mental status
DIGOXIN
• Increased digoxin concentration (verapamil)
• Bradydysrhythmias
PRAZOSIN
• Potentiation of effect
• Decreased blood pressure
QUINIDINE
• Increased quinidine concentrations (diltiazem, verapamil)
• Bradydysrhythmias
• Decreased quinidine concentrations (nifedipine)
• Tachydysrhythmias

ment such as confusion, hallucination, dementia, and depression are among the most common clinical presentations of drug-induced illness. Falls also are frequent presenting complaints.[25,26] A common pitfall for the clinician is to attribute these nonspecific clinical manifestations erroneously to the patient's aging state or underlying medical illness. The clinician unwittingly may prescribe a new drug to treat the manifestations of an adverse drug reaction, placing the patient at additional risk of experiencing adverse drug effects.[27] It is essential that the clinician directly question the patient several times about medication history, since many patients initially forget to mention their use of over-the-counter drugs or herbal preparations. Specific questioning regarding medication use has been shown to be more sensitive in detection of their use.[28]

Some pathology caused by the adverse effect of polypharmacy is not subtle. Hypotension, bradycardia, coma, and bleeding diatheses are well-documented results of inappropriate drug combinations. Drug-related complications always should be considered in clinical presentations involving significant derangements of physiology, and can be checked easily by reviewing the patient's current medication usage.

Legal Considerations

Current medical systems rely heavily on error-free performance, as evidenced by the lack of fail-safe mechanisms. Many medical institutions deal with medical errors by placing the emphasis on individual accountability and not on system failures.[29] The typical response to medical error usually includes increased training efforts and punitive measures directed at the "imperfect" clinician. The public expects physicians to have knowledge of all the current pharmaceuticals on the market and, in particular, potential side effects and drug and food interactions. A survey conducted by the National Patient Safety Foundation found that many people believed that when mistakes did happen, they were the result of physician carelessness, stress, faulty training, or bad communication. Three out of four respondents believed the best solution to medical mistakes would be to get rid of the bad health care providers.[30] Emergency clinicians increasingly are being held to an unachievable standard of care, with dire consequences resulting when inevitable human errors do occur.[31,32]

Studies have shown that a substantial number of patients each year suffer serious morbidity and mortality from medical errors.[33] Although the overall rate of medical errors occurring in the emergency setting is unknown, it is no doubt quite high given the brisk and complex nature of this medical specialty. In one study, the ED was shown to have the highest number of adverse events from negligent care, ranging from 52-70%.[34,35] A study performed in an intensive care unit revealed that there were an average of 178 activities per patient per day with an error rate of 1.7 per day.[36] However, many medication errors are unavoidable and are not due to negligence. It is impossible for the clinician to know what the impact of age-related changes in physiology and disease on drug handling and drug response will be in every patient. Thus, it is difficult to predict which patients will experience significant drug side effects. Idiosyncratic reactions are unpredictable.

Physicians who commit mistakes that have resulted in serious injury or death not only must deal with emotional devastation, but also the fear of potential litigation, including criminal indictment.[30,31,37] Frequently, drug injuries result in malpractice claims. When malpractice suits do arise, it is common for the defense to offer a settlement even when there is no negligence. One large study of closed claims revealed that drug injuries accounted for the highest total expenditure.[38] The severity of the patient's disability, not the occurrence of an adverse event, was more predictive of payment to the plaintiff.[39] Fortunately, however, most medication errors do not cause injury, and many medical injuries caused by negligence do not result in a malpractice claim.

When a medical error does occur, the best policy is full and timely disclosure of the error to the patient and his or her family.[40-42] Patients feel betrayed and angry when they believe health care providers are trying to cover up an error. Many lawsuits are motivated not by negligence, but by poor communication and a breakdown in trust between providers and patients. Institutions that have established guidelines for honest and full disclosure of medical errors and a provision for equitable compensation for loss have found both a cost-effective and ethical solution to the problem.[43,44]

The Role of the ED and the Emergency Physician

Self-education. Emergency medicine physicians have a large number of yearly patient encounters yielding drug treatment.[45] Physicians' prescribing practices contribute significantly to ADEs.[46-48] Common medication errors that occur due to physician prescribing errors include incorrect drug product, dosage

Table 4. Some Drug Information Resources

CONSULTANTS
- Medical toxicologist
- Clinical pharmacist or pharmacologist
- Department of pharmacy
- Hospital-based pharmacist
- Poison control center

INTERNET
- American College of Medical Toxicology (www.acmt.net)
- EMRonline (www.emronline.com)
- Food and Drug Administration (www.fda.gov)
- Institute for Safe Medication Practices (www.ismp.org)
- MDconsult (www.mdconsult.com)
- Medscape (www.medscape.com)
- Medwatch (www.fda.gov/medwatch)
- Physicians' Desk Reference (www.pdr.net)
- PubMed (www.ncbi.nlm.nih.gov/pubmed)
- RxList (www.rxlist.com)
- United States Pharmacopoeia (www.usp.org)
- WebMD (www.webmd.com)

PUBLICATIONS AND TEXT
- *Drug Interaction Facts*
- *Physicians' Desk Reference*
- Product inserts

SOFTWARE
- mobilePDR (via PDA)
- LexiDrugs

Table 5. Strategies to Prevent Polypharmacy Adverse Drug Reactions in Elderly Patients

HAVE A HIGH SUSPICION OF RISK
- Always consider the diagnosis
- Complete illness history/medication history

ENHANCE KNOWLEDGE
- Study drug information sources
- Understand geriatric prescribing principles

LIMIT THE NUMBER OF PRESCRIPTIONS

LOOK FOR HIGH-RISK COMBINATIONS TO AVOID POTENTIAL DRUG INTERACTION

FOLLOW A LOW-DOSE PHILOSOPHY IN PRESCRIBING

AVOID PRESCRIBING ERRORS
- Use legible handwriting
- Avoid abbreviations
- Take care with decimal points

CONSIDER THE USE OF SAFER ALTERNATIVE DRUGS

ADJUST DOSE FOR ORGAN FUNCTION IMPAIRMENT

form, dosage amount, administration route, and dosing frequency. Illegible handwriting, the use of abbreviations, decimal point misplacements, or miscalculation of dose can have tragic consequences.[49-51] The majority of prescribing errors are due to lack of knowledge about pharmaceuticals and geriatric prescribing principles. In one study, 22% of errors were caused by lack of knowledge of the drug prescribed—the most common cause of error.[47] One group reviewed similar concepts in their study of medication errors and found that almost 60% of prescribing errors were due to deficits in knowledge and application of knowledge regarding drug therapy and patient characteristics.[46] The patient factors most commonly not accounted for in selecting a drug or drug dose were advanced age, renal impairment, and patient weight. They also found that inappropriate concurrent drug therapies involving drug-drug interactions and duplicative therapies were frequent.

More sophisticated systems can check for drug-drug and drug-allergy interactions. Clinicians must make it their responsibility to educate themselves continually regarding medication errors and polypharmacy issues in the elderly. Since it is impossible for a clinician to have in-depth knowledge about every pharmaceutical product available on the market, the use of easily accessible, up-to-date databases has become imperative. Software that allows for drug-drug interaction recognition is available to all practitioners. For example, medical screening software, such as PDA-based mobilePDR is updated regularly and can screen out dangerous drug combinations to help prevent potentially serious interactions. Other sources of pharmaceutical information are listed in Table 4.

Medication Screens. The ED is the hospital's primary contact with the community. Conversely, for many individuals in the community, the ED serves as their primary source of medical care. Historically, more than 40% of patients treated in the ED lack a usual source of health care.[13] The number of ED visits nationally in 1999 was 102.8 million. This allows for a vast screening of the general population for polypharmacy issues. Conscientious attempts must be made to obtain a complete medicine history, including herbal and over-the-counter preparations, from the patient and attendant family. This information can be obtained by reviewing all of the patient's medication bottles or medication lists. For patients who are unable to provide information or cannot remember their medications, an old medical chart can be extremely useful. Several hospital information systems are designed to maintain and display a current medication list. The patient's current drug regimen must be assessed fully before a new drug is prescribed to prevent potential drug interactions.

The ED may set up a system that reviews patients' medication lists to recognize any pharmaceutical problems. An example would be a protocol requiring that all patients who present to the ED and who have multiple medications automatically have their drug lists reviewed by a pharmacist or computerized query system. If a problem with high-risk drug combinations or dosage was identified, the patient, ED clinician, and the primary care physician would be notified. This concept needs to be investigated further to establish its clinical utility and efficacy.

Clinical Guidelines/Pathways. Treatment guidelines are becoming increasingly popular in clinical medicine. They are designed to serve as safeguards and to standardize and improve medical therapy for some of the most common and highest-morbidity pathologies.[52] Guidelines should include strict medication regimens and internalized restrictions to minimize potential adverse polypharmacy effects. Examples are the use of weight-

Table 6. Strategies for Preventing Adverse Drug Events

- Self-education
- Medication screens
- Pharmaceutical history
- Guidelines/pathways
- Communication with staff
- Coordination and problem-solving with pharmacy
- Utilization of support services
- Patient education/discharge instructions
- Discharge prescription screens
- Adverse drug event reporting

based heparin in thrombolytic pathways to reduce the possibility of hemorrhage, and sildenafil citrate advisories regarding nitroglycerin use to avoid inducing serious hypotension. Nearly 700 evidence-based treatment guidelines are available easily to clinicians from the National Guideline Clearinghouse. The web site is www.guideline.gov.

Communicate with Staff. Nurses often experience a more extensive and relaxed communication with patients and their families than ED physicians do. Nurses spend much more time with patients than physicians do, and they usually are the first and last point of medical contact for patients. Nurses may encounter information that the ED physician is not privy to, as patients may become annoyed and uncooperative if they must give their histories more than once and therefore may leave out pertinent details when questioned repeatedly. Therefore, nurses can provide valuable clinical information to the treating clinician. In addition, since nurses administer medications and give the patient discharge instructions, they can serve as a screen for prescribing mistakes. In one study, nurses were the principal interceptors of medication errors, detecting half of physician ordering errors.[47] This result occurred within a hospital-wide system that included pharmacists; in the ED, nurses are the emergency physician's only check and balance.

Utilize Supportive Services for the Patient. Employ social service consultation to arrange patient and family education regarding medication usage. Social services also can aid in ensuring completion of prescriptions, communication with primary care providers, referral to consultants, lab follow-up to obtain serum testing, and transportation to appointments.

Simplify Treatment Regimens. One group showed that patients with multiple daily doses of a medication have a 75% rate of noncompliance.[53] Because more mature patients have even greater difficulty with multiple daily dosing, try to utilize once- or twice-daily schedules. If possible, discuss the opportunity to simplify already existing treatment regimens with the primary care physician or consultant.

Conservative Initial Drug Dosing. The use of lower initial drug doses may help avoid serious adverse reactions in older patients. In addition, lower drug dosages may reduce drug side effects and interactions while improving patient compliance. Elderly individuals have a reduced rate of drug clearance due to decreased renal and hepatic function in comparison to younger adults. Despite these pharmacokinetic differences, most drug inserts do not recommend reduced initial doses for elderly patients. Many times, lower doses are appropriate because a large number of studies have been conducted that support the therapeutic effectiveness of lower drug doses. For example, multiple studies show the effectiveness of ibuprofen at 200 mg doses three to four times per day.[54] Furthermore, for many drugs, pharmacokinetic data for the elderly are not available. Patients who describe long histories of numerous drug intolerances are likely to be slow metabolizers and require low-dose medication. For all other elderly patients, the adage "start low and go slow" should be heeded.

Safer Alternative Drug Therapy. The potential benefits of any medication must be weighed against the risks of adverse drug effects. Many times, safer alternative drug options can be utilized for elderly patients. For example, an elderly patient who requests medication to aid sleep may be served better by the use of an antihistamine, such as diphenhydramine or low-dose trazodone, instead of a benzodiazepine. Antihypertensive agents provide another example. Thiazide diuretics are quite effective in lowering blood pressure, but they cause several adverse effects that limit their use. In addition to causing potassium and sodium loss, they may cause extremity swelling, which can resemble gout-like symptoms. In a study of more than 9000 Medicaid patients who were age 65 or older, the risk of being started on treatment for gout was almost double in patients who received thiazide diuretics when compared to patients who were treated with non-thiazide therapies. In addition, the risk of being treated for gout was much less when a lower dose of thiazide was prescribed, and the lower dose was found to be effective in lowering blood pressure.[55] NSAIDs also are responsible for a huge number of adverse drug effects in the general population. Safer treatment alternatives include acetaminophen or cyclooxygenase-2 inhibitors.[12,13] Finally, cimetidine is responsible for a large number of clinically significant drug interactions. Cimetidine, a potent inhibitor of the P450 system, causes increases in serum concentrations of many concurrently administered drugs.[24,56] Ranitidine, famotidine, and nizatidine are safer alternative H_2-blocker drugs.

Discharge Instructions/Prescriptions. Patients always should be counseled regarding potential drug side effects and interactions. Elderly patients who take multiple medications, or who appear particularly frail or incompetent, should be encouraged to have a family member or close friend listen to discharge instructions with them. Patients also should be encouraged to seek medical advice for any concerns in identifying drug side effects.

A significant trend in ED management has been the introduction of computerized discharge instructions and prescriptions. Prescription programs provide a dose selection menu, which includes drug route and dosing frequency and generates a legible copy. Several current platforms automatically compare discharge prescriptions for compatibility to provide the clinician with the potential for intervention. For instance, a patient who is maintained on warfarin therapy is diagnosed with diverticulitis and is

prescribed metronidazole. Metronidazole, an inhibitor of the cytochrome P450 system, would increase warfarin levels, leading to significant bleeding complications. Inputting the new prescription with the baseline medication list would result in an alert of the drug interaction to the practitioner.[57] The net effect of the application of this software should parallel one group's findings of inpatient physician order entry where there was an overall 55% reduction in "serious medication errors."[58]

In addition, a copy of discharge instructions, including prescriptions, should be forwarded to the primary care provider and/or consultant. This would provide them with an updated pharmaceutical list to avoid any unintended error on their part.

Adverse Drug Event Reporting. All ADEs suspected in the ED should be reported. This allows intervention, education, policy revision, and tracking of epidemiology on a national scale. Although fear of litigation deters many clinicians, full disclosure of errors is the best policy and is simply the right thing to do.[59,60]

In this age of increased public awareness and sensitivity to the issue of medical errors, EDs should have a protocol for responding to serious errors, particularly those resulting in significant patient injury or death.[61,62] This plan should address how the staff should interact with patients, families, federal regulatory bodies, accreditation agencies, and the media. Procedures for safeguarding event documentation, containers, and equipment should be included. Arrangements for psychological counseling and other forms of support for staff, patients, and their families should be addressed. *(See Tables 4, 5, and 6.)*

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Physician CME Questions

91. Which of the following drugs were found to be responsible for the most serious drug-related complications?
    A. Anticoagulants
    B. Carbamazepine
    C. Digoxin

D. NSAIDs and narcotic analgesics
E. All of the above

92. Which of the following is (are) considered to be particularly troublesome when combined with warfarin?
A. Acetaminophen
B. Aspirin
C. NSAIDs
D. Antibiotics
E. All of the above

93. NSAID use is associated with what increase in risk of peptic ulcer disease in the elderly?
A. Tenfold
B. Twofold
C. Three- to fivefold
D. Four- to sixfold

94. What is the most common cause of prescribing errors?
A. Lack of knowledge about the drug prescribed
B. Poor handwriting
C. Use of abbreviations
D. Use of PDAs

95. One study showed which rate of noncompliance among patients with multiple doses of medication?
A. 100%
B. 75%
C. 50%
D. 25%

96. What is a common pitfall in diagnosing adverse drug effects in elderly patients?
A. Attributing nonspecific clinical manifestations to the patient's age or underlying medical illness
B. Questioning the patient several times about medication history
C. Considering drug-related complications in presentations involving significant derangement of physiology
D. Reporting adverse drug events

97. Which of the following medications promotes hyperkalemia when used with ACE inhibitors?
A. NSAIDs
B. Spironolactone
C. Potassium supplements
D. All of the above

98. All of the following may be successful strategies in reducing adverse polypharmacy events *except*:
A. use of medication screening software.
B. maintaining a "physicians-only" pharmacology management technique.
C. simplification of treatment regimens.
D. self-education.

In Future Issues: **Ophthalmologic Emergencies**

Emergency Medicine Reports

CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- be educated about how to correctly perform necessary diagnostic tests;
- take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;
- apply state-of-the-art therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur;
- and provide patients with any necessary discharge instructions.

Emergency Medicine Reports
The Practical Journal for Emergency Physicians

Polypharmacy in the Elderly, Part II

High-Risk Drugs

- ACE inhibitors
- Benzodiazepines
- Calcium channel blockers
- Digitalis
- Lithium
- Nonsteroidal anti-inflammatory drugs
- Theophylline
- Anticoagulants
- Beta-blockers
- Carbamazepine
- Insulin
- Narcotics
- Serotonergic enhancing drugs

Partial List of Medicinal Substances that Have Clinically Significant Interactions with Warfarin

[redacted]

Ciprofloxacin, clarithromycin, erythromycin, metronidazole, trimethoprim-sulfamethoxazole

[redacted]

Fluconazole, itraconazole, ketoconazole

[redacted]

Bromelains, danshen, dong quai, garlic, Ginkgo biloba

[redacted]

Calcium Channel Blocker Interactions

[redacted]

- Additive effect on chronotropy, inotropy, and conduction
- Hypotension, bradydysrhythmias

[redacted]

- Increased carbamazepine concentration (diltiazem, verapamil)
- Ataxia, altered mental status

[redacted]

- Increased digoxin concentration (verapamil)
- Bradycysrhythmias

[redacted]

- Potentiation of effect
- Decreased blood pressure

[redacted]

- Increased quinidine concentrations (diltiazem, verapamil)
- Bradycysrhythmias
- Decreased quinidine concentrations (nifedipine)
- Tachycysrhythmias

Some Drug Information Resources

- Medical toxicologist
- Clinical pharmacist or pharmacologist
- Department of pharmacy
- Hospital-based pharmacist
- Poison control center

- American College of Medical Toxicology (www.acmt.net)
- EMRonline (www.emronline.com)
- Food and Drug Administration (www.fda.gov)
- Institute for Safe Medication Practices (www.ismp.org)
- MDconsult (www.mdconsult.com)
- Medscape (www.medscape.com)
- Medwatch (www.fda.gov/medwatch)
- Physicians' Desk Reference (www.pdr.net)
- PubMed (www.ncbi.nlm.nih.gov/pubmed)
- Rx List (www.rxlist.com)
- United States Pharmacopoeia (www.usp.org)
- WebMD (www.webmd.com)

- *Drug Interaction Facts*
- *Physicians' Desk Reference*
- Product inserts

- mobilePDR (via PDA)
- LexiDrugs

Role of the Emergency Physician in Preventing Adverse Drug Events

- Self-education
- Medication screens
- Pharmaceutical history
- Guidelines/pathways
- Communication with staff
- Coordination and problem-solving with pharmacy
- Utilization of support services
- Patient education/discharge instructions
- Discharge prescription screens
- Adverse drug event reporting

Stragegies to Prevent Polypharmacy Adverse Drug Reactions in Elderly Patients

- Always consider the diagnosis
- Complete illness history/medication history

- Study drug information sources
- Understand geriatric prescribing principles

- Use legible handwriting
- Avoid abbreviations
- Take care with decimal points

Supplement to Emergency Medicine Reports, June 3, 2002: "Polypharmacy in the Elderly: Clinical Challenges in Emergency Practice—Part II: Overview, Etiology, and Drug Interactions." *Authors*: **Katherine M. Prybys, DO, ACTM,** Assistant Professor of Emergency Medicine, University of Maryland Medical System, Baltimore; **Kraig A. Melville, MD, FACEP, FAAEM**, Chief, Emergency Medical Services, Calvert Memorial Hospital, Prince Frederick, MD; **Jeahan R. Hanna, MD**, Chief Resident, Emergency Medicine, University of Maryland Medical System, Baltimore.

BIOTERRORISM WATCH
Preparing for and responding to biological, chemical and nuclear disasters

They don't call it bio*terror* for nothing: Fear is the foe when anthrax spores are found within hospital walls

'We feel we were able to ward off a panic . . .'

Clinicians nationwide were beset with hoax powder scares last year at the height of the anthrax attacks, but at one hospital, the threat turned out to be real. Positive cultures for *Bacillus anthracis* were found within hospital walls, setting off a wave of anxiety that threatened to descend into panic.

"There was a mounting level of anxiety among our health care workers," said **Maureen Schultz**, RN, infection control coordinator at Veterans Affairs (VA) Medical Center in Washington, DC. "It had to be dealt with before we could work out any other aspect of the situation."

The events began to unfold last October, when it was discovered that the anthrax letter sent to Sen. Tom Daschle (D-SD) might have contaminated other federal buildings through cross-contamination of mail processed at the Brentwood postal building in Washington, DC.

"It was several days before the contamination was discovered, and by that time, several downstream facilities, including our VA hospital, were contaminated," she said recently in Salt Lake City at the annual meeting of the Society for Healthcare Epidemiology of America (SHEA).[1] In light of the situation, it was recommended that mailrooms in federal buildings be cultured for anthrax.

"One of the things we found frustrating was that we were not given any guidance as to how we should screen the mail," Schultz said. "So we [took] cotton swabs and ran each swab over an approximately 10 to 50 square inch area."

Four of 34 environmental swabs taken in the hospital mailroom grew *B. anthracis*, with colony counts varying from one to 11. The anthrax was found on a canvas mail tote, a cardboard box that had been mailed, on the top of a mailroom speaker, and on a canvas mail cart.

The fear factor

"Even before the contamination was discovered, [we] decided to take some action because of the growing concern among our employees," she said. "So [we] convened a group from the emergency response team, infection control, safety, and public affairs."

The focus of the response was to determine risk level, provide prophylaxis as needed, decontaminate the environment, and get accurate information to all 1,700 health care workers, patients, and visitors, Schultz said. In order to reduce the high level of anxiety, a series of educational sessions were held, information was posted on the hospital web page, press releases were distributed, and printed materials were given to staff, patients, and families. In addition, a series of "town-hall" meetings was held to fully air the concerns of employees.

"These were informal sessions that we had in our auditorium where many health care workers could come and interact on an informal basis," Schultz said.

The risk to hospital workers was determined to

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be low, and only eight staff members were started on prophylactic antibiotics. Those included five mailroom employees who were encouraged to take full 60-day regimens. Another three workers, considered at lower risk, were given 10-day regimens due to possible contact with contaminated mail. The mailroom and surrounding area were decontaminated by an outside contractor.

Overall, some 500 health care workers attended the education sessions, and each town-hall meeting drew more than 200 staff members. With the colony counts low and the contamination limited, the decision was made to limit prophylaxis to only the eight aforementioned employees. That approach was not well received by other health care workers who feared they could have been unknowingly exposed.

"We refused treatment to all other employees, and initially, this created a lot of anxiety among the health care workers, particularly in these large town-hall meetings," Schultz said. "They were demanding ciprofloxacin or doxycycline in case they had come in contact with something contaminated. But we did hold firm on this, and we did not provide prophylaxis to any other employees."

Still, at the SHEA meeting, the Centers for Disease Control and Prevention (CDC) conceded that many of its initial assumptions about anthrax turned out to be false, including the perception that mail handlers were not at risk for inhalational anthrax. Given that acknowledgment, *Bioterrorism Watch* asked Schultz if she would now reconsider the decision to limit antibiotic prophylaxis to a few workers. "Based on the information we have now, no. I don't think we would change that decision." There really was no evidence that any widespread contamination had occurred, she added.

A total of 34 workers reported to the occupational health service for clinical evaluation, but there were no reports of staff refusing to work, and patient care was not interrupted. The initial level of fear and anxiety among many of the workers eased off under the continuous education and communication effort.

"We feel we were able to ward off a panic situation by the actions that we took," she said.

NYC hospital faces similar situation

A similar contamination incident was feared at Memorial Sloan Kettering Institute, a 431-bed cancer center in New York City. Some 1,200 health care workers at Sloan Kettering work in the same building as Gov. George Pataki's Manhattan office, which was reported to be the target of anthrax mailing. On Oct. 17, possible anthrax (positive by polymerase chain reaction test) was discovered in the governor's office. Pataki and staff vacated their part of the building, and infection control staff and hospital administration at Sloan Kettering developed a response plan to protect their workers.

The hospital employees worked on 10 floors of the 40-story building, including three floors that shared an air-ventilation system with the governor's offices. The response was honed to focus on mailroom staff and some 250 employees who worked on the three floors with shared air. With incomplete information on the scope of potential contamination of Pataki's offices, hospital clinicians decided to perform nasal cultures on the employees on the three floors, **Janet Eagan**, RN, an infection control professional at Sloan Kettering reported at the SHEA conference.[2] All of the 245 cultures taken were negative.

"I think the nasal swabs were more to allay fear," she said. "We wanted to do something that was proactive."

Public health investigators first used the nasal swab approach after the first anthrax case in Florida, but the CDC would later advise against routine use of the practice. The reliability of the swabs came into question, in part, because even those exposed may test negative as the nose clears of spores. At a Nov. 1, 2002, press briefing, the CDC advised against using nasal swabs "as a nonspecific probe to determine whether anthrax has ever been present in an environment."

Of course, clinicians at Sloan Kettering were dealing with a situation before that clarification was issued, but even then there were doubts about the wisdom of swabbing the workers.

"By the time we agreed to do the nasal swabs, I was kicking myself, thinking what on earth are we going to do with this information," **Ken Sepkowitz**, MD, epidemiologist at the hospital told SHEA attendees. "The nasal swabs was a screw-up, but with the information we had . . ."

With all the swabs negative, no antibiotics were administered. Additional efforts were needed to reassure the "worried well" that they were not at risk. Personnel from infection control, safety, security, and social work all met with the staff. Building management conducted an independent environmental survey of the building.

"E-mails went to all staff that all 245 employees tested had negative results," Eagan said.

"Communication is key. We believe that by having a hands-on approach — actually being there meeting with staff — prevented panic in employees that were very vulnerable."

Then word came that the original specimen from the governor's office had been found culture negative on retesting. The hospital had been through an intense false alarm drill, but overall had met the challenge, Eagan said.

"Decisions were made using incomplete information at a time-sensitive pace," she said. "Staff responded in a positive manner to the high visibility of administrative leadership, infectious disease, and infection control in numerous educational sessions and e-mail alerts."

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APIC: Smallpox plan uses outdated infection control

Designating patient facilities a mistake

The Centers for Disease Control and Prevention (CDC) has based its smallpox bioterrorism response plan on "outdated concepts," and entire sections need to be revised to reflect current epidemiologic strategies, the nation's leading group of infection control experts warned.

The Association for Professionals in Infection Control and Epidemiology (APIC) commented on the *CDC Interim Smallpox Response Plan and Guidelines*, which has been released as something of a work in progress.

"In general, we are concerned that the draft guidelines appear to be based on outdated strategies used to control this disease decades ago and do not appropriately integrate those infection control strategies and environmental controls utilized in our hospitals today," the APIC letter stated.

The CDC response plan calls for investigators to rapidly immunize a "ring" around the first cases. The ring concept uses isolation of confirmed and suspected smallpox cases followed by contact tracing, vaccination, and close surveillance of contacts. The ring approach was used to successfully eradicate smallpox from the world in 1980. But the ring concept was effective when the demographics of smallpox were very different, when few were infected, and the vast majority of people already were immune.

As part of the ring response, vaccine would be administered to people involved in the direct medical care, public health evaluation, or transportation of confirmed or suspected smallpox patients.

"Vaccination, like any preventive strategy, is more effective if given prior to exposure," APIC argued. "If health care workers are not immunized prior to case identification, these individuals [especially emergency department staff, direct caregivers, and laundry personnel] should be vaccinated immediately upon documentation of a case in their community. It is crucial that we not wait for a case to present in the facility before taking preventative action."

In addition, it may not be possible to distinguish between febrile response to vaccine or actual exposure in health care workers, APIC warned.

"Approximately 20% of vaccinated employees will develop fever and not be able to work if vaccine is given in response to a suspect or confirmed case," the association stated. "We need to develop strategies for dealing with staffing shortages whether they are due to febrile reaction to vaccination, true infection / disease, or refusal to care for patients in a smallpox emergency."

'Misuse of resources'

APIC also questioned the CDC concept of a "Type C isolation facility" for smallpox patients. As proposed, the sites would be facilities that are at least 100 yards from any other occupied building, or those that have nonshared air-ventilation systems with filtered exhaust.

"We believe it would be a misuse of resources to design, build / retrofit, and maintain a designated facility that is not integrated with the existing health care system," APIC stated. "Using alternative structures rather than enhancing the current infrastructure is not a wise use of our limited resources."

Instead, existing facilities could substantially

benefit from dedicating resources to ensuring appropriate air handling and ventilation systems for existing clinics, emergency departments, and isolation rooms. "This would provide the added benefit of controlling more likely exposures to infectious droplet nuclei [tuberculosis, disseminated zoster, chicken pox, measles, etc.] in addition to minimizing or eliminating the likelihood of intrafacility transmission of smallpox," APIC stated.

The association expressed concern that health care delivery might be compromised in separate Type C facilities, particularly if they are not designed to provide services such as intensive care, ventilator support, dialysis, and laboratory resources. Rather then designate facilities for smallpox patients, each hospital should be prepared in advance to activate its program when the first case is identified, APIC argued.

"There needs to be a predetermined area [building or wing, etc.] that meets the 'Type C' facility requirements for isolation," APIC noted. "Part of a facility's planning would include a determination regarding the number of patients that could be housed in the designated area."

Some of the cleaning and disinfection recommendations in the document are out of date with current sterilization principles and practices. That includes "fogging" rooms to disinfect environmental surfaces, the association charged.

"CDC has not recommended the fogging of rooms for many years," APIC stated. "We strongly suggest the deletion of any archaic references to fogging." ■

Stanford sets the standard for bioterrorism planning

A separate piece: Stand-alone plan advised

It's not enough merely to update the bioterrorism component of your current disaster preparedness plan, experts say; you must create a detailed bioterrorism response plan that stands on its own.

That's precisely the philosophy behind the Stanford (CA) Hospital and Clinics (SHC) & Lucile Packard Children's Hospital (LPCH) Bioterrorism Response Preparedness Plan, which is gaining widespread recognition as a model for such plans. In fact, several Kaiser Permanente facilities in California already have adopted the plan.

"You need a separate [bioterrorism] plan," asserts **Eric A. Weiss**, MD, assistant professor of emergency medicine at Stanford, associate director of trauma at Stanford Hospital, and chairman of the disaster committee and bioterrorism task force. "During most disasters, for instance, you don't rely on the microbiology lab to identify pathogens. Also, infectious disease and infection control staff take on a major, heightened role."

In disasters such as an earthquake, Weiss notes, you generally don't have to worry about the quarantine of patients or the spread of infectious agents. Similarly, you may not have to put on protective clothing or worry about cross-contamination of existing patients who may be immunosuppressed.

A bioterrorism plan had been in place prior to 2001, Weiss says, "but it was really just a skeleton plan — not very comprehensive. It was part of a larger disaster preparedness plan, but a plan to deal with mass casualties from bioterrorism is very different."

When you have a major disaster such as the collapse of the World Trade Center, Weiss notes, local health care providers are likely to come to the hospital and offer to chip in and help wherever they can.

"But what happens when the word goes out that patients are walking around with smallpox?" he asks. "Are providers going to want to stream down to the hospital and potentially infect themselves and their families? You need a response plan to address the safety of health care providers, so they will feel comfortable and want to show up for work."

To create such a plan, the Bioterrorism Planning Task Force was formed, incorporating personnel from 30 or more different departments at both facilities. Those departments include infectious diseases, infection control, emergency medicine, pediatrics, critical care, intensive care units, nursing and hospital administration, dermatology, psychology, social services, and environmental health and safety.

"We began putting the plan together when we identified the fact that the current plan was not adequate," notes Weiss. "We accelerated our activities after Sept. 11. After Sept. 11, *everybody* wanted to be part of it."

[Editor's note: The bioterrorism plan is available on the Stanford web site at www.stanfordhospital.com.] ■