

**JOHN D. CLOUGH, MD**Editor-in-Chief, *Cleveland Clinic Journal of Medicine***ROGER M. MACKLIS, MD**

Department of Radiation Oncology, Cleveland Clinic

DEBORAH M. NADZAM, PHD, RNDirector, Cleveland Clinic Health System
Quality Institute

It's time medicine stopped burying its mistakes

ACCORDING TO A RECENT, well-publicized report from the Institute of Medicine,¹ medical errors kill an estimated 44,000 to 98,000 patients in American hospitals each year. We can quibble about the numbers, which were extrapolated from several studies,^{2,3} but it is clear that a frontal attack on this problem is long overdue.

We in the health care professions, especially those of us in hospitals, routinely look for and learn from medical errors. But despite our current efforts, we continue to make errors, occasionally with disastrous consequences.

We clearly need a better approach to patient safety as our treatments become more potent and effective, but at the same time more complicated and dangerous. And as health care moves out of the hospital into outpatient centers and physicians' offices, the creation of error-identification and prevention systems becomes even more important.

Fortunately, the Institute of Medicine's report is crystallizing and legitimizing these efforts across the country. The challenge is to improve the current systems and remove the barriers standing in the way of error-prevention programs that will work truly well.

■ HOW ERRORS SHOULD BE ANALYZED

Most medical errors are "minor" in that they result in no discernible harm to the patient, who may not even recognize them as having taken place. In the study of Brennan et al,² over half fell into this category. Some errors are not minor, however, and in Brennan's study, 13.7% of them resulted in death of the patient.

Accident theory provides a way to approach this problem. Viewing medical errors as predictable outcomes of imperfect processes provides a rational basis for applying well-studied industrial process-improvement algorithms to health care.

The basic premise of this approach is that complex, tightly coupled processes, such as health care, are prone to accidents, ie, errors.^{1,5} Health care delivery processes are made up of many subprocesses that are complex (nonlinear), tightly coupled (highly interdependent), and not always under common managerial control. Although the error rates in each of the subprocesses may be very small, the compounding effect of these small error rates in sequentially occurring subprocesses predictably results in a high error rate for the overall process.⁶ This suggests that reducing the number of subprocesses and the number of interfaces between them is likely to be more successful in reducing the overall error rate than trying to perfect each subprocess individually.

■ BARRIERS TO REPORTING ERRORS

Before the root cause of an error can be fixed and further errors prevented, somebody has to notice that an error has occurred and report it. And two main barriers—fragmentation of medicine and a potential "culture of blame"—impede our ability to obtain and use the data we need to mount an effective attack on medical errors.

Health care is fragmented

Most hospitals have multiple systems for recording errors, and in many cases there is little sharing of data between these systems: they "don't talk to each other." For instance, a typical hospital might have a myriad of separate databases residing in its incident-reporting office, pharmacy, ombudsman service, radiation safety office, quality management office, infection control department, care pathways department, risk management office, and general counsel's office. The systems are directed at recording, archiving, classifying, analyzing, prioritizing, and otherwise studying the errors, not at detecting them in the first place. The existence of these redundant systems reflects the sheer magnitude



and complexity of the error-prone processes with which we are dealing.

At least these systems exist in many hospitals. Not so in most private physicians' offices, where reporting and recording of errors is a highly individual phenomenon. Initiatives to consolidate the many pieces of the health care system into integrated systems and networks provide an opportunity to reduce this fragmentation.

Reporting leads to a 'culture of blame'

The second barrier is the threat of developing a "culture of blame,"⁴ with the eagerness of government and internal management to punish a scapegoat for anything that goes wrong.

How the hospital approaches error reporting and its consequences is extremely important in determining the degree to which errors actually get reported. If people who make or observe errors fear for their jobs, they are far less likely to report them than they would be if management viewed errors as an opportunity to learn about and improve the processes of care. This managerial gestalt is probably more important than the physical systems for quantifying and studying errors.

Then there are the personal-injury lawyers. As we gear up to study and publish our errors, our friends in the legal profession will be waiting in gleeful anticipation of the rich table we are setting before them. The problem of tort liability has not been resolved for the modern era of consolidation, networking, and managed care. Currently, peer-review activities, done within a single institution for the purpose of quality improvement, are legally privileged and, hence, not discoverable. All bets are off, however, when we talk about networks of hospitals, outpatient clinics, and physicians' offices. One of the Institute of Medicine's major recommendations is that this issue be addressed legislatively to permit greater openness in sharing information about errors,

a prerequisite to learning the lessons needed to prevent them.¹ Tort reform is a difficult path, however, and most of the gates are guarded by lawyers, both in the legislature and the judiciary.

Finally, as we begin to discuss errors more openly, it is important not to confuse the results of better error detection and reporting with increased frequency of errors.

■ INNOVATORS IN ERROR REDUCTION

The conclusions of the Institute of Medicine report that medical errors that occur frequently should not have come as a surprise to anyone who has spent much time around hospitals or read the newspapers in recent years. A few famous cases—such as the chemotherapy overdose of Boston Globe writer Betsy Lehman⁷ and the "wrong leg" surgery in a Florida hospital⁸—were highly publicized years before the report. These incidents prompted several important efforts in confronting the problem of medical errors—efforts that should be recognized even as the Institute of Medicine report galvanizes further reform efforts.

Jerod Loeb of the Joint Commission on Accreditation of Healthcare Organizations and the late Mark Eppinger of the Annenberg Center for Health Sciences conceived the First Annenberg Conference devoted to medical errors in 1996. And the Joint Commission went on to develop and define the concept of the "sentinel event," which uses an event resulting in a serious injury or death to trigger an analysis of the root cause of the error, so that the system can be analyzed and recurrences of the error prevented.

These early efforts at systemizing our approach were an important step. Further reduction of errors is one important aspect of an effective overall quality improvement program. It will be difficult, and the learning curve will be steep, but the payoff will be well worth the effort and the risk. ■

■ REFERENCES

1. Kohn LT, Corrigan JM, Donaldson MS, editors. Institute of Medicine Committee on Quality of Health Care in America: To Err is Human. National Academy Press, Washington, DC, 1999.
2. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. *N Engl J Med* 1991; 324:370-376.
3. Thomas EJ, Studdert DM, Burstin HR, et al. Incidence and types of adverse events and negligent care in Utah and Colorado. *Med Care*. In press.
4. Waller R, Grealy M. Avoid "culture of blame." *USA Today*, Dec 3, 1999; 28A.
5. Cook R, Woods D. Operating at the sharp end: the complexity of human error. In Bogner MS, editor, *Human Error in Medicine*. Hillsdale, NJ: Lawrence Erlbaum Associates, 1994.
6. Berwick DM. Taking action to improve safety: how to increase the odds of success. In *Proceedings of Enhancing Patient Safety and Reducing Errors in Health Care*, Annenberg Center for Health Sciences at Eisenhower, Rancho Mirage, CA, 1998.
7. Knox RA. Doctor's orders killed cancer patient: Dana-Farber admits drug overdose caused death of Globe columnist, damage to second woman. *The Boston Globe* 1995, March 23; metro/region 1.
8. Stanley D. Amputee recovering after wrong leg taken. *The Tampa Tribune* 1995, Feb 28; A1.

ADDRESS: John D. Clough, MD, *Cleveland Clinic Journal of Medicine*, NA32, 9500 Euclid Avenue, Cleveland, Ohio 44195; e-mail ccjm@ccf.org.

In hypertension or angina... Convenient once-daily dosing

The usual starting dose is 5 mg in hypertension or angina

—In hypertension, small, fragile, or elderly individuals, or patients with hepatic insufficiency may be started on 2.5 mg once daily

Titration can proceed to 10 mg

—Most angina patients will require 10 mg

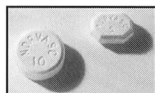
Can be taken with or without food

An excellent side-effect profile

DOSE-RELATED SIDE EFFECTS	NORVASC 5 mg (%) (N=296)	NORVASC 10 mg (%) (N=268)	PLACEBO (%) (N=520)
ADVERSE EVENT			
Edema	3.0	10.8	0.6
Dizziness	3.4	3.4	1.5
Flushing	1.4	2.6	0.0
Palpitation	1.4	4.5	0.6

Once-Daily 5-mg and 10-mg tablets
NORVASC[®]
(amlodipine besylate)

The most prescribed cardiovascular agent in the world^{4*}



Rx
Norvasc 5 mg
30
Sig: 1 tablet
po daily

Among branded cardiovascular agents indicated for hypertension and/or angina.

References: 1. Velasco M, Urbina A, Silva H, et al. A double-blind, parallel, comparative evaluation of amlodipine vs. captopril in the monotherapeutic treatment of mild and moderate essential hypertension. *J Cardiovasc Pharmacol.* 1991;17(suppl 1):S19-S21. 2. Kloner RA, Sowers JR, DiBona GF, Cobb M, Wein M, Gaffney M. Women have a higher response rate than men to the antihypertensive calcium channel blocker amlodipine. *J Am Coll Cardiol.* February 1995;32A. Abstract. 3. Hayduk K, Adamczak M, Nowitzki G. Is initial dose titration of amlodipine worthwhile in patients with mild to moderate hypertension? *Curr Med Res Opin.* 1999;15:39-45. 4. IMS International Prescription Data (based on 29 countries moving annual total), June 1999; IMS National Prescription Audit (total prescriptions), YTD October 1999.



Pfizer U.S. Pharmaceuticals

Brief Summary NORVASC[®] (amlodipine besylate) Tablets

For Oral Use

CONTRAINDICATIONS: NORVASC is contraindicated in patients with known sensitivity to amlodipine.

WARNINGS: Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

PRECAUTIONS: General: Since the vasodilation induced by NORVASC is gradual in onset, acute hypotension has rarely been reported after oral administration of NORVASC. Nonetheless, caution should be exercised when administering NORVASC as with any other peripheral vasodilator particularly in patients with severe aortic stenosis.

Use in Patients with Congestive Heart Failure: In general, calcium channel blockers should be used with caution in patients with heart failure. NORVASC (5-10 mg per day) has been studied in a placebo-controlled trial of 1153 patients with NYHA Class III or IV heart failure on stable doses of ACE inhibitor, digoxin, and diuretics. Follow-up was at least 6 months, with a mean of about 14 months. There was no overall adverse effect on survival or cardiac morbidity (as defined by life-threatening arrhythmia, acute myocardial infarction, or hospitalization for worsened heart failure). NORVASC has been compared to placebo in four 8-12 week studies of patients with NYHA Class I/III heart failure, involving a total of 697 patients. In these studies, there was no evidence of worsened heart failure based on measures of exercise tolerance, NYHA classification, symptoms, or LVEF.

Beta-Blocker Withdrawal: NORVASC is not a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of the dose of the beta-blocker.

Patients with Hepatic Failure: Since NORVASC is extensively metabolized by the liver and the plasma elimination half-life ($t_{1/2}$) is 56 hours in patients with impaired hepatic function, caution should be exercised when administering NORVASC to patients with severe hepatic impairment.

Drug Interactions: *In vitro* data in human plasma indicate that NORVASC has no effect on the protein binding of drugs tested (digoxin, phenytoin, warfarin, and indomethacin). Special studies have indicated that the co-administration of NORVASC with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers; that co-administration with cimetidine did not alter the pharmacokinetics of amlodipine; and that co-administration with warfarin did not change the warfarin prothrombin response time.

In clinical trials, NORVASC has been safely administered with thiazide diuretics, beta-blockers, angiotensin converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, digoxin, warfarin, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic drugs.

Drug/Laboratory Test Interactions: None known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Rats and mice treated with amlodipine in the diet for two years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 mg/kg/day showed no evidence of carcinogenicity. The highest dose (for mice, similar to, and for rats twice* the maximum recommended clinical dose of 10 mg on a mg/m² basis), was close to the maximum tolerated dose for mice but not for rats.

Maternity studies revealed no drug related effects at either the gene or chromosome levels. There was no effect on the fertility of rats treated with amlodipine (males for 64 days and females 14 days prior to mating) at doses up to 10 mg/kg/day (8 times* the maximum recommended human dose of 10 mg on a mg/m² basis).

Pregnancy Category C: No evidence of teratogenicity or other embryo/fetal toxicity was found when pregnant rats or rabbits were treated orally with up to 10 mg/kg amlodipine (respectively 8 times* and 23 times* the maximum recommended human dose of 10 mg on a mg/m² basis) during their respective periods of major organogenesis. However, litter size was significantly decreased (by about 50%) and the number of intrauterine deaths was significantly increased (about 5-fold) in rats administered 10 mg/kg amlodipine for 14 days before mating and throughout mating and gestation. Amlodipine has been shown to prolong both the gestation period and the duration of labor in rats at this dose. There are no adequate and well-controlled studies in pregnant women. Amlodipine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether amlodipine is excreted in human milk. In the absence of this information, it is recommended that nursing be discontinued while NORVASC is administered.

Pediatric Use: Safety and effectiveness of NORVASC in children have not been established.

ADVERSE REACTIONS: NORVASC has been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. In general, treatment with NORVASC was well-tolerated at doses up to 10 mg daily. Most adverse reactions reported during therapy with NORVASC were of mild or moderate severity. In controlled clinical trials directly comparing NORVASC (N=1730) in doses up to 10 mg to placebo (N=1250), discontinuation of NORVASC due to adverse reactions was required in only about 1.5% of patients and was not significantly different from placebo (about 1%). The most common side effects are headache and edema. The incidence (%) of side effects which occurred in a dose related manner are as follows: edema (1.8% at 2.5 mg, 3.0% at 5.0 mg, and 10.8% at 10.0 mg, compared with 0.6% placebo); dizziness (1.1% at 2.5 mg, 3.4% at 5.0 mg, and 3.4% at 10.0 mg, compared with 1.5% placebo); flushing (0.7% at 2.5 mg, 1.4% at 5.0 mg, and 2.6% at 10.0 mg, compared with 0.0% placebo); and palpitation (0.7% at 2.5 mg, 1.4% at 5.0 mg, and 4.5% at 10.0 mg, compared with 0.6% placebo).

Other adverse experiences which were not clearly dose related but which were reported with an incidence greater than 1.0% in placebo-controlled clinical trials include the following: headache (7.3%, compared with 7.8% placebo); fatigue (4.5%, compared with 2.8% placebo); nausea (2.9%, compared with 1.9% placebo); abdominal pain (1.6%, compared with 0.3% placebo); and somnolence (1.4%, compared with 0.6% placebo).

For several adverse experiences that appear to be drug and dose related, there was a greater incidence in women than men associated with amlodipine treatment as follows: edema (5.6% in men, 14.6% in women, compared with a placebo incidence in men of 1.4% and 5.1% in women); flushing (1.5% in men, 4.5% in women, compared with a placebo incidence of 0.3% in men and 0.9% in women); palpitations (1.4% in men, 3.3% in women, compared with a placebo incidence of 0.9% in men and 0.9% in women); and somnolence (1.3% in men, 1.6% in women, compared with a placebo incidence of 0.8% in men and 0.3% in women).

The following events occurred in $\leq 1\%$ but $>0.1\%$ of patients in controlled clinical trials or under conditions of open trials or marketing experience where a causal relationship is uncertain; they are listed to alert the physician to a possible relationship: **cardiovascular:** arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, hypotension, peripheral ischemia, syncope, tachycardia, postural dizziness, postural hypotension; **central and peripheral nervous system:** hypoesthesia, paresthesia, tremor, vertigo; **gastrointestinal:** anorexia, constipation, dyspepsia, dysphagia, diarrhea, flatulence, vomiting, gingival hyperplasia; **general:** asthenia, back pain, hot flushes, malaise, pain, rigors, weight gain; **musculo-skeletal system:** arthralgia, arthrosis, muscle cramps; **myalgia;** **psychiatric:** sexual dysfunction (male** and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization; **respiratory system:** dyspnea, epistaxis; **skin and appendages:** pruritus, rash, rash erythematous, rash maculopapular; **special senses:** abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus; **urinary system:** micturition frequency, micturition disorder, nocturia; **autonomic nervous system:** dry mouth, sweating increased; **metabolic and nutritional:** thirst; **hemopoietic:** purpura.

The following events occurred in $\leq 0.1\%$ of patients: cardiac failure, pulse irregularity, extrasystoles, skin discoloration, urticaria, skin dryness, alopecia, dermatitis, muscle weakness, twitching, ataxia, hypertension, migraine, cold and clammy skin, apathy, agitation, amnesia, gastritis, increased appetite, loose stools, coughing, rhinitis, dysuria, polyuria, parosmia, taste perversion, abnormal visual accommodation, and xerophthalmia.

Other reactions occurred sporadically and cannot be distinguished from medications or concurrent disease states such as myocardial infarction and angina.

NORVASC therapy has not been associated with clinically significant changes in routine laboratory tests. No clinically relevant changes were noted in serum potassium, serum glucose, total triglycerides, total cholesterol, HDL cholesterol, uric acid, blood urea nitrogen, creatinine or liver function tests.

NORVASC has been used safely in patients with chronic obstructive pulmonary disease, well compensated congestive heart failure, peripheral vascular disease, diabetes mellitus, and abnormal lipid profiles.

OVERDOSAGE: Single oral doses of 40 mg/kg and 100 mg/kg in mice and rats, respectively, caused deaths. A single oral dose of 4 mg/kg or higher in dogs caused a marked peripheral vasodilation and hypotension.

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. In humans, experience with intentional overdosage of NORVASC is limited. Reports of intentional overdosage include a patient who ingested 250 mg and was asymptomatic and was not hospitalized; another (120 mg) was hospitalized, underwent gastric lavage and remained normotensive; the third (105 mg) was hospitalized and had hypotension (90/50 mmHg) which normalized following plasma expansion. A patient who took 70 mg amlodipine and an unknown quantity of benzodiazepine in a suicide attempt, developed shock which was refractory to treatment and died the following day with abnormally high benzodiazepine plasma concentration. A case of accidental drug overdose has been documented in a 19 month old male who ingested 30 mg amlodipine (about 2 mg/kg). During the emergency room presentation, vital signs were stable with no evidence of hypotension, but a heart rate of 180 bpm. Ipecac was administered 3.5 hours after ingestion and on subsequent observation (overnight) no sequelae were noted.

If massive overdose should occur, active cardiac and respiratory monitoring should be instituted. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine), should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. As NORVASC is highly protein bound, hemodialysis is not likely to be of benefit.

*Based on patient weight of 50 kg.
**These events occurred in less than 1% in placebo controlled trials, but the incidence of these side effects was between 1% and 2% in all multiple dose studies.

More detailed professional information available on request.
Revised June 1996