ADVERSE DRUG EVENTS AND MEDICATION ERRORS:

LESSONS LEARNED AT THE SHARP END

Internal Medicine Grand Rounds
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Drug therapy is the most powerful tool used by internists in modern medical practice. New drugs are developed and approved for marketing at a pace never seen before. This boon of therapeutics has come with several difficult issues. Drug related morbidity and mortality have been estimated to cost thousands of lives and billions of dollars each year in the United States alone.[1,2,3,4,5] Recent estimates list drug related mortality among the leading causes of death.[6] Public awareness of the hazards of medications is rising due to media coverage and legislation passed by the U.S. Senate requiring reporting of drug safety to the public. The Health Care Financing Administration has proposed requirements for monitoring adverse drug events and sanctions for hospitals that fail to do so.[7] HCFA may someday view passing on charges for averse dug events as fraud.[8] For these and many other reasons the focus on pharmacotherapeutics will continue to sharpen. The benefits of drug therapy outweigh the risks, but it is our responsibility to scrutinize the risks carefully. These grand rounds will discuss adverse drug events (ADE) and Medication Error as they affect patients and physicians.

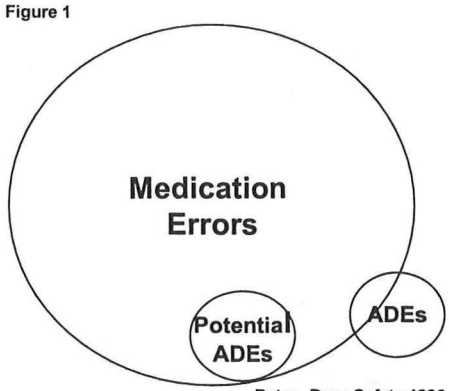
Patient safety has been foremost in the minds of all physicians since the inception of the Hippocratic Oath with the vow, *primum non nocere*. The effect of untoward events in patient care on the practitioners is often under-emphasized. Studies of human error in high-risk industries shed light on management and prevention of error. The successes of this "systems error" approach to mistakes could be applied to the practice of medicine. Examination of ADEs and medication errors, the preventable and the unavoidable, can be a valuable exercise in developing an approach to adverse events. The goals of a new approach will include error-proofed medication systems in health care to avoid patient harm, new mechanisms for monitoring drug safety, and optimal exchange of information among practitioners.

DEFINITIONS

The World Health Organization defined an adverse drug reaction (ADR) as any noxious, unintended, and undesired effect of a drug that occurs at doses used in humans for prophylaxis, diagnosis or therapy.[9] The definition excludes therapeutic failures, intentional and accidental poisoning (i.e. overdose), drug abuse, and noncompliance. Recent preference is to use the term adverse drug event (ADE) which is an injury resulting from medical intervention related to a drug (thereby including errors in administration). For example, oversedation caused by ten fold overdose of Versed (order for 1.0mg misread as 10mg) that leads to aspiration pneumonia would not be considered an ADR by the WHO definition, but is clearly an ADE. As in the above example, many ADEs are dose-dependent, related to the pharmacologic characteristics of a drug and predictable.[10]

Medication errors are a larger group defined as any error in the process of giving patients a drug. These can include errors in prescribing, ordering, transcribing, dispensing, administering and consuming of medications. Only about one in one hundred medication errors result in an ADE. However, seven in one hundred medication errors are caught as "near misses" or potential ADEs (fig 1).

Figure 1



Bates, Drug Safety 1996

There is disheartening evidence that medication error deaths are on the rise, even at a rate disproportionate to the rise in prescribing rates.[11] Fatal medication errors are often the most publicized types of ADEs. Examples from the last decade include the Dana Farber chemotherapy overdose incidents, and the death of a newborn in Denver after IV administration of Benzathine Penicillin G.

In 1981 Naranjo and colleagues suggested a method for estimating the probability that a given outcome is the result of an ADR.[12] It has remained the standard in this field of study. Table one includes their ten criteria and scoring system. Using physicians and pharmacists as reviewers, the intraclass correlation coefficient of reliability of the method was 0.92 in the original paper. Of course, with increasing complexity of pathophysiology and increasing numbers of drugs involved, the method becomes less reliable.

Table 1

ADR probability scale

To assess the adverse drug reaction, please answer the following questions and give the pertinent score.

	Yes	No	Don't Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4. Did the adverse reaction reappear when the drug was re-administered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10. Did any objective evidence confirm the adverse event?	+1	0	0	

Scoring: >9 definite, 5-8 probable, 1-4 possible, and <1 doubtful

Naranjo et al. Clin Pharmacol Ther August 1981.

Certain classes of drugs are frequently associated with ADEs (table 2). Many studies list the drugs involved in the majority of incidents at their institutions. Table two includes a representative list. Antibiotics, narcotics, sedatives and toxic drugs such as chemotherapeutic agents are commonly cited culprits. The remainder of the list includes many drugs of narrow therapeutic index such as anticoagulants, anticonvulsants, antiarrhythmics and other cardiovascular agents.

Table 2

Drug Classes Associated with ADEs	
Analgesics (Narcotics)	Sedatives
Antibiotics	Anticonvulsants
Cardiovascular	Diabetes (Hypoglycemics)
Anticoagulants	Electrolytes
Chemotherapy	Others

INCIDENCE AND PREVELANCE OF ADES

The incidence and prevalence of ADEs and medication errors are difficult to determine. Methods for gathering data rely on retrospective chart review, self-reporting and computer generated reports, all of which can be expensive and inaccurate. Spontaneous reporting, such as incident reporting, is the preferred method of tracking ADEs in most institutions and is widely recognized to underestimate the number of events, detecting only about 5%.[13,14,15] Even the FDA's MedWatch[16] program, a large enough database to identify rare ADRs, is limited in that it does not track ADEs due to error. Table 3 shows the characteristics of ADRs reported to the FDA between 1985 and 1989. There was little difference in the proportions of reports associated with death or hospitalization when newer drugs were compared with older drugs. In 1994 the FDA received 73,887 reports of ADRs, only 5.2% of which were directly from physicians.[17] Some investigators have looked at what prompts a physician to report, and what barriers exist. Underreporting has been attributed to ignorance of reporting procedures, fear of involvement in litigation, complacency about drug safety, diffidence about reporting mere suspicions, and lethargy.[18] Factors that increase reporting are severe reactions, idiosyncratic versus pharmacologic reactions, and previous publicity about reactions.[19]

Table 3

Severity of Adverse Drug Reactions Reported to the Food and Drug Administration by Age or Suspect Drug

Severity	**New Drugs,* No. (%)**	**Older Drugs, No. (%)**
Death	1220 (3.8)	5420 (4.7)
Hospitalization	4885 (15.4)	18992 (15.8)
Neither	25695 (80.8)	96097 (79.5)
Total	31800 (100.0)	120509 (100.0)

Faich. Arch Intern Med August 1991.

The FDA MedWatch program is the only formal way of documenting post-marketing drug safety. More than 51% of approved drugs have serious adverse effects discovered in post-marketing surveillance.[20] There are concerns about the FDA's ability to safely police the greater than 5000 drugs in use today, let alone the new medications that it approves each year (92 drugs in 1996-97). The questions concern the reliability of voluntary reporting, the amount of resources available for thorough and appropriate investigation, and the possibility of conflict of interest. Pharmaceutical companies are required by law to report adverse events, but they must first receive documentation of the event. Dispassionate investigation by either the manufacturer, or FDA personnel who feel personally responsible for approving a drug, may be difficult. The costs of these investigations can be staggering—and cannot legally be defrayed by the New Drug Application Fees (c.f. Modernization Act of 1997). As it stands the FDA's Division of Pharmacovigilance and Epidemiology (to be renamed the Office of Post-Marketing Drug Risk Assessment) is overwhelmed and often must rely on the manufacturer to complete investigation of the reports.

Research on ADEs is sparse and underfunded when compared with other major causes of morbidity. The study of ADEs does not fall into the realm of any one medical specialty, though pharmacy research has made some strides. The FDA is not a funding agency and other sources of moneys for this research are scarce.[21] It is widely accepted that a large number of ADRs are unpreventable (e.g. previously undocumented allergy, idiosyncratic reactions, etc.) In reality, many "unavoidable" events are, at second glance, preventable. Avoiding readministration of the same drug requires appropriate documentation of the reaction, patient education and communication of the information to other practitioners and pharmacies that may care for the patient outside the site of the initial incident. As the study of medical genetics progresses we may some day be able to predict some "unavoidable" reactions—there are already well-described genetic polymorphisms in P450 cytochromes among ethnic groups.[22]

The Harvard Medical Practice Study published in 1991 is still widely quoted as an important study in determining the incidence and nature of adverse outcomes in hospitalized patients. They studied a randomly selected sample from patients hospitalized in New York in 1984.[3,5] From 30,195 hospital records they defined an adverse outcome as an unintended injury caused by medical treatment that resulted in measurable disability. The overall incidence was of these serious events was 3.7% (1133 patients). Drug misadventures were implicated in 19% of all injuries to patients. There were 153 incidents of errors in drug treatment analyzed. Errors in choosing therapy, dosing drugs, following therapy, recognizing drug-drug interactions, and delaying therapy were all cited amongst the preventable events.

To look at the incidence of actual and potential ADEs, a group at Brigham and Women's Hospital undertook a prospective study in 1993. Extrapolated event rates for the hospital were 6.5 ADEs and 5.5 potential ADEs per 100 nonobstetrical admissions. Of all ADEs almost 1% were fatal, 12% were life-threatening and 30% were serious. Preventable ADEs comprised 28% of the total, but 48% of the life-threatening and

serious ADEs. None of the fatal ADEs were judged preventable. Of interest, errors resulting in ADEs were common at several steps of the medication use process. Ordering errors were most common and were intercepted almost half the time. On the other hand administration errors were never intercepted during the study (table 4).[2]

Table 4

Stages of Primary Errors Associated with Preventable and Potential Adverse Drug Events (ADEs)				
	Stage of Event			
	Ordering No. (%)	Transcription No. (%)	Dispensing No. (%)	Administration No. (%)
Preventable ADEs (n=70)	39 (56)	4 (6)	3 (4)	24 (34)
Intercepted potential ADEs (n=83)	62 (75)	7 (8)	14 (17)	0 (0)
Non-intercepted potential ADEs (n=111)	27 (24)	19 (17)	21 (19)	44 (40)
All above events (n=264)	128 (49)	30 (11)	38 (14)	68 (26)

Bates. JAMA July 1995.

Lazarou et al published a meta-analysis of thirty-nine heterogeneous prospective studies of ADRs in 1998. They studied hospitalized patients and suggested an overall serious ADR incidence of 6.7% with fatal ADR incidence of 0.32%. When applied to the sum of all hospitalized patients in 1994 they generated a death toll of between 76,000 and 106,000 victims of ADRs in that year alone, ranking between the fourth and sixth most common cause of death. By including only ADRs and excluding medication errors, the authors comment that their study points out the hazards of drugs even when properly prescribed and administered.

Table 5

Studies on ADRs in Patients while in the Hospital (ADRIn)*

Source, y	Wards Studied†	Study Size	Incidence of ADRs, %‡ All Severities	Serious	Fatal
Bates et al, 1995	1, 7	379	5.3	0.8	0
Bates et al, 1995	1, 2	4031	4.4	1.5	0.08
Bowman et al, 1994	1	1024	10.3	1.1	. . .
Bates et al, 1993	1, 2, 6, 8	420	3.6	1.9	0
Steel et al, 1981	1	815	14.8	2.8	. . .
Mitchell et al, 1979	4	1669	16.8	. . .	. . .
Bennett & Lipman, 1977	1, 2	152	7.2	1.4	. . .
May et al, 1977	1	334	10.2	. . .	. . .
Miller, 1973§	1	11526	22.5	2.4	0.29
McKenzie et al, 1973	4	658	12.2	2.3	0.15
Wang & Terry, 1971	1, 2	8291	1.2	. . .	0.01
Gardner & Watson, 1970	1	939	10.5	2.1	0.85
Borda et al, 1968	1	830	24.1	6.0	. . .
Sidel et al, 1967	1	267	10.9	. . .	. . .
Seidl et al, 1966	1	714	13.6	0.8	0.42
Smith et al, 1966	1	900	10.8	. . .	0.22
Reichel, 1965	1	500	8.2	. . .	. . .
Schimmel, 1964	1	1014	10.2	0.8	0.39

* ADR indicates adverse drug reaction; ADRIn, an ADR occurring in patients while in the hospital; and ellipses, data not available.

† Wards studied: 1, medical; 2, surgical; 3, geriatric; 4, pediatric; 5, psychiatriac; 6, internal medicine; 7, intensive care; and 8, obstetric.

‡ Incidence of ADRs = (number of patients with ADR/total patients studied) x 100.

§ This study performed by the Boston Collaborative Drug Surveillance Program was categorized as United States in our analysis since only 1787 of the 11526 patients were from hospitals outside the United States.

Lazarou et al. JAMA April 1998

There are several criticisms of this meta-analysis and other studies of the incidence of ADEs.[23] The inherent limitations of the meta-analysis readily apply to Lazarou's data particularly with the heterogeneity of the primary data. Also, these studies are conducted in academic, tertiary care institutions with a sicker patients and may not be generalizable to the U.S. hospital patient population. The sites of care in many studies overrepresent medical wards where the most medications are used in the oldest patients. These considerations lead to a conclusion that these studies may overestimate the importance of ADEs. Gathering this data is difficult and fraught with error, but it is intended to help justify devoting more resources to developing systems that reduce preventable ADEs. There is value in examining why there is such discrepancy between these studies and what is perceived as the true incidence. There are strong incentives not to identify ADEs in hospitals. These include scrutiny and negative attention from the media, the public and regulatory bodies. For instance, though nurses are an invaluable resource for recognizing and reporting ADEs, in Texas the State Board of Nursing requires automatic review for nurses involved in more than 3 incidents in a year (an incident includes a medication error).[24] Understandably, reporting could be seen as self-incrimination.

ECONOMIC IMPACT

Studies of the costs of ADEs in hospitalized patients uniformly demonstrate substantial costs related to increased length of stay, increased hospital cost and disability.[5,25] Classen's study of 91,574 admissions to LDS hospital in Salt Lake City, Utah in 1997 found that 2.43 per hundred patients suffered a severe ADE.[26] The low incidence relative to other large studies was felt to reflect the computer order entry system at LDS that can intercept many potential ADEs.[21,27,28] Analysis suggested that each ADE increased the length of stay of 1.91 days, and increased direct hospital cost at $2262 per incident. The relative risk of death in patients who suffered an ADE versus those who did not was 1.88.

Table 6 outlines the costs associated with some of their most commonly identified ADEs. The Adverse Drug Events Prevention Study Group in Boston also studied cost to the hospital for ADEs. They found an average cost of $2595 per event, but for preventable events the cost was $4685 probably because the preventable events tended to be more severe. Other potential costs of ADEs not measured in these studies include injury to the patient and malpractice litigation. Drug injuries frequently result in malpractice claims, accounting for the largest total awards of any procedure-related claim in the 1970s.[29]

Table 6

Attributable Costs for Various Types of Adverse Drug Events

Type of ADE	Total # of Patients	Attributable Cost, $	Attributable Length of Stay, d
Cardiac arrhythmia	561	4410	3.93
Diarrhea	182	4631	4.40
Fever	26	9022	5.49
Nausea/vomiting	526	712	1.37
Renal failure	324	1371	4.54
Confusion	98	232	2.50
Rash	108	1868	1.37
Itching	548	677	0.72
Hypotension	75	3563	2.94
Bleeding	26	6702	4.89

Classen et al. JAMA January 1997.

There is also data regarding ADEs that result in hospital admission, and the entire cost of the hospital stay. Drug-related illness represents a significant impact of ADEs and account for 1-4% of all hospital admissions.[30,31,32] This was confirmed by Lazarou et al in their 1998 meta-analysis that determined a 4.7% incidence of serious ADRs leading to admission. (Recall that measuring ADRs excludes errors of administration and noncompliance.) Einarson's 1993 meta-analysis estimated that 5% of all hospital admissions resulted from drug-related problems. He studied events related to both OTC and prescribed drug therapies, including compliance, but excluding overdoses and intentional poisoning, suicide attempts, and drug abuse. At the time of his review only one report had involved folk remedies or herbal medicines. A study in Hong Kong in 1990 identified 0.2% of acute medical admissions due to the use of herbal medicines.[33] With the increasing popularity of herbal medicines, this can be expected to have risen significantly. In one study, 21.7% of urban emergency department patients reported the use of herbal preparations, 15.6% were using the herbs to treat their chief complaint.[34] Emergency Department visits for drug-related illnesses account for about 5% of all visits. About two thirds of these ED visits are felt to be preventable, partly because they include a large proportion of the events involving prescribing errors and noncompliance.[35] Noncompliance is a significant factor in ED visits in particular and might be reduced by specific counseling provided by pharmacists. Obviously, many physician office visits are also prompted by adverse drug events.

Table 7

Characteristics of Drug-Related Illnesses (DRIs) in Patients Visiting the Emergency Department (n=50)

DRI Characteristic	No. (%) DRIs with Characteristic
Cause	
Noncompliance[a]	29(58)
Inappropriate prescribing[b]	5 (10)
Adverse drug reaction[c]	16 (32)
Manifestation	
Allergic reaction	7 (14)
Asthma exacerbation	7 (14)
Hypoglycemia or hyperglycemia	6 (12)
Seizures	3 (6)
Bleeding	3 (6)
Heart disease	3 (6)
Other	21 (42)
Severity	
Mild	9 (18)
Moderate	33 (66)
Severe	8 (16)
Medication involved	
Albuterol	5 (10)
Insulin	4 (8)
Warfarin	4 (8)
Phenytoin	3 (6)
Prednisone	2 (4)
Glyburide	2 (4)
Other	30 (60)

[a]Attributable to the patient running out of medication (10 DRIs), stopping a medication regimen intentionally (7), taking medication inconsistently (6), taking medication incorrectly (5), and taking the wrong medication (1). Drugs most commonly involved in these 20 DRIs were those in metered-dose inhalers (7 DRIs) and insulin and phenytoin (3 each).

[b]Attributable to prescribing an excessive dosage (2 DRIs), failure to prescribe therapy for an expected drug-related complication (1), prescribing a drug for which an allergy was documented (1), and giving improper dosage instructions (1).

[c]Classified as untoward (8 DRIs, most commonly upset stomach from antimicrobials or nonsteroidal anti-inflammatory drugs and bleeding from Warfarin), hypersensitivity related (5, most commonly antimicrobial-related pruritis or rash), and idiosyncratic (3).

Recommendations of an Expert Panel. Am J Health Syst Pharm June 1996.

CAUSES OF ADVERSE DRUG EVENTS

Prescribing errors have been identified as a major cause of ADEs.[1,2,3,5] Researchers have identified many factors contributing to these errors. Specific factors described include: calculation of drug dosage, placement of decimal points, inappropriate consideration of pathophysiologic characteristics of the patient, use of abbreviations, complicated dosage regimens, and poor patient history taking (e.g. known drug allergy).[36] Therapies are often duplicated within the same class of medication, subject to drug-drug interactions, or improperly dosed for renal or hepatic impairment. The etiologies of these errors are lack of knowledge, inadequate access to detailed drug and patient information, and mental slips.

Studies of prescribing errors document increases in errors per order written, per admission and per patient day between 1987 and 1995.[36] As the numbers of drugs used rises, so does the opportunity for these errors (figure 2).[37] The number of prescribed medications per patient per hospitalization is currently about ten on average, more in critically ill patients.[38] Cullen et. al. found the rate of preventable and potential ADEs was twice as high in intensive care units compared with non-ICU settings. However, after adjustment for the number of drugs ordered, the likelihood of error was the same.[39] In a study of elderly nursing home residents, the probability of mortality was positively correlated with the number of inappropriate drugs prescribed, the number of prescribers, and the number of pharmacies used.[40]

Figure 2

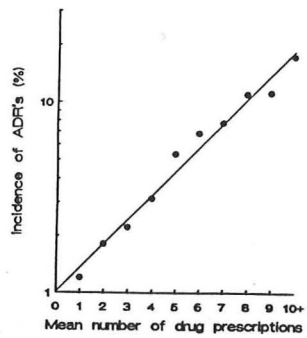


FIGURE 4. Incidence of ADR's (on logarithmic scale) stratified by number of drug prescriptions administered during hospitalization to each patient. Chi-square in 2 × 10 table = 349, $P < 0.0001$.

Carbonin JAGS 1991

DETECTION OF ADVERSE DRUG EVENTS

Computerized detection of ADEs, predominantly by pharmacy computer systems is effective in both reducing and detecting ADEs.[21,28,41] Alerts based on known allergies and drug-drug interactions print up in the pharmacy before drugs are dispensed. Drug ordering can be linked to forcing functions that won't allow the pharmacist to enter an order that conflicts with an allergy. More sophisticated systems flag the use of antidote drugs such as naloxone and protamine, or pick up prescriptions of antimotility drugs and antihistamines as possibly indicating ADEs such as diarrhea or rash. When the pharmacy computer can integrate laboratory data, warnings such as thrombocytopenia can be provided for patients receiving heparin. These alerts are not always appropriate (true-positive alerts), as rule based programming of the computer is understandably complex. However, these systems provide an opportunity to catch prescribing errors and create near-miss medication errors instead of actual ADEs.

Many investigators enlisted physicians as part of their efforts to identify ADEs. Often the method was retrospective chart review. Pharmacist reviewers were likely to catch some events missed by physicians. Further, the weakness inherent in relying on documentation in the medical chart is well described. In an interesting study at Brigham and Women's Hospital, housestaff physicians were asked to participate in a prospective e-mail based reporting system. The results compared with standard chart review. The number of reports generated by each method was similar, but only identified about 50% of the same patients. Notably, the housestaff based reporting system identified twice as many preventable ADEs at 28% of the cost of chart review. Interviews with the physicians who participated revealed that they did not feel scrutinized, or under any pressure to "snitch" on one another. They believed that their contribution would

contribute to the quality of patient care. The willingness to participate may have stemmed some from the reassurance that the investigators were completely independent of any line of authority over the residents.[42]

PREVENTION OF ADEs

Computerized decision support and computer order entry are touted as important deterrents to prescribing errors. Hospital computer systems that integrate patient-specific data (such as major diagnoses), laboratory values, medication allergies, pharmacy, and radiology orders have been shown to reduce avoidable ADEs in both the community hospital and teaching hospital settings.[27,28] Systems of computer order entry are designed to provide the physician with appropriate dosing information, indicate duplicate therapies, warn about allergies and drug interactions, and alert the physician to critical lab values that affect prescribing, e.g. rising creatinine in a patient on aminoglycosides.[43] The reduction in serious medication errors was 55% and in ADEs 17% with this type of system.[21]

Figure 3

IHC ANTIBIOTIC ASSISTANT AND ORDER PROGRAM

00000000 Doe, John Q. E615 77yr M Diagnosis:PANCREATITIS
Max 24 hr WBC = 26.3 ↑ (21.1) Admit: 06/21/96.17.50 Max 24 hr Temp = 38.3 ↑ (37.8)
RENAL FUNCTION: Impaired, CrCl = 28, Max 24hr Cr = 2.0 ↓ (2.2) IBW: 77kg
Patient's Diff shows a left shift, Max 24hr Bands = 20 ↑ (8)
ANTIBIOTIC ALLERGIES: Ofloxacin
CURRENT ANTIBIOTICS:
1. 07/14/96.17:23 AMPHOTERICIN B, VIAL 45 Q 24hrs
2. 07/18/96.12:19 VANCOMYCIN (VANCOCIN), VIAL 1000 Q 72hrs
Total amphotericin given = 181 mg

IDENTIFIED PATHOGENS	SITE	COLLECTED
Enterococcus	T-Tube	07/17/96.10:57
Staphylococcus aureus	Blood	07/17/96.10:28
Candida albicans	Abdomen	07/14/96.06:23

ABX SUGGESTION	DOSAGE	ROUTE	INTERVAL
Vancomycin	*1000 mg	IV	*q72h (infuse over 1hr)
Amphotericin B	45 mg	IV	q24h (infuse over 2-4hr)

Suggested antibiotic duration: 28 days
*Adjusted based on patient's renal function
<1> Micro, <2> OrganismSuscep, <3>Drug Info, <4>ExplainLogic, <5>Empiric Abx
<6>Abx Hx <7>ID Rnds, <8>Lab/Abx Levels, <9>Xray, <+ or F12> Change Patient
<Esc>Exit, <F1>Help, <0>User Input, <.>Outpatient Models
ORDERS:<*>Suggested Abx, <Enter>Abx List, </>D/C Abx, <->Modify Abx

Example of the Type of Information Initially Displayed When the Computerized Antiinfectives-Management Program is used.
Dx denotes diagnosis, max maximal, WBC white cell count, CrCl creatinine clearance, Cr serum creatinine, IBW ideal body weight, Diff differential, arrows direction of change, IV intravenous, Abx antiinfective, Hx history, ID Rnds infectious disease rounds, Lab laboratory and D/C discontinue.
Evans et al. NEJM 338(4)1998.

LDS hospital in Salt Lake City has one of the most advanced clinical information systems in the country. In 1998, Evans, Pestotnik and Classen described their disease management program for antibiotics.[27] The program used computerized clinical decision support system (CDSS) for all patients receiving antibiotics during the study period. Their computer automatically provided physicians with patient, laboratory, and cost data before order entry (figure 3). Though the computer made suggestions, the physician could bypass the recommendations with impunity. Their results showed impressive decreases in cost of antibiotics and total hospital stay, ADEs, and prescribing errors related to known allergies and pathogen's drug sensitivities. Time savings were also striking: an infectious disease consultant used on average 14 minutes to find all the data provided by the computer screen in 3.5 seconds. Currently these pilot programs have integrated computer systems that are available in only about thirty percent of U.S. hospitals.[44]

Unfortunately, computer-based strategies for improving care are often met with resistance. Hunt, et al. reviewed 65 studies assessing the impact of clinical decisions support systems on clinician behavior. "Improvement" in behavior could be demonstrated in providing preventative care such as vaccinations (74%) and drug dosing (60%), but only one in five systems with diagnosis and management protocols had positive results.[45] Physicians resent the implication that a machine can do what they are long-trained to do and believe that a machine could never appreciate the subtleties and complexities of patient care. In studies evaluating computer based strategies of medication use, concurrence between computer-derived alerts and professional opinion ranges from 10-50%. Compendiums of drug information often don't agree on which of the described events are clinically significant. The danger inherent in these systems, then, is that their benefits may be outweighed by indifference and irritation brought on by overload of questionably valuable information.[21,46] Bainbridge described the two major "ironies of automation" as: a) Designer's errors make significant contributions to the accidents and events they are intended to prevent. b) Despite the design to eliminate human beings, the operator is still left with the tasks the designer cannot think how to automate.[47] To computerize a highly complex task such as drug prescribing and dispensing requires a huge investment in operator training and a very sophisticated and expensive system.

AN APPROACH TO ERROR IN MEDICINE

The concepts of preventable ADEs and medication errors open up a whole topic of discussion that is uncomfortable for many physicians and other health care providers. The medical literature has presented evidence over the last several decades of the real hazards of medical care. In 1964 Schimmel reported that 20% of patients admitted to a university hospital medical service suffered iatrogenic injury, 20% of which were fatal.[48] Steel again studied iatrogenic events in teaching hospitals in 1981 and found 36% of patients suffered an adverse outcome, half related to the use of a medication.[49] The Harvard Medical Practice Study showed a 3.7% rate of injury to hospitalized patients. If the death rate of 14% in those events were extrapolated to the entire U.S. hospital population, the death rate would be 180,000 patients per year. Lucian Leape of the

Harvard School of Public Health pointed out that this would be equivalent to 3 jumbo jet crashes every two days.[50] It is not surprising that so many "errors" occur when one examines how many actions are performed on a hospitalized patient each day. Even at a 99% level of proficiency, there is a lot of room for error. In other hazardous industries such as aviation and nuclear power, such an error rate was long ago deemed intolerable. Health care may be able to learn some valuable lessons from their approach to improving systems and reducing error.

Discussions of safe systems often include the example of aviation safety. Allnut observed that pilots and physicians are similar in that they are carefully selected, highly trained, and determined to maintain high standards while performing difficult tasks in life-threatening situations.[51] Of course there are important distinctions such as the unpredictability of the human organism and the fact that pilots' lives are on the line as well as those of the passengers. Design for safety in aviation incorporates characteristics that could be useful in medicine. System design in aviation assumes errors and failures are inevitable, therefore the system must absorb them. Procedures are standardized to the maximum extent possible to minimize the use of knowledge based thinking during operation. Pilots willingly submit to external authority, the air traffic controller, when in dangerous situations such as take-off and landings.[50] Studies on the flight decks of aircraft carriers with nuclear weapons reveal the secret to safe operations despite the high potential for serious accidents. In these tightly coupled systems, the "organizational mind" and the social and interpersonal skills of the crew create safety. An autonomous individual is a liability. In emergency situations, hierarchy degrades and the crew becomes more interrelated, subordination is replaced by cooperation and trust.[52] In a medical world, this could be likened to a well-run resuscitation. Everyone knows his or her role, and no one person's observations or contribution are less important than any other's.

Like aviation and nuclear power, medical care involves a host of complex interactions that engineers describe as "tightly coupled".[53] Some characteristics of tightly coupled systems are listed below:

1. Processing delays are unacceptable.
2. Production sequences are relatively invariant
3. There are few ways of achieving a particular goal.
4. Little variance is permissible in supplies, equipment and personnel.
5. Buffers and redundancies are deliberately designed into the system.

Tight coupling means that what happens in one part of the system directly and often quickly and powerfully affects other parts. It is the nature of complex, tightly coupled, highly interactive systems to "spring nasty surprises" on its operators.[54] In any one person's actions, many deviations from ideal performance are tolerated. The medication use process is one example of a system within health care that fits Perrow's description. As mentioned previously, only about one in one hundred medication errors result in an actual ADE. Everyday errors, such as writing the wrong dose, are innocuous but are the same ones that rarely cause accidents. These accidents can be

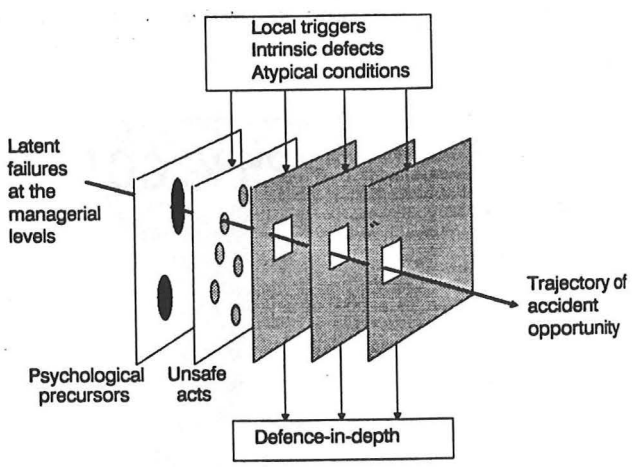
viewed as "errors with sad consequences".[55] Accidents can result from errors when they occur at an inopportune time or under inopportune circumstances. What creates these circumstances is the key to separating human error from system error.

SYSTEMS ERROR VERSUS HUMAN ERROR

In a complex system requiring precise coordination of multiple human and mechanical elements, there are many layers of defense against error. Taken alone, no small failure would breach the system defenses. However, a coincidence of failures of several system components creates opportunity for an accident. These small failures are termed "latent failures".

Reason describes latent failures as "decisions or actions, the damaging consequences of which may lie dormant for a long time, only becoming evident when they combine with local triggering factors to breach the defenses. Their defining feature is that they were present within the system well before the onset of a recognizable accident sequence. They are most likely to be spawned by those whose activities are removed in both time and space from the direct human-machine interface: designers, high-level decision makers, regulators, managers and maintenance staff."[54,56] On the other hand, "active failures" are those errors that result in immediate adverse effects.

Figure 4



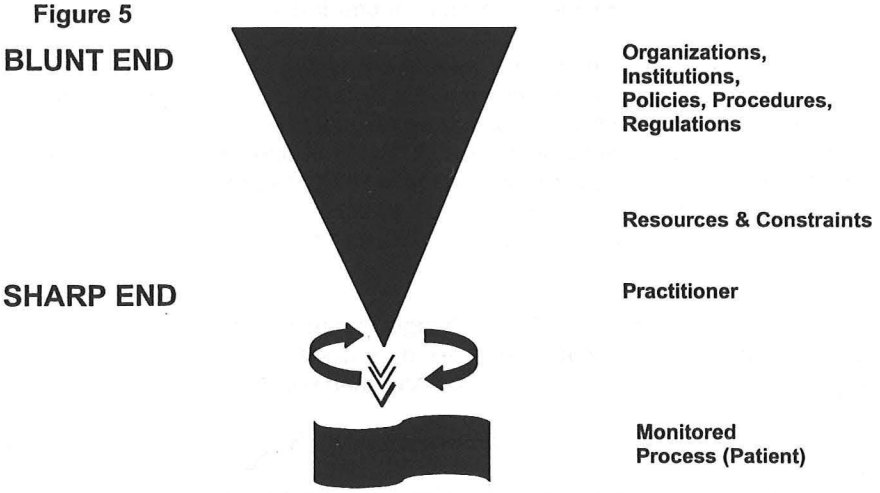
The dynamics of accident causation. The diagram shows a trajectory of accident opportunity penetrating several defensive systems. This results from a complex interaction between latent failures and a variety of local triggering events. It is clear from this figure, however, that the chances of such a trajectory of opportunity finding loopholes in all of the defenses at any one time is very small indeed.

Human Error, Reason, 1995

Reason used an apt medical analogy by describing latent errors as "resident pathogens". Resident pathogens cause disease only in combination with external factors such as immunosuppression or injury. What are the external factors that turn a latent failure into an accident? First, the likelihood of accidents is a function of the total number of latent failures. In large, very complex, tightly coupled systems there will be a greater number of latent failures, but also a proportionate number of defenses against accidents. Those making decisions at the blunt end have a greater opportunity to create latent failures than do those at the sharp end. It is virtually impossible to foresee all the scenarios in which accidents might occur, but latent failures can be assessed given knowledge of and access to the system.

The "sharp end" is the part of a system where there is the most hazard and opportunity for accidents.[57] In medicine, physicians, nurses, pharmacists, and others involved in direct patient care are functioning at the sharp end. The blunt end is composed of organizations (HMO's), institutions, policies and procedures, and regulatory bodies. The "latent failures" created at the blunt end bear down on the practitioners caring for the patient. At the sharp end there are always competing demands, time constraints, dilemmas, and conflicts that operate while we are making decisions and choosing safe actions. These forces introduce latent failures into all levels of the system. Any practitioner has the capacity to be stressed, to fail to perceive hazard, to have inadequate knowledge of equipment, or to suffer less than ideal motivation for the task at hand.

Figure 5



Practitioners at the *sharp end* of the system interact directly with the hazardous process. The conflicts and dilemmas in their technical work arise from institutional, management, regulatory and technological *blunt end factors.*

Cognitive Technologies Lab, Chicago, 1991-1998, Modified from Woods 1991

Learning the right lessons from adverse events in medicine is difficult for many reasons. Our ethical obligation not to harm patients is foremost; but, legal ramifications of adverse events and erosion of public confidence in institutional safety are extremely important. When an accident occurs, those at both the sharp and blunt ends tend to look back at the incident and identify human error as the most important cause of the incident. Too much of the focus after an accident is placed on the "active failure" or the "human error" that was proximal to the event. Part of this phenomenon is due to "hindsight bias".[58] It has at least two important aspects:

a) The 'knew-it-all-along' effect, where observers of past events exaggerate what others should have been able to anticipate in foresight.
b) The unawareness of the influence of outcome knowledge on perceptions of past events.

Wells further refined this concept as the "hindsight illusion". He defined this concept as the belief that something was obvious once the outcome is known (e.g. Monday morning quarterbacking); incorporating the inability to see that a different outcome might change that belief entirely.[59] After an accident, people can be concerned, sad, anxious, and angry. These emotional contexts help to propagate a move to identify blame, thereby allowing assimilation of the event. Finding one cause is simple and comforting. In looking for a cause, or something/someone to blame, people tend to try to "mentally undo" steps leading up to the incident. In these examinations, actions are often easier to "undo" than inaction. However, addressing only the human factors in an accident can be likened to seeing only the "active failure" tip of the iceberg.[54]

What occurs at the blunt end is similar. Institutional reactions to accidents and adverse events are subject to (at least) two human failings. The first is called "fundamental attribution error", or the tendency to blame bad outcomes on the actor's personal deficiencies.[60] The second is "fundamental surprise error", where an incident reveals a profound discrepancy between one's perception of the world and the reality. Fundamental surprises require major reappraisals, whereas situational surprises are more localized events requiring the solution of specific problems.[61] The designers and administrators in a system prefer to respond to fundamental errors as if they were only situational. In this way latent errors persist, hidden in a complex system, awaiting their next victim.

The objectives of a system designed for safety are twofold: first, make it difficult for individuals to err and, second, make the system absorb errors by permitting detection and correction before harm occurs.[62,63]

THE PSYCHOLOGY OF ERROR IN MEDICINE

Physicians are socialized in medical school and residency to strive for error free performance. Perfection is praised and expected, and mistakes are unacceptable. Physicians in training also develop a strong sense of responsibility for their patients. Sometimes the goal of perfection and an overdeveloped sense of responsibility create confusion: the physician feels responsible for any error that occurs in the care of a patient. It is easy to see why this might happen. The word iatrogenic is derived from the Greek root, *iatros* and means "harm originating with the physician". This concept was promoted in the AMA's 1847 Code of Ethics:

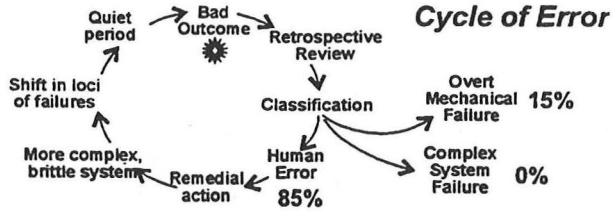
> A physician should not only be ever ready to obey the calls of the sick, but his mind imbued with the greatness of his mission, and the responsibility he habitually incurs in its discharge. (This responsibility is) More deep and enduring, because there is no tribunal other than his own conscience to adjudge penalties for carelessness and neglect.

When errors or accidents occur, physicians can be emotionally devastated by guilt, doubts about competence, and fears of censure or litigation.[64,65] The culture of other caregivers such as nurses and pharmacists is laden with similar stigmata.[66] Most physicians would like to examine and learn from error and ideally begin doing this as medical students. Looking back again provides some insight into why many continue to deal with errors all alone. Pervical in 1803 advised that "errors of omission and commission should be brought into mental view", but the professional etiquette of the era dictated that this not involve discussion with colleagues. This construct implies that errors that don't cause harm are only opportunities for personal improvement or development of moral integrity and technical skill.[67,68] Certainly, opportunities for learning from error should not be limited to one's own error, nor should they stop with reflection on personal failures.[64,68,69] The goals should be educational and practical: linked to improvement of all caregivers, not to the punishment of those who err, and directed toward improvement in patient care.[50,69,70]

Too frequently, the only response to error is to increase knowledge and motivation. Most errors are viewed as being someone's fault and as being rectifiable with more teaching. Leape refers to this as the perfectibility model. The methods used to achieve results are known as "blame and train". Punishment is through peer disapproval and professional censure or, for negligence, through the malpractice tort litigation system.[50] Tort law was designed to reduce the accident rate and to provide a sensible system of compensation insurance for individuals who suffer product or service related accidents. The current system, however, largely impairs accident reduction by requiring responsibility be placed on an individual or corporation.[71] Corrective measures are then directed toward preventing recurrence of a similar error often by that particular person. Casarett, et. al. published a paper in early 1999 addressing the need to find a balance between systems errors and physicians' errors. Though the authors give credence to the concept of system error, they raise concerns about the possibility that attributing errors to system causes decreases the likelihood of learning from mistakes. There is evidence that physicians who ascribe error to system causes are less likely to try and modify their behavior in the future.[68] They propose a balanced solution for academic medical centers. Systems approaches to quality improvement should be a part of formal residency training, and faculty should encourage house officers to search for external causes of their errors and participate in correcting them. Role models and programs must also encourage reflection of "internal" causes of error such as inadequate knowledge or lack of attention to detail.[69,72] Social psychologists have documented the appeal of a "high-status person" (here, the attending) who admits his mistake when confronted with serious consequences and ambiguous evidence.[73]

Using Reason's approach to latent failures could enrich our understanding of errors and allow constructive investigation that prevents multiple future accidents. As mentioned above, human factors introduce both latent and active errors. Sometimes it is appropriate to focus part of the corrective action on the individual, while excessive blame or punishment are harmful. To stop at examining only the human factor is to miss the opportunity to improve the system and make it safer for other practitioners and patients in the future.[50,70,74] We should strive for balance in investigating errors in medical care.

Figure 6



Cook RI. Cognitive Technologies Lab, Chicago, 1991-1998

MEDICATION ERRORS AS A MODEL OF SYSTEM ERROR

Of all the events that lead to patient injury, medication errors are most well studied and documented in both the professional and the lay literature.[75,76,77] As mentioned above in the discussion of ADEs, only about 1% of medication errors lead to an adverse event in a patient. Those that do not cause patient harm are minor, such as missed dose or wrong timing of dose. Systems analyses of ADEs are helpful in pointing out parts of the process that deserve most attention.[63,78] Physician prescribing and nurse administration each comprise about 38% of all medication errors. Pharmacist transcription and dispensing made up the rest.

Dosing errors are the most common type of error, accounting for 28% of all errors. Most dosing problems begin at the physician ordering stage, but are caught by pharmacists and nurses almost three quarters of the time. The proximal causes included lack of knowledge of the drug itself, or of potential drug-drug interactions, simple slips, and memory lapses. Clarity of handwriting and accuracy of phone orders are also cited. Inadequate familiarity with the patient was involved in 14% of errors (e.g. Giving KCl in wrong dose, not knowing the patient had renal failure). Administration errors by nurses were only intercepted 6% of the time as opposed to the safety net for physician errors. Their proximal causes included lack of knowledge of the drug, misuse of infusion pumps, faulty drug identity checking and faulty dose checking. In the pharmacy, failures in drug identity due mostly to sound-alike names and look-alike packaging were common.

Table 8

Common Causes of Medication Errors
• **Ambiguous strength designation on labels or in packaging.**
• **Drug product nomenclature (look-alike or sound-alike names, use of lettered or numbered prefixes and suffixes in drug names).**
• **Equipment failure or malfunction.**
• **Illegible handwriting.**
• **Improper transcription.**
• **Inaccurate dosage calculation.**
• **Inadequately trained personnel.**
• **Inappropriate abbreviations used in prescribing.**
• **Labeling errors.**
• **Excessive workload.**
• **Lapses in individual performance.**
Cohen, Hospital Pharmacy, 1994

A technique called "error mode and effects analysis" has been proposed in examining systems and errors.[62,79] The process looks at a system, identifies possible or likely errors, and gauges what their effects will be even before they take place. An incident is examined with several criteria: the likelihood of occurrence, the severity of failure, and the probability of detection. When this system is used, the value of the near-miss medication error cannot be overstated. Often a physician's incorrect order is intercepted by a pharmacist, or an inappropriately dispensed drug is recognized by a nurse. In both cases an ADE and patient harm are averted. A good approach to preventing these errors in the future involves equal attention to these critical near miss incidents. Investigating a near-miss should involve the same questions used to investigate mistakes. The approach requires the investigators to ask what happened, what caused or allowed it to happen, and what to do about it.[80] The insight of the providers at the sharp end can be invaluable in making improvements. Positive feedback about safety changes should be reported back to those involved, thereby increasing personal investment in the culture of safety.

The medication delivery system is one that has been a focus for error reduction with some successes.[81] What are the systems failures identified from these proximal causes? First, the education and knowledge component: drug therapy is becoming incredibly complex. The Health and Public Policy Committee of the American College of Physicians acknowledged that we have not dealt as effectively as we should with the education of physicians in therapeutics.[82] In their position paper from 1988, they recommended increasing education in therapeutics both in medical school and house officer training programs. It is still generally true that the last formal training in pharmacology occurs in the second year medical school curriculum, before significant clinical exposure. The suggested syllabus would include: rational use of drugs, basic pharmacokinetics, awareness of particular patient populations, interpretation of clinical trials for evaluating new therapies, and wise skepticism of pharmaceutical industry claims. This information should be based in new techniques for providing physicians with timely information about drug efficacy and toxicity, new computer systems concerning drug interactions, and on communication with pharmacists. Several studies have noted the efficacy of clinical pharmacists on rounds in decreasing medication errors and ADEs.[21,63,83] Dissemination of information from hospital drug information centers, the pharmacy and therapeutics committee, and the formulary are also

mentioned as beneficial, though with due acknowledgement of the poor response of physicians to written materials.

The ACP also emphasized the importance of communication between healthcare providers and patients regarding medications. In a study of ADEs at a teaching hospital in Australia, authors employed a postdischarge questionnaire to determine patient knowledge of ADEs. Only 46% were aware they had suffered an adverse drug event. Further, just 34% knew which drug was involved, 12% could describe the reaction but not identify the drug, and only 11% knew to avoid reexposure to the offending drug.[84] Enlisting the patient in the fight against adverse drug events makes sense. Pharmacist counseling and monitoring of drug therapy has been very successful. Lastly, a reevaluation of the relationship between the pharmaceutical companies and practicing physicians is in order. The lay press has recently focused on what has been documented in the medical literature: physicians prescribing preferences are heavily influenced by the pharmaceutical industry.[85,86] Direct-to-patient advertising has spread their influence to the patients. At best, this practice encourages doctors and patients to discuss the possible benefits and risks of drug therapies and might even help us identify patients who could benefit from life saving therapies (e.g. HMG CoA-reductase inhibitors). Sadly, the ACP neglected to mention the role of physicians in reporting ADEs as a critical part of monitoring for drug safety and increasing knowledge of drugs. Many others have proposed and pleaded that this is a responsibility of all physicians.[18,87,88]

There are many common causes of medication errors (table 8). Look-alike and sound-alike drugs have been documented as problematic in the transcription and dispensing stage.[89] Many letters to the editor describe drug confusion and the adverse outcomes suffered by patients.[90,91,92] Some well-known examples are in table 9. Packaging has also created problems that used to exist equally in the nursing stations as in the pharmacy, but with the advent of unit dosing are less common.[93,94]

Table 9

PRILOSEC	**PROZAC**
LOSEC	**LASIX**
CISPLATIN	**CARBOPLATIN**
FLOMAX	**FOSAMAX**
NORFLOX	**NORFLEX**
DIAMOX	**DIABENESE**
NARCAN	**NORCURON**

A cooperative project of the Institute for Safe Medication Practices (ISMP) and RxMark, Incorporated uses a scale to analyze the suitability of proposed drug names. Important factors to consider are in table 10. Poor clarity of drug dosage and concentration has also created adverse events, particularly in drugs with narrow therapeutic indices, such as anti-arrhythmics. Packaging can also be helpful for patients who might require tactile cues—the best example was the now defunct practice of packaging NPH insulin in a square bottle and regular in a round one.[76,77]

Table 10

ISMP/Prescription Mark Factors for Analyzing New Drug Names

1. **Likelihood of being mistaken in a written document.**
2. **Likelihood of being mistaken in a verbal order.**
3. **Degree of dose range overlap.**
4. **Degree of dosage forms overlap.**
5. **Similarity of dosage forms with different routes of administration.**
6. **Similarity of directions.**
7. **Similarity of clinical indications.**
8. **Popularity of established products—(Is there a similar name in the top 100?).**
9. **Manufacturer the same as established product.**
10. **Miscellaneous factors (both narcotics, both refrigerated, same lettered suffixes).**

Cohen, Hospital Pharmacy, 1994.

Access to patient information is a critical piece of the safe medication use process.[63] Too often, pharmacist's ability to intercept an error is missed because critical clinical data are not available in the pharmacy. When patients are hospitalized, clinical pharmacists have the opportunity to make rounds to gather information. Cross-covering physicians sometimes prescribe without full knowledge of the patient's status. Sophisticated computer systems like the one at LDS Hospital in Utah can obviate some of these potential errors. Outpatient prescriptions are much harder to impact.[95] Prescriptions at hospital discharge are often filled at outside pharmacies, and there is usually no way to communicate drug sensitivities between pharmacies. In the era of the hospitalist, communication of ADEs must occur between outpatient and inpatient caregivers. Currently, patient education is the best tool in preventing outpatient ADEs, and preventing rechallenge with drugs identified to have caused ADRs.

What to do about handwriting? The pharmacy literature has long documented and bemoaned the dangers of illegible prescriptions, including delays in patient care because the prescribing doctor can't be identified to clarify his or her illegible order! There seems to be no successful way to impact our penmanship. Most literature now suggests that computer order entry is the only solution. Use of punctuation and, especially, abbreviations has also been a source of hazard. Many physicians are already well versed in the evils of trailing zeros on dosages and the use of the abbreviation U for units in insulin prescribing.

Failures of communication are well described in many types of errors and accidents.[51,54,96,97] Once again using an aviation example, research into the cause of commercial airline accidents revealed a prominent role for miscommunication in more than three fourths of incidents. Sociologic barriers to communicating crucial information "against the authority gradient" often lay at the root of these failures.[41,98] Studies of communication in the operating room confirm the importance of these barriers in medical settings.[99] The authority gradient in the medication use process involves patients, pharmacists, nurses, and physicians The roles of each care provider are firmly entrenched in medical society and difficult to overcome. Creating safety involves the ability to degrade the hierarchy for the sake of the patients' well being.

RECOMMENDATIONS FOR IMPROVEMENT

The American Society of Health-System Pharmacists (ASHP) published steps that hospitals can take to prevent ADEs in hospitals in 1993. Their recommendations included the following. First, computer systems for order entry and clinical information should be established. Use of bar coding technology for medication identification was mentioned, but would first require commitment from pharmaceutical manufacturers to participate. Systems for monitoring and reporting ADEs should be improved, with preventable events as top priority. Unit dosing and pharmacy based intravenous admixture systems should be in place. Pharmacists should be involved in direct patient care areas to encourage collaboration with physicians, nurses and patients. A pharmacist should routinely review medication orders. Resolution of any question regarding medication use should be a goal before administering the drug. The approach to medication errors should focus on system failures and system solutions using input from physicians, pharmacists, nurses, and administrators.

In 1996 the ASHP convened an expert panel to create more extensive guidelines for preventing medication errors with specific suggestions for each group involved in the medication use process. Provided below in outline form are some of their suggestions.

At the organizational level:

1. Active pharmacy and therapeutics committee with multi-disciplinary representation to review the entire process.
2. Intelligently developed formulary based on clinical research and reviewed by the P and T committee.
3. Adequate staffing and appropriate guidelines for workload and hours.
4. Systematic programs to review medication practices for safety, including Drug Usage Evaluation studies.
5. Access for health care professionals to appropriate clinical information when prescribing and dispensing drugs.
6. Accurate medication profiles for all patients in the system.
7. Twenty-four hour pharmacy services.
8. Minimize storage of drug products in floor stock, particularly drugs with a narrow therapeutic margin of safety.
9. Adequate drug information resources available to all health care providers.

For prescribers:

1. Continue medical education in the area of therapeutics. Special mention is made of physicians prescribing drugs outside his or her usual practice.
2. Evaluate patients total status and full medication profile before writing new prescriptions.
3. Write complete, clear, and legible prescriptions that optimally include indication and desired therapeutic outcome. (Avoid verbal orders where possible.)
4. Communicate indication, desired effect and possible adverse effects of medications to patients and nursing staff.

For pharmacists:

1. Participate in drug therapy monitoring and patient care wherever possible.
2. Be available as a resource for other caregivers
3. Clarify any questionable order.
4. Provide discharge and ambulatory counseling as well as inpatient counseling.

For nurses:
1. Continue education in therapeutics
2. Verify orders if any question exists.
3. Double check calculations, drip rates and drug concentrations with a colleague.
4. Maintain familiarity with drug administration routes, and equipment for drug administration.

For patients:
1. Know all current medications including OTC drugs and indications.
2. Know all drug allergies and sensitivities.
3. Carry a list of all items listed in numbers 1 and 2.
4. Attempt to follow instructions, but voice questions and concerns to physicians and pharmacists without hesitation.

For pharmaceutical companies:
1. Involve health care providers in decisions about drug names, labeling and packaging.
2. Avoid sound-alike, look-alike names and similar proprietary appearances of drugs.
3. Avoid suffixes and coined abbreviations.
4. Highlight special warnings and safety information at expense of trade names and logos.

Monitoring medication errors should involve consideration of known risk factors such as stress and fatigue, special patient populations (geriatrics and oncology), polypharmacy and poor communication amongst health care providers. Managing errors must involve incident reporting, risk management, education and intervention policies, based not only on adverse events, but on near misses. The first priority is the care of affected patients, then prompt and thorough investigation with confidential reporting and adequate documentation for patient safety. Investigation should aim to identify system errors that can be corrected for future patient safety. Reporting at the national level should be encouraged as it can identify trends among what are otherwise rare events in one institution.[100]

Recent editorials in the New England Journal of Medicine and the Journal of the American Medical Association propose development of new mechanisms for monitoring drug safety.[101,102] Both suggest the creation of an independent drug safety board. The first concept behind their arguments is borrowed in part from the airline industry's approach to accidents in which the Federal Aviation Administration sets standards and the National Transportation Safety Board investigates and suggests changes. This separation of powers markedly increases safety. Compare the large discrepancy between the number of U.S. airline fatalities (511 between 1995 and 1997) and the estimates of close to 100,000 annual patient fatalities related to drug use. Most people

would agree that the airline crashes were thoroughly investigated by the NTSB and often subjected to public hearings. By contrast, investigations of plaintiff injuries related to drugs are erratic and often lacking in hard evidence. This need for independent monitoring of drug safety has long been recognized, by the National Academy of Sciences in 1970(Drug Research Board), by the Joint Commission on Prescription Drug Use in 1980(Jt Com on Pres Drug), and by expert consultants review of the FDAs post-market safety monitoring program in 1993.[103]

Second, these editorials point out the weakness of safety data that relies on spontaneous reporting. Both propose more formal,[101] or mandatory[102] reporting to help develop a database to promote safer prescribing and dispensing processes. The hope is that better reporting will help identify causes of drug-related injury and their relative importance. Possible causes include inadequate initial testing, prescribing errors, poor post-marketing surveillance, and poor patient compliance.[101] Currently it is difficult to distinguish the role of drug therapy in causation of outcomes that can be plausibly ascribed to the disease process they are used to treat. From this comes the third suggestion that the database should generate comparative drug data, such as safety of different classes of antihypertensives. Wood's editorial in the NEJM suggests that surrogate endpoints used in marketing approval be confirmed by evidence gathered in population-based usage studies.[102] Moore et. al. mention two more specific goals. Drug safety monitoring should assure that new warnings and restrictions are included in product labeling and provide effective messaging to prescribers, pharmacists and the public. Sentinel programs could focus on most common drug induced medical problems rather than on specific drugs (e.g. active surveillance for agranulocytosis, aplastic anemia, and arrhythmias).

FDA Medwatch has a toll free number for reports and inquiries regarding ADRs at 1(800)FDA-1088. The Medication Errors Reporting System , operated by the United States Pharmacopeial Convention Inc. (USP) in cooperation with the Institute for Safe Medication Practices provides a confidential error reporting system at 1 (800)23-ERROR. Sample reporting forms are included at the end of the protocol for your reference. The JCAHO includes serious medication errors as a voluntarily reportable Sentinel Event. As of April, 1998 organizations that report voluntarily are spared from placement on a public "accreditation watch" list if they report the incident to JCAHO within 5 days and submit a root-cause analysis within 30 days, along with an action plan to correct the root cause. Sentinel events are reported through the quality and risk management departments of an institution, not by individual practitioners.

In conclusion, though the scope of medication errors and ADEs remains undefined, their importance is undeniable. Factors that affect reports of ADEs include such far-reaching influences as tort reform litigation, psychological models for response to error, and political and financial aspects of modern health care. There is a need for more structured, "no-fault" methods of identifying and investigating these important medical events, that represent one of the top ten causes of morbidity in the US each year. The legal system will continue to impede progress as long as unintentional errors are seen as prosecutable offenses. Changes in the way we address adverse events (and near misses) in the future will depend on our ability to examine them in the context of systems in which they occur. Health care systems and regulatory bodies must stop

blaming only the individuals involved in error and take full account of the problems in systems with intent to correct them. Education of health care providers should provide more emphasis on therapeutics and provide models of proven effective ways of dealing with error. With these goals, we can continue to use our most powerful weapon against disease wisely and safely.

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USP MEDICATION ERRORS REPORTING PROGRAM

Presented in cooperation with the Institute for Safe Medication Practices

The USP Practitioners' Reporting Network℠ is an FDA MedWatch partner

MEDICATION ERRORS REPORTING PROGRAM

❑ ACTUAL ERROR ❑ POTENTIAL ERROR

Please describe the error. Include description of sequence of events, personnel involved, and work environment (e.g., code situation, change of shift, short staffing, no 24-hr. pharmacy, floor stock). If more space is needed, please attach separate page.

Was the medication administered to or used by the patient? ❑ Yes ❑ No Date of Event _____

Please describe outcome (e.g., death, type of injury, adverse reaction). _____

When and how was error discovered? _____

If practitioner intervened, what type of staff discovered the error? _____

Where did the error occur (e.g., hospital, outpatient or retail pharmacy, nursing home, patient's home)? _____

At what time of day? _____

What type of staff or health care practitioner made the initial error? _____

Was the error perpetuated by another practitioner? _____

Was patient counseling provided? ❑ Yes ❑ No If yes, before or after error was discovered? _____

Please complete the following if a product was involved.

	Product #1	Product #2
Brand Name of Product Involved		
Generic Name		
Manufacturer		
Labeler (if different from mfr.)		
Dosage Form		
Strength/Concentration		
Type and Size of Container		

If available, please provide patient information that may be relevant, including age, gender, diagnosis, etc. (pt. identification not required).

Reports are most useful when relevant materials such as product label, copy of prescription/order, etc., can be reviewed.

Can these materials be provided? ❑ Yes ❑ No Please specify _____

Please retain these materials/samples for 60 days, if possible.

Do you have any recommendations to prevent recurrence of this error, or have you instituted policies or procedures to prevent future similar errors?

A copy of this report is routinely sent to the Institute for Safe Medication Practices (ISMP), the manufacturer/labeler, and to the Food and Drug Administration (FDA). **USP may release my identity to: (check boxes that apply)**

❑ ISMP ❑ The manufacturer and/or labeler as listed above ❑ FDA ❑ Other persons requesting a copy of this report ❑ Anonymous to all

Your Name and Title

Telephone Number (include area code)

Your Facility Name, Address, and Zip

Signature

Date

Return to: **USP PRN℠** 12601 Twinbrook Parkway, Rockville, Maryland 20852-1790

Call Toll Free: **1-800-23-ERROR** (1-800-233-7767) or FAX 1-301-816-8532

Date Received by USP:

File Access Number:

HOSPITAL PHARMACY

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For VOLUNTARY reporting by health professionals of adverse events and product problems

Page ___ of ___

Form Approved: OMB No. 0910-0291 Expires: 12/31/94
See OMB statement on reverse

FDA Use Only

Triage unit sequence #

A. Patient information

1. Patient identifier	2. Age at time of event: or Date of birth:	3. Sex	4. Weight
In confidence		☐ female ☐ male	___ lbs or ___ kgs

B. Adverse event or product problem

1. ☐ **Adverse event** and/or ☐ **Product problem** (e.g., defects/malfunctions)

2. **Outcomes attributed to adverse event** (check all that apply)
   - ☐ death ___ (mo/day/yr)
   - ☐ life-threatening
   - ☐ hospitalization – initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other: ___

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)

5. **Describe event or problem**

6. **Relevant tests/laboratory data,** including dates

7. **Other relevant history, including preexisting medical conditions** (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1. **Name** (give labeled strength & mfr/labeler, if known)
   #1
   #2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1	#1
#2	#2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1	#1 ☐ yes ☐ no ☐ doesn't apply
#2	#2 ☐ yes ☐ no ☐ doesn't apply

6. Lot # (if known)	7. Exp. date (if known)	8. Event reappeared after reintroduction
#1	#1	#1 ☐ yes ☐ no ☐ doesn't apply
#2	#2	#2 ☐ yes ☐ no ☐ doesn't apply

9. **NDC #** (for product problems only)
   – –

10. **Concomitant medical products** and therapy dates (exclude treatment of event)

D. Suspect medical device

1. **Brand name**

2. **Type of device**

3. Manufacturer name & address	4. Operator of device
	☐ health professional ☐ lay user/patient ☐ other: ___

6.
- model # ___
- catalog # ___
- serial # ___
- lot # ___
- other #

5. Expiration date (mo/day/yr)	7. If implanted, give date (mo/day/yr)	8. If explanted, give date (mo/day/yr)

9. **Device available for evaluation?** (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on ___ (mo/day/yr)

10. **Concomitant medical products** and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. **Name, address & phone #**

2. Health professional?	3. Occupation	4. Also reported to
☐ yes ☐ no		☐ manufacturer ☐ user facility ☐ distributor

5. **If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box.** ☐

FDA

Mail to: MEDWATCH
5600 Fishers Lane
Rockville, MD 20852-9787

or **FAX to:**
1-800-FDA-0178

ADVICE ABOUT VOLUNTARY REPORTING

Report experiences with:

- medications (drugs or biologics)
- medical devices (including in-vitro diagnostics)
- special nutritional products (dietary supplements, medical foods, infant formulas)
- other products regulated by FDA

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- death
- life-threatening (real risk of dying)
- hospitalization (initial or prolonged)
- disability (significant, persistent or permanent)
- congenital anomaly
- required intervention to prevent permanent impairment or damage

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Report product problems – quality, performance or safety concerns such as:

- suspected contamination
- questionable stability
- defective components
- poor packaging or labeling

How to report:

- just fill in the sections that apply to your report
- use section C for all products except medical devices
- attach additional blank pages if needed
- use a separate form for each patient
- report either to FDA or the manufacturer (or both)

Important numbers:

- 1-800-FDA-0178 to FAX report
- 1-800-FDA-7737 to report by modem
- 1-800-FDA-1088 for more information or to report quality problems
- 1-800-822-7967 for a VAERS form for vaccines

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. The reporter's identity may be shared with the manufacturer unless requested otherwise. However, FDA will not disclose the reporter's identity in response to a request from the public, pursuant to the Freedom of Information Act.

FDA Form 3500-back **Please Use Address Provided Below – Just Fold In Thirds, Tape and Mail**

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Rockville, MD 20857

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Penalty for Private Use $300

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The FDA Medical Products Reporting Program
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