

Medication Errors

Hospital Pharmacist Perspective

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Abstract

In recent years medication error has justly received considerable attention, as it causes substantial mortality, morbidity and additional healthcare costs. Risk assessment models, adapted from commercial aviation and the oil and gas industries, are currently being developed for use in clinical pharmacy.

The hospital pharmacist is best placed to oversee the quality of the entire drug distribution chain, from prescribing, drug choice, dispensing and preparation to the administration of drugs, and can fulfil a vital role in improving medication safety. Most elements of the drug distribution chain can be optimised; however, because comparative intervention studies are scarce, there is little scientific evidence available demonstrating improvements in medication safety through such interventions.

Possible interventions aimed at reducing medication errors, such as developing methods for detection of patients with increased risk of adverse drug events, performing risk assessment in clinical pharmacy and optimising the drug distribution chain are discussed. Moreover, the specific role of the clinical pharmacist in improving medication safety is highlighted, both at an organisational level and in individual patient care.

The issues of medication safety and medication errors have received considerable attention in recent years. Several landmark publications, such as *To Err is Human: Building a Safer Health System*^[1] in the US, and *Building a Safer NHS for Patients: Improving Medication Safety*^[2] and *A Spoonful of Sugar: Medicines Management in NHS Hospitals*^[3] in the UK, have made people realise that the risks associated with the administration of drugs are considerable and the costs due to medication errors are high. It has been estimated that 44 000–98 000 people die each year in hospitals in the US as a result of medical errors, exceeding the number attributable to

the eighth leading cause of death. More people in the US die in a given year as a result of medical errors than from motor vehicle accidents, breast cancer or AIDS.^[1] A substantial proportion of these medical errors, probably between 10% and 20%, are due to medication errors^[4,5] and are estimated to account for >7000 deaths, either in or out of hospital, in the US annually. The cost per year of medication errors in the US have been estimated to be \$US2.8 million for a 700-bed teaching hospital, while the cost to the National Health System in the UK in additional days in hospital was estimated at £500 million (year of values not stated).^[3] Moreover, estimates in Austra-

lia indicate that 80 000 people are admitted to hospitals with medication errors, at a cost of \$A350 million per year (year of values not stated).^[6]

The idea that risk is associated with the administration of drugs is not new and has received much attention, but almost all of that attention has been paid to the intrinsic events, such as the adverse effects of drugs. Extrinsic drug events, for example as a result of medication errors, have only been appreciated in recent years. The differentiation between these types of adverse drug events (ADEs) has led to a useful classification of medication errors. An ADE is defined as "any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment".^[7] A widely accepted and applied classification of medication errors, proposed by the National Coordinating Council for Medication Error Reporting and Prevention, shown in table I, is helpful in comparing studies in the field of medication safety.^[8]

Methods for quantification and qualification of medication errors are numerous. Faults or near accidents (FONA) committees in hospitals, which record and analyse spontaneously reported medical errors, usually study individual incidents, reconstructing causes and advising on preventive measures to minimise repetition of those types of incident. However, there are a number of problems with such reactive approaches. One important drawback is that incident reports provide a slow and unsystematic source of information, which is especially problematic in fast-moving fields such as modern medicine. Moreover, spontaneous reporting systems depend highly on the willingness of people to report their own and others' faults and near misses, which may lead to biased reporting. There is, for example, structural under-reporting, especially from physicians and of near misses (as opposed to faults).^[9] Finally, the analysis process by the FONA committee requires an advanced and detailed understanding of processes that may lead to errors, and even then it is sometimes difficult to predict, using a theoretical process analysis, where and how failures may occur. In complex socio-technical systems, such as modern medicine, there are many ways in which disastrous outcomes can occur. In reality, individual incidents

Table I. Medication error classification by the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP)^[8]

Category	Description
No error	
A	Circumstances or events that have the capacity to cause error
Error, no harm	
B	An error occurred but the error did not reach the patient (an 'error of omission' does reach the patient)
C	An error occurred that reached the patient, but did not cause patient harm
D	An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude it
Error, harm	
E	An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention
F	An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalisation
G	An error occurred that may have contributed to or resulted in permanent patient harm
H	An error occurred that required intervention necessary to sustain life
Error, death	
I	An error occurred that may have contributed to or resulted in the patient's death

represent only a fraction of the total 'space' of possibilities for error and, therefore, analysis of individual incidents may better reflect the imagination of the analyst rather than the true possible sources of a problem. Systematic and trend analysis of individual incidents and harm scenario descriptions may, in part, overcome this problem. Obviously, incident reports from FONA committees can hardly be used for estimating quantitative figures on medication errors, however, they may provide a useful source of qualitative information.

The disguised observation method is usually applied in clinical studies, when studying the effect of certain interventions on the occurrence of medication errors or when estimating frequencies of errors. Using this study design, the healthcare workers involved in the process being studied, with the exception of the analyst performing the study, are neither

informed nor aware of the aim of the study. Hence, bias due to performing the study may be avoided.

One problem that many approaches face is that not all medication errors result in ADEs. Nevertheless, the mechanisms leading to medication errors, whether a specific outcome is benign or not, can also result in disastrous outcomes under appropriate circumstances.

This commentary article critically examines possible interventions aimed at reducing medication errors and the role of the pharmacist in these interventions, from the perspective of the hospital pharmacist. Topics covered include ADEs, risk assessment in clinical pharmacy, the drug distribution chain and the role of the clinical pharmacist.

1. Adverse Drug Events

ADEs are caused either by intrinsic toxicity of the drug (adverse effects) or by the way the drug is used, that is, extrinsic toxicity. ADEs attributable to drug-drug or drug-food interactions, double medication (e.g. the concomitant use of more than one benzodiazepine), the unwillingness of the patient to take the drug and medication errors are all examples of extrinsic drug toxicity. In several studies it has been reported that 4–30% of hospitalisations are drug related; that is, caused by an ADE.^[7,10] Other studies have shown that ADEs in hospitalised patients, which resulted in excess length of stay, costs and attributable mortality, were evident in approximately 2% of patients.^[11,12] The wide range in estimated frequencies of ADEs in these studies is probably due to differences in study population (age, extent of polypharmacy, comorbidity), in definitions (of ADE), and especially in study design and detection methods.

Although medical chart review appears to be a systematic approach for detecting ADEs, it is not efficient, insensitive, subjective or, more importantly, preventive. Obviously, estimating ADE frequencies is important to illustrate the extent of the problem, but preventing ADEs is much more challenging and is worthwhile for individual patient care as well as for cost reduction in healthcare. Detection of ADEs by computerised data extraction from an electronic patient database on the basis of defined algorithms could be a much more sensitive and efficient

methodology.^[13] Jha et al.^[14] compared this method with chart review and spontaneous error reporting (FONA). From their results it appeared that computerised ADE detection and chart review were almost equally effective at detecting ADEs, but the latter was 60-fold more time consuming (60 hours vs 1 hour per week for a 700-bed hospital). As expected, spontaneous error reporting resulted in an underestimation of the frequency of ADEs.

Principally, algorithms or so-called clinical rules described to date concentrate on detecting ADEs after they have occurred. Examples of these clinical rules include laboratory test results (both drug concentrations and biochemical levels [e.g. ALT, creatinine]), use of drugs to relieve or treat symptoms associated with ADEs, or the use of antidotes. However, more recently, algorithms designed to prevent ADEs have been developed and described in the literature.^[15] One approach is to investigate the nature of preventable ADEs.^[16] In this meta-analysis cardiovascular, psychoactive (and other CNS drugs), analgesic and anticoagulant drugs were found to be most frequently associated with preventable ADEs. Adverse outcomes could also provide a suitable source to develop algorithms. Allergic reactions, hepatotoxicity or nephrotoxicity, effects on the cardiovascular system, haematological effects and CNS effects were the most prevalent outcomes in this meta-analysis. By combining these drug- and organ-associated determinants for ADEs, a more sensitive and preventive algorithm could be designed.

In our institution we have chosen a multiple source approach for development of clinical rules aimed at detecting patients potentially susceptible to ADEs. In addition to the methodology already discussed, we include current treatment guidelines (to detect suboptimal treatment); alerts generated by the US FDA, the European Medicines Agency (EMA) or the pharmaceutical industry; FONA reports; and over-ruled medication safety alerts generated by the computerised physician order entry (CPOE) system which necessitated retrospective interventions by hospital pharmacists (drug interactions, duplicate medications, overdoses). With regard to the latter, we follow the procedure that all medication safety alerts generated by the CPOE system during prescribing that are over-ruled by the prescriber are

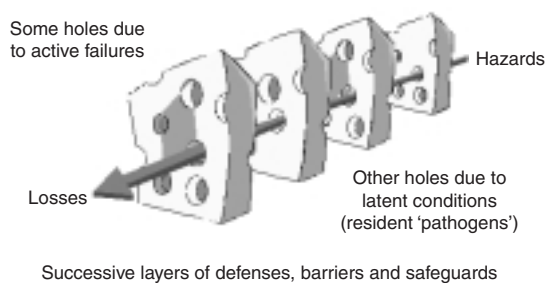


Fig. 1. Reason's Swiss Cheese Model (courtesy J. Reason). The active failures of front-line individuals have to be seen as finishing off the hazards propagated by the latent conditions upstream.

reviewed by a hospital pharmacist on a daily basis and interventions are made when necessary. In our clinical rule system for selecting patients with the potential for ADEs, clinical pharmacists use the information on at-risk patients to make specific consultations and to discuss these patients with physicians. Recently, it has been shown that the implementation of this type of methodology offers an economical and effective method for increasing medication safety in hospitalised patients.^[15]

A clinical rule monitor can also identify patients with drug-related hospital admissions. In The Netherlands, almost all community pharmacists and the majority of general practitioners use computerised systems for checking drug dosage, double medication and drug interactions. Nevertheless, the incidence of drug-related hospital admissions in The Netherlands is estimated at 4–30%.^[7,10] By applying the clinical rule monitor to detect these patients and exploring the causes of these ADEs, we also aim to improve medication safety in the outpatient setting. Of course, such rules require a proper analysis of the extrinsic risks associated with medications, an understanding of where the problems lie, what the major risks are and what methods will be most effective in combating them.

2. Risk Assessment in Clinical Pharmacy

Conventional risk analyses in pharmacy have been devoted to the intrinsic effects of drugs but medication errors fall under extrinsic factors. In fact, classical intrinsic risk analyses ignore the extrinsic risks because they are not relevant for the assessment of the risks associated with a particular drug; the assumption is made that the drug will have been

given appropriately. Therefore, it is necessary to look in other directions when developing methods to analyse the risk of medication errors. The commercial aviation and oil and gas industries have a rich history of developing and applying models for risk assessment and accident analysis aimed at a better understanding of how accidents are caused and can be prevented within these industries.^[17] Medicine, including clinical pharmacy, has recently started to adopt these models and methods, which may help to assess and understand the risks within a pharmaceutical system.

Reason's Swiss Cheese Model (figure 1) can be described as a number of barriers ('slices of cheese') interposed between the hazards and the outcomes to be avoided.^[18] The barriers represent the defences and the holes ('in the slices of cheese') represent the weaknesses in those defences. The holes allow propagation of failures so that hazards can turn into losses such as accidents or other negative outcomes. The risk of propagation of failures is determined by the number, size and nature of the holes. The strength of the model is that it enables us to analyse accidents as the outcome of a set of possible causal elements of a chain ('how did the system allow this to happen?') instead of just pointing to the individual or element nearest to the negative outcome. In a

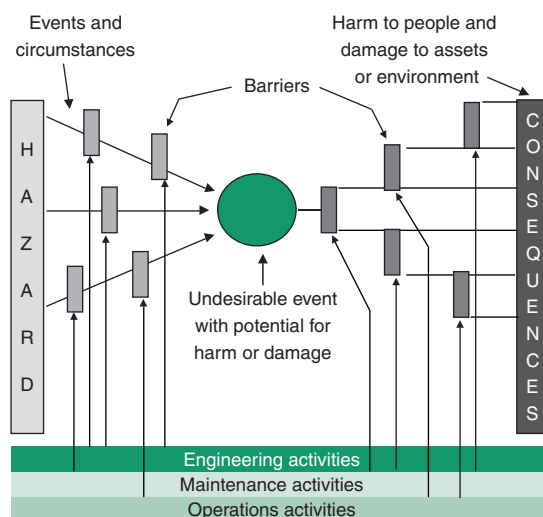


Fig. 2. The Bow Tie Model combines the concepts of fault and event trees used in quantitative risk assessment (courtesy Shell International Exploration & Production).

pharmaceutical system, checks and controls are very common and, in fact, represent barriers aimed at preventing the propagation of possible failures. Identifying latent conditions that represent weaknesses in the system and assessing risks may help to prevent failures and increase the safety of the entire system.

Many techniques are available to help assess risks, often based on fault trees, analysing forwards to or backwards from disastrous outcomes. In one standard technique, Failure Mode and Effect Analysis, one specifies the process in detail, examines how and where things can go wrong (failure modes), and estimates the frequencies and consequences of a whole range of possible outcomes (effects). Alternatively, working backwards rather than forwards, one can take specific undesired consequences, and fill in all the possible pathways and necessary combinations that could lead to that event.

The Bow Tie Model, originally developed by Shell International, combines the concepts of fault and event trees used in quantitative risk assessment^[19] (figure 2). The left-hand side of the bow tie describes how events and circumstances can release a hazard, and can lead to an undesirable event with the potential for harm, called a top event. The right-hand side represents the various consequences of the undesirable event, and the methods and effectiveness of the system to stop or limit progression to harm. Therefore, barriers in the model are aimed at preventing undesirable events from occurring (as in the Swiss Cheese Model) or at mitigating the consequences of these negative events should they occur.

In a pharmaceutical system there are a large number of possible ways in which medication errors can occur that should be defended against. The Academic Medical Center (AMC) model^[20] expresses these in terms of bow ties, with a limited number of top events with distinct aetiologies. These aetiologies are:

- wrong patient
- wrong diagnosis
- wrong drug
- wrong dose
- wrong delivery
- wrong timing.

For example, neonatal twins, of whom only one should be receiving treatment, run considerable

risks. One twin may receive unnecessary medication, while the other misses out. The model identifies the possible control measures for this specific wrong-patient threat, such as barcoding, positive identification protocols and separate housing in the hospital, and then identifies how these control measures could be degraded, such as by failures of barcode readers, lack of training in protocols or the need to keep the babies together so they can be fed by their mother. Another threat, administration of the wrong drug, would be when patients bring in their own medicine, which would require controls to identify and replace these drugs to avoid the risk of unexpected interactions. These controls can be degraded when patients are not questioned and their medication identified and, usually, removed and replaced by the hospital medication regimen. Once the controls have failed and the top event is reached, it is necessary to mitigate the possible clinical consequences. Currently, we have identified in excess of 120 such aetiological pathways in the AMC model.

The AMC model, which is based on industrial risk assessment approaches and is still under development, differs slightly from the more traditional approach of using the medication cycle, which is the approach used in the rest of this article. A risk analysis of the medication system involves identifying the threats with their associated barriers and degradation mechanisms, as well as the mitigation barriers between the top events and possible extreme outcomes, up to the death of the patient. Armed with a complete analysis, it is possible to perform a risk assessment of the system, as opposed to an individual drug, by seeing whether the necessary controls are in place and effective. A quantitative assessment would involve estimating the frequencies of threats and the effectiveness of the relevant controls in reducing the occurrence of top events and undesired final outcomes.

3. The Drug Distribution Chain

For physicians, prescribing drugs is one of the most common and frequently applied methods of medical treatment. Failures may occur in each part of the continuum of prescribing, dispensing, administering and applying drugs, and have the potential to cause patient harm (figure 3). Recognising the

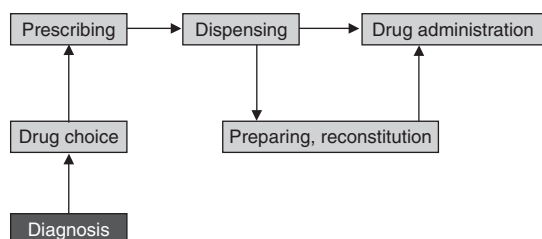


Fig. 3. The drug distribution chain is the continuum of prescribing, dispensing, preparation and administration of drugs. Failure may occur in each part of the chain.

most vulnerable steps in the drug distribution chain, as identified by risk analysis, may help to expose critical intervention methods that will most efficiently improve the entire process. However, there are important problems with this rational approach (starting with the weakest part of the chain). The first is that judgement of risk and sense of safety are very subjective and dependent on individual factors such as habit, experience, knowledge and personal situation. Risk is usually expressed as the product of negative outcome and probability, enabling one to balance bad but unlikely outcomes with less bad but more frequent ones. People also find it difficult to estimate the actual chance of becoming a victim, especially when the outcome is extremely negative, such as death, and they are inclined to take no chances in such situations. Problems arise in defining what is meant by an outcome and how the probability is assessed.

Outcomes may be discrete events, such as death, or continua, such as getting better or worse. In a risk-based approach to the management of medication errors, we have to be careful in defining what types of outcomes are covered. Clearly, medication errors can generate a wide variety of adverse outcomes, not necessarily pharmacological but also, for instance, the number of extra days of hospitalisation required. Probabilities are generally derived from frequency information, requiring accurate estimates of both base and failure rates. A major problem that makes estimation of frequency rates difficult is that any remedial action taken may immediately render those estimates meaningless, even if reliable information was available in the first place.

A second important problem with the rational approach of improving a serial process is that changes in methods, techniques and systems them-

selves often lead to unstable, untried and risky situations. Gawande^[21] described this learning curve of improvements. In their example, the introduction in 1986 of a novel surgical technique in a London clinic for patients with a severe cardiac defect called 'transposition of the main arteries' was a success. The number of patients dying per year decreased by >75% and the life expectancy of the patients increased from 47 years with the conventional method to 63 years with the new technique. However, it appeared that the 'price' for introducing this technique was extremely high. For the first 70 operations using the new technique, the mortality rate was 25%, as opposed to only 6% with the conventional technique. During the introductory phase twice as many babies died than in the entire 20-year period of conventional surgery, illustrating that even introducing a change itself may raise risk temporarily. From our own studies, it appears that the introduction of a CPOE system for prescribing drugs not only introduces new types of medication errors during the introduction phase but also influences error rates in other parts of the drug distribution chain, for example drug administration,^[22] and may reduce the attentiveness of physicians to the details of the prescriptions. When making the decision to introduce an advancement aimed at improving safety, an implicit decision is made on the acceptance of a possible and temporary period of increased risk and errors compared with the current situation.

3.1 Medical Diagnosis

Obviously, rational pharmacotherapy starts with making a correct and conclusive medical diagnosis, and establishing the precise aim of pharmacotherapy. However, a pharmacotherapeutic intervention may form part of the process of making the diagnosis. For example, to diagnose acid-related intestinal diseases the use of a proton pump inhibitor for some weeks may be prescribed.

Drugs are frequently prescribed for illnesses that are clearly not sensitive to medication, for example the treatment of influenza or viral tonsillitis with antibacterials, and in fact this could be considered a medication error. The extent of this type of medication error is unclear, as it is usually not included in studies on medication errors and is difficult to estimate.

Another type of medication error related to the estimation of whether the disease under consideration is sensitive to medication could, for instance, appear in immunisation of possibly infected patients. In our practice, we were consulted by a physician for the immunisation of a group of paediatric oncology patients who had been in contact with a patient with a varicella-zoster virus infection. It was intended that the immunocompromised patients would be treated by vaccination; however, in this group of patients passive immunisation by immunoglobulin administration was indicated.

3.2 Drug Choice

It is well known that several factors influence an individual prescriber's decision-making when choosing a drug.^[23] Ideally, drug choices are evidence-based, supported by high-quality publications in peer-reviewed journals, while taking clinical expertise and patient values into account. However, in practice, other factors such as the marketing strategies of the pharmaceutical industry and prescribing patterns of colleagues or supervisors appear to be important determinants of the drug choice of individual physicians.^[24] Furthermore, a strong association between authors' published opinions and their financial relationships with the pharmaceutical industry has been demonstrated in several studies.^[25] On the basis of these data, decision-making is a difficult task for an individual prescriber.

In a more structured manner, scientific associations and institutional pharmacotherapy and therapeutics (P&T) committees make decisions on drug choice by developing treatment guidelines and drug formularies. They have the difficult task of evaluating the risks each drug poses to patients, and choosing whether to recommend for or against the use of a particular drug. Obviously, the accessibility of novel innovative drug therapies is important. However, from a medication safety perspective, it has to be realised that when an established, safely used and effective therapy already exists, any new drug should be considered as a potential risk factor.

Newer roles of P&T committees include reviewing medication error and/or ADE trends for possible modifications in the drug distribution chain.^[26]

Obviously, the application of an objective and structured methodology for the formulary management process is essential. Decision-supportive models designed specifically for making drug choices, such as the System of Objectified Judgment Analysis developed by Janknegt and Steenhoek^[27] may be useful for structured decision-making. Moreover, medication usage evaluation and drug utilisation reviews designed to improve the quality of prescribing are increasingly being performed by P&T committees,^[28] and include the evaluation of clinical outcomes information, including quality-of-life issues.^[29,30]

Nevertheless, there may still be room for improvement. A recent Dutch study^[31] demonstrated that some P&T committees still make decisions in a unstructured manner instead of using validated structured selection matrices or decision-supportive models, thereby questioning whether their decisions can be considered to be evidence based. Finally, P&T committees could take into account site-specific characteristics, such as demographics or the seriousness of the disease, when integrating best research evidence into local treatment guidelines. Currently, once such guidelines have been established and implemented in clinical practice, it is unusual for a structured evaluation to take place to determine whether the new guideline leads to improvements in terms of efficacy, safety and pharmacoeconomics.

Drug formularies are implemented in most hospitals, but their restrictive nature may pose a problem in clinical practice and can lead to non-adherence. In this respect, drug formulary management is a critical factor for a successful institutional drug formulary. Factors that contribute to non-adherence are the design of the formulary (product- or disease-oriented formularies), differences between primary care formularies and the hospital formulary, which lead to discontinuities when a patient is admitted to the hospital or discharged, and the perceived unwillingness of patients. By applying a simple pharmacoepidemiological model, it has been proven possible to assess indicators for hospital drug formulary non-adherence in a specific hospital;^[32] these indicators can be used to improve adherence. An example of such an intervention is the antimicrobial control programme that was implemented in our hospital to

increase the quality of antimicrobial drug prescribing.^[33]

3.3 Prescribing

When pharmacotherapy is indeed chosen as the appropriate treatment for a patient, an important first step is choosing the right drug at the right dose, with the right frequency, duration, etc., taking into account the possible specific conditions of the patient, such as renal and liver function, age, bodyweight, co-medication and known allergies. Traditionally, such decisions are made by the physician. This process of individualising and prescribing the ideal drug therapy is becoming increasingly complex. At the moment of prescribing, all of the knowledge about the patient and all recent scientific evidence must be integrated, in order to make the best choice for the patient. In many countries, the support of the clinical pharmacist at this point is increasing. Computer systems are also being developed to support prescribing.

A basic system for this purpose is a CPOE system, which helps to generate clear, readable and unambiguous medication orders and has the potential to reduce prescription and transcription errors. When integrated with pharmacy logistics, efficiency of drug distribution can be improved and drug distribution errors can also be reduced.^[34-36] The impact of a CPOE system on medication safety can be further increased by implementing different features and integrating the system with other hospital systems. However, it has been shown that while the implementation of a basic CPOE system in a hospital may cause a major improvement of medication safety, there were only marginal improvements upon addition of sophisticated features in new releases of the system.^[37] Most CPOE systems generate medication safety alerts during prescribing, such as signalling of drug interactions, duplicate medication, drug overdose and allergies. It is possible that these features improve medication safety but no broad scientific evidence for this hypothesis can be found in the literature. A problem encountered in handling medication safety alerts is that it is often difficult for prescribers to interpret the clinical relevance of the signals and to translate the alert into a practical adjustment of the prescription. Moreover,

and possibly because of these problems, alert signals are being over-ruled to a considerable extent.^[38] Improving the selectivity and specificity of alerts,^[39,40] together with more guidance on the interpretation of alerts, may help to overcome this problem.

However, a recent study showed that CPOE systems can facilitate errors in prescribing in addition to reducing them.^[41] Examples include fragmented CPOE displays that prevent a coherent view of a patient's medications, pharmacy inventory displays mistaken for dosage guidelines, ignored antibacterial renewal notices placed on paper charts rather than in the CPOE system, separation of functions that facilitate double-dosage and incompatible orders, and inflexible ordering formats generating wrong orders.

More sophisticated CPOE systems are integrated into the hospital information system and enable features such as protocol-guided prescribing. Integration with, for example, laboratory and clinical systems enables the involvement of information on biochemical parameters (such as renal function, liver function and serum potassium levels) or disease states in prescribing. Another possible feature of a CPOE system is the use of medication protocols. We have experience with protocol-guided prescribing in the CPOE system *Medicator*[®] (iSoft, Leiden, The Netherlands), which is in use in several Dutch hospitals.^[42] Complex treatment protocols are presented to the prescriber as a standardised series of individualised medication orders that only need authorisation by the physician. In oncology, for example, where high-risk medication is being prescribed in complicated schedules that often require dose individualisation, protocol-guided prescribing certainly has the potential to reduce medication errors.

A further development is the construction of clinical decision support systems (CDSS), in which clinical evidence and treatment protocols are integrated into the CPOE system. The system assists the physician to take the appropriate pharmacotherapeutic decisions, leading to the optimal prescription for the specific patient. Currently, most available CDSS are developed for specific medications or diseases, such as care of diabetes mellitus or heart failure.^[36]

3.4 Dispensing

The objective of responsible drug dispensing in hospitals is to ensure that each physician-ordered and pharmacist-reviewed drug is available to the nurse for administration to the correct patient, in the correct dosage form and dose, via the correct route of administration and at the correct time (see the AMC model described in section 2 for risk analysis). Dispensing of medication can be automated and, if linked with point-of-care barcode scanning and information systems, automated dispensing machines (ADMs) have the potential to decrease medication errors and to increase effectiveness and work efficiency of the distribution process. ADMs in hospitals may include both centralised and decentralised automated devices. The advantages of decentralised devices over the traditional distribution (unit-dose) systems are automated dispensing for controlled substances and floor-stock medications, availability of all authorised medications in specific medication pockets, access for only authorised users with secure passwords, forced entry of obligatory data into the system, logging of all data and the possibility of barcoded drug selection. Additional benefits of (some) centralised devices are automatic unit-dose and barcode-controlled drug dispensing per patient and per administration time, the ability to barcode all drugs and solutions that are on the market, and automatic handling of returns.

There are only a few controlled studies that show improvement of medication safety upon implementation of ADMs.^[40] Studies on the effects of ADMs on medication error rates and cost effectiveness compared with traditional systems are inconclusive. Comparing these studies is difficult because of differences in distribution systems, variability in linkage to other information systems and methods of data collection. Overall, ADMs alone have the least support for their effectiveness in preventing medication errors. However, implementation of new technology in the drug distribution process necessitates a complete redesign of services and considerable financial requirements. Therefore, novel technology in this area should have proven benefits on medication safety and a complete evaluation of appropriateness before broad implementation can be recom-

mended. Development of a standard evaluation model using performance indicators is necessary to compare available ADMs with regard to performance, cost effectiveness, and prevention of medication errors and enhancement of safety.^[43]

3.5 Preparation

The preparation of medications is a critical step, especially in intravenously administered drugs. Errors in this phase can have serious consequences as it is the last step before administration and these errors are difficult to detect. Experimental data on error rates and types of errors in this field are scarce. In a recent study involving ten wards in two hospitals in the UK, it was shown by using the disguised observation technique that one or more errors occurred in 57 of 430 intravenous doses.^[44] Lack of training, the design of the technology itself, poor communication and workload were all factors contributing to this high error rate. Using the same technique, we investigated the error rate in intravenous preparations by nurses in our own hospital. With the exception of a poor aseptic technique, we detected significant clinical errors in 64 of 90 intravenous doses, and in a second study in which we excluded repeated errors, such as drawing up the whole content of an 1mL ampoule instead of the precise 1.0mL volume, one or more errors occurred in 26 of 254 intravenous doses.

An intravenous admixture unit at the patient care unit, where preparation is done by pharmacy personnel, has the potential to reduce both medication errors and microbiological contamination. In such a unit, medication is prepared according to standardised protocols in laminar down-flow hoods. Several institutions have implemented decentralised pharmacy intravenous admixture units;^[45] however, the evidence base for the success of such a service is currently weak. In our own experience, again using the disguised observation method for error detection, the error rate at a decentralised pharmacy intravenous admixture unit operated by skilled pharmacy technicians was 2% (7 of 330 intravenous doses were judged as errors because of poor aseptic technique) compared with 71% when nurses made the preparations on the ward.

3.6 Barcode-Enabled Point of Care Systems

Barcode-enabled point-of-care (BPOC) systems combine barcode scanning with sophisticated medication administration software that provides the nurse with an additional check. The software can communicate important clinical information to the nurses, improving their ability to safely administer medications, while barcode technology contributes to safer patient care through real-time confirmation of patient identification, medication, dose, time and route of administration.^[46] When medication orders are sent from a computerised order entry system or pharmacy system to the BPOC system, the patient's wristband and medication barcodes are scanned and the system provides an automated double-check, ensuring that patients receive the medication treatment specified in the pharmacy order. BPOC technology therefore provides a safe automated identification and feedback system in real time. BPOC systems may utilise, store and forward radio frequency, wireless and even cellular communications. They have been built for personal computers, mobile laptops and centrally located stationary computers.^[40] BPOC closes the loop of a safe distribution process: CPOE, pharmacy system, ADM and BPOC.^[47] According to several studies, most errors occur in the ordering part of the distribution process, with one-third occurring in the administration process. Although error rates can be reduced in each part of the medication use process separately, the only solution that can provide an overall reduction in medication errors is an integrated approach spanning each of the components.

In many industries barcoding is an effective tool to reduce error rates. Several factors have to be considered when implementing a BPOC system in healthcare organisations, such as the availability of unit-dose barcoded products, the format of barcodes used, scan technology issues and system platform choices. According to US FDA regulations, all new human drug products and biological products currently in the market must be barcoded by 2007, but pharmaceutical manufacturers have yet to agree on a standard approach to the implementation of barcoding. Studies evaluating point-of-care systems that verify patient and drug information are not yet available and, therefore, this new development warrants

justification before wide implementation can be expected.^[43]

4. The Role of the Clinical Pharmacist

Hospital pharmacists are best placed to oversee the quality of the entire drug distribution chain, from prescribing, drug choice, dispensing and preparation to administration of drugs, and can fulfil an important role in improving medication safety. The hospital pharmacist usually plays a prominent role in institutional committees dedicated to patient safety and quality of prescribing, such as the P&T committee, the FONA committee or the integrated patient safety team. This role enables the pharmacist to improve the quality of pharmacotherapy at an organisational level. Pharmacist participation on medical rounds is common in many hospitals and has been proven to prevent errors, lower drug costs and reduce ADEs in, for example, intensive care and general medicine units.^[48,49] The essential difference of this approach to that of traditional pharmacy practice is the proactive role of the pharmacist in influencing prescription at the time that the decisions are made. Compared with the traditional reactive approach, for example by checking prescriptions and correcting prescribing errors, participation on medical rounds is much more effective and challenging and the specific expertise of the pharmacist is much better utilised.

Limited human resources may restrict pharmacist participation on ward round teams in all of the medical units of a hospital, necessitating selection of patients at risk for ADEs. Because of a lack of comparative intervention studies, no clear criteria for selection of high-risk patients are available. However, in clinical practice, patients are selected who are severely ill, have complex and multiple diseases, are using multiple drug therapies, are of either age extremity, have organ failure or are receiving multidisciplinary treatment. In fact, such identification of patients with potential for ADEs using clinical rules is an effort to select patients at high risk and to use limited resources most efficiently.

Hospital pharmacists should take initiatives to develop, introduce and implement novel technologies and methods such as CPOE systems, ADMs, BPOC systems and intravenous drug admixture ser-

vices in order to optimise the drug distribution chain. Moreover, the specific knowledge of the hospital pharmacist can also be utilised in the training and education of medical and pharmacy students, medical residents, physicians and nurses.

5. Conclusion

Hospital pharmacists are best placed to oversee the quality of the entire drug distribution chain, from prescribing, drug choice, dispensing and preparation, to the administration of drugs, and they can fulfil a vital role in improving medication safety. Most elements of the drug distribution chain can be optimised; however, because comparative intervention studies are scarce, there is little scientific evidence available to demonstrate improvements in medication safety through particular interventions.

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References

- Kohn LT, Corrigan JM, Donaldson MS. To err is human: building a safer health system. Committee on quality of health care in America; Institute of Medicine. Washington, DC: National Academy Press, 1999
- Department of Health. Building a safer NHS for patients: improving medication safety. London: The Stationery Office, 2001
- Audit Commission. A spoonful of sugar: medicines management in NHS hospitals. London: Audit Commission Publications, 2001
- Leape LL, Brennan TA, Laird N, et al. The nature of adverse events in hospitalized patients: results of the Harvard Medical Practice Study II. *N Engl J Med* 1991; 324 (6): 377-84
- 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 (6): 370-6
- Australian Council for Safety and Quality in Health Care. Improving medication safety: report of a medication safety workshop, July 2001 [online]. Available from URL: <http://www.safetyandquality.org> [Accessed 2005 Jun 13]
- Chan M, Nicklason F, Vial JH. Adverse drug events as a cause of hospital admission in the elderly. *Intern Med J* 2001; 31 (4): 199-205
- National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) [online]. Available from URL: www.nccmerp.org [Accessed 2005 Jun 13]
- Busse DK, Wright DJ. Classification and analysis of incidents in complex medical environments. *Top Health Inf Manage* 2000; 20 (4): 1-11
- Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. *Pharm World Sci* 2002; 24 (2): 46-54
- Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA* 1998; 279 (15): 1200-5
- Classen DC, Pestotnik SL, Evans RS, et al. Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality. *JAMA* 1997; 277 (4): 301-6
- Bates DW, Gawande AA. Improving safety with information technology. *N Engl J Med* 2003; 348 (25): 2526-34
- Jha AK, Kuperman GJ, Teich JM, et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. *J Am Med Inform Assoc* 1998; 5 (3): 305-14
- Silverman JB, Stapinski CD, Huber C, et al. Computer-based system for preventing adverse drug events. *Am J Health Syst Pharm* 2004; 61 (15): 1599-603
- Kanjanarat P, Winterstein AG, Johns TE, et al. Nature of preventable adverse drug events in hospitals: a literature review. *Am J Health Syst Pharm* 2003; 60 (17): 1750-9
- Hudson PTW. Applying the lessons of high risk industries to health care. *Qual Saf Health Care* 2003; 12 Suppl. 1: i7-21
- Reason J. Human error: models and management. *BMJ* 2000; 320 (7237): 768-70
- van der Graaf GC, Milne D, Primrose M. HSE cases: some lessons learned. Exploration and Production Newsletter. The Hague: Shell International, 1996
- Hudson PTW, Guchelaar H-J. Risk assessment in clinical pharmacy. *Pharm World Sci* 2003; 25 (3): 98-103
- Gawande A. Complications. New York: Metropolitan Books, Henry Holt and Company, 2002
- Molmans BHE, Kalmeijer MD, Reitsma RB, et al. Invloed van een elektronisch voorschrijfsysteem op medicatiegerelateerde foutmeldingen. *Pharm Weekbl Ziekenhuisfarmacie* 2004; 139 (47): 1547-9
- Denig P, Haaijer-Ruskamp FM. Therapeutic decision making of physicians. *Pharm Weekbl Sci* 1992; 14 (1): 9-15
- Schumock GT, Walton SM, Park HY, et al. Factors that influence prescribing decisions. *Ann Pharmacother* 2004; 38 (4): 557-62
- Studdert DM, Mello MM, Brennan TA. Financial conflicts of interest in physicians' relationships with the pharmaceutical industry: self-regulation in the shadow of federal prosecution. *N Engl J Med* 2004; 351 (18): 1891-900
- Silverman JB, Stapinski CD, Churchill WD, et al. Multifaceted approach to reducing preventable adverse drug events. *Am J Health Syst Pharm* 2003; 60: 582-6
- Janknegt R, Steenhoek A. The System of Objectified Judgement Analysis (SOJA): a tool in rational drug selection for formulary inclusion. *Drugs* 1997; 53 (4): 550-62
- Pedersen CA, Schneider PH, Santell JP. ASHP national survey of pharmacy practice in hospital settings: prescribing and transcribing - 2001. *Am J Health Syst Pharm* 2001; 58: 2251-66
- Wade WE, Spruill WJ, Taylor AT, et al. The expanding role of pharmacy and therapeutics committees: the 1990s and beyond. *Pharmacoeconomics* 1996; 10 (2): 123-8
- Weekes LM, Brooks C. Drug and therapeutics committees in Australia: expected and actual performance. *Br J Clin Pharmacol* 1996; 42 (5): 551-7
- Fijn R, Brouwers JRBJ, Knaap RJ, et al. Drug and therapeutics (D&T) committees in Dutch hospitals: a nation-wide survey of structure, activities, and drug selection procedures. *Br J Clin Pharmacol* 1999; 48 (2): 239-46
- Fijn R, Lenderink AW, Egberts AC, et al. Assessment of indicator for hospital drug formulary non-adherence. *Eur J Clin Pharmacol* 2001; 57 (9): 677-84

33. Kweekel DM, le Cessie S, Guchelaar HJ, et al. Outcomes of an antimicrobial control program in a Dutch hospital. *Am J Health Syst Pharm* 2004; 61 (16): 1702-6
34. Bates DW, Leape LL, Cullen DJ, et al. Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. *JAMA* 1998; 280 (15): 1311-6
35. Guchelaar HJ, Kalmeijer MD. The potential role of computerisation and information technology in improving prescribing in hospitals. *Pharm World Sci* 2003; 25 (3): 83-7
36. Kaushal R, Shojania KG, Bates DW. Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review. *Arch Intern Med* 2003; 163 (12): 1409-16
37. Bates DW, Teich JM, Lee J, et al. The impact of computerized physician order entry on medication error prevention. *J Am Med Inform Assoc* 1999; 6 (4): 313-21
38. Weingart SN, Toth M, Sands DZ, et al. Physicians' decisions to override computerized drug alerts in primary care. *Arch Intern Med* 2003; 163 (21): 2625-31
39. Hsieh TC, Kuperman GJ, Jaggi T, et al. Characteristics and consequences of drug-allergy alert overrides in a computerized physician order entry system. *J Am Med Inform Assoc* 2004; 11 (6): 482-91
40. Oren E, Shaffer ER, Guglielmo BJ. Impact of emerging technologies on medication errors and adverse drug events. *Am J Health Syst Pharm* 2003; 60 (14): 1447-58
41. Koppel R, Metlay JP, Cohen A, et al. Role of computerized physician order entry systems in facilitating medication errors. *JAMA* 2005; 293 (10): 1197-203
42. Kalmeijer MD, Holtzer W, van Dongen R, et al. Implementation of a computerized physician medication order entry system at the Academic Medical Centre in Amsterdam. *Pharm World Sci* 2003; 25 (3): 88-93
43. Colen HB, Neef C, Schuring RW. Identification and verification of critical performance dimensions: phase 1 of systematic process redesign of drug distribution. *Pharm World Sci* 2003; 25 (3): 118-25
44. Taxis K, Barber N. Causes of intravenous medication errors: an ethnographic study. *Qual Saf Health Care* 2003; 12 (5): 343-7
45. Poley MJ, Bouwmans CA, Hanff LM, et al. Efficiency of different systems for medication distribution in an academic children's hospital in The Netherlands. *Pharm World Sci* 2004; 26 (2): 83-9
46. Lewis RF, editor. The impact of information technology on patient safety. Chicago (IL): Healthcare Information and Management Systems Society, 2002
47. Lenderink BW, Egberts TC. Closing the loop of the medication use process using electronic medication administration registration. *Pharm World Sci* 2004; 26 (4): 185-90
48. Leape LL, Cullen DJ, Dempsey Clapp M, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA* 1999; 281 (3): 267-70
49. Kucukarslan SN, Peters M, Mlynarek M, et al. Pharmacists on rounding teams reduce preventable adverse drug events in hospital general medicine units. *Arch Intern Med* 2003; 163: 2014-8

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