Current status of preparation and distribution of medicines

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The scope of hospital pharmacy practice has expanded over the past several decades beyond drug-product-oriented tasks to include patient-oriented clinical pharmacy services, investigational drug research, and pharmacist services in the emergency department. However, in most countries, pharmacists still devote considerable time to the dispensing and preparation of medicines. In my own estimation, Japanese hospital pharmacists spend about 60% of their time dispensing medicines to inpatients and outpatients, 15% of their time preparing injectable products, another 15% providing clinical pharmacy services on the wards, and 10% performing other services (e.g., drug information services, therapeutic drug monitoring, inventory management, pharmaceutical manufacturing, investigational drug studies). Improving the efficiency of dispensing and preparing medicines through the use of computer technology can reduce the amount of time spent on product-oriented activities and can enable pharmacists to devote more time to specialized patient-oriented clinical services. Nevertheless, dispensing and preparing medications are core pharmacy functions needed to ensure the safety and effectiveness of drug therapy. Analyses of medication-error reports reveal that errors occur in the dispensing and preparation steps of the medication-use process and that some of these errors result in patient harm or death.1,2

The results of the Global Survey of Hospital Pharmacy Practices reveal marked differences among countries in pharmacy systems and the nature and extent of involvement of pharmacists in dispensing and preparation activities. Ideally, all medication orders should be reviewed by a pharmacist for appropriateness before dispensing and administering medications, regardless of the clinical setting. Some medicines are obtained in ready-to-use form from manufacturers, and other medicines require preparation before administration. The nature of the preparation process depends on the stability of the product, need for sterility, dosage form, route of administration, and other factors. All medicines should be stored under proper temperature and lighting conditions, with appropriate security to prevent access by unauthorized persons.

The dispensing and preparation of medicines may take place in the pharmacy or patient care area, depending on the urgency of patient care, availability of human resources, and other factors. Medicines for parenteral administration must be sterile. The preparation of sterile products that are not available commercially is best performed in the pharmacy, although this is not always feasible in urgent cases. Most medicines for inpatient use are dispensed and prepared in a centralized pharmacy; however, some hospitals have satellite pharmacies in patient care areas.3,4 Some medicines are kept in the patient care area (e.g., on the wards and in intensive care units and the emergency department), but the use of such medicines is limited for safety reasons in some hospitals with unit dose drug distribution systems. Some patients bring their own medicines for use in the hospital, but this practice is limited for safety reasons in some hospitals.5

Many hospital pharmacies dispense medicines to outpatients. The dispensing of cancer chemotherapy for administration on an outpatient basis has become increasingly common because of economic reasons,
and the availability of supportive care for the adverse effects from chemotherapy in ambulatory patients.

General overview

Medicines are dispensed, prepared and distributed to patients in the hospital through several pathways, depending on whether the patient is an inpatient or outpatient and the location in the hospital (Figure 1). There are five primary tasks in dispensing and preparing medicines: 1. accurate and efficient communication of medication orders to the pharmacy department, 2. review of medication orders for appropriateness by a pharmacist, 3. verification of proper medicine storage, 4. accurate preparation of medicines for dispensing if they are not commercially available in ready-to-use form, and 5. accurate and efficient dispensing and distributing medicines to hospital inpatients and outpatients. Verifying the identity and appropriateness of patient medicines brought from home and providing a mechanism for dispensing and preparing medicines appropriately and efficiently when the pharmacy is closed may also be required.

Communicating medication orders to pharmacy. In many hospitals, transmitting medication orders to the pharmacy department entails making a handwritten copy of the order (i.e., transcribing the order) and sending the copy to the pharmacy. Alternatively, a carbon copy or no-carbon-required copy may be created at the time an order is written, and this copy is then sent to the pharmacy. Scanning and facsimile transmission of the original order to the pharmacy have been used to expedite the order transmission process and shorten the turnaround time for order processing. Computerized prescriber order entry (CPOE) systems with a pharmacy interface are being increasingly used to circumvent the need to transcribe orders, eliminate errors associated with poor handwriting and the transcription process, and reduce delays associated with the transmission of orders.

Medication order review for appropriateness. Although review of all medication orders by a pharmacist for appropriateness is preferred before dispensing, this review is not always feasible in urgent care situations and facilities without 24-hour pharmacy services. A retrospective review of a random sample of all orders is performed in some institutions where prospective review is not possible. Many hospitals have identified high-risk medicines and taken steps to ensure that the order-review process is performed before dispensing medicines in order to reduce the risk of harm.

In the Global Survey, 48% of respondents indicated that a pharmacist reviews all nonemergency medication orders before dispensing in most (more than 60%) hospitals in their country, and 34% of respondents indicated such practices in few (less than 40%) hospitals in their country. In the same survey, 34% of respondents indicated that medication orders are reviewed by a pharmacist for appropriateness of the drug, dose, frequency, and route of administration in most hospitals in their country, but 48% of respondents indicated that this function is performed in few hospitals in their country.

Computer software with screening capabilities to detect drug allergies, drug interactions, therapeutically and inappropriate dosing is used for medication-order review in some hospitals. This software may be part of a CPOE system or a standalone pharmacy computer system. The use of CPOE or preprinted orders facilitates the medication-order-review process by standardizing orders.

In many hospitals, it is difficult to obtain sufficient patient-specific information (e.g., the diagnosis, laboratory test results) to judge the appropriateness of medication orders, especially for outpatients, because of a lack of computerization of patient information or an interface between the hospital mainframe computer and the pharmacy computer system. In the Global Survey, 39% of respondents indicated that most hospitals in their country have access to sufficient medical information about patients, and 45% of respondents indicated...
that few hospitals in their country have such access. In its Statement of Professional Standards on Electronic Prescriptions, the International Pharmaceutical Federation (FIP) requires that electronic systems provide the pharmacist with access to information about the patient as necessary to judge the appropriateness of prescribed drug therapy and include the diagnosis, intended use of the medication, or both. Most hospitals use an electronic or manually maintained outpatient medication profile, including drug allergies, as part of the medication-order-review process. Some hospitals with electronic patient-medication profiles use computer software with screening capabilities for drug allergies, drug interactions, inappropriate dosing, and therapeutic duplication.

Some hospitals have policies and procedures for the review of cancer chemotherapy orders requiring pharmacists to verify the appropriateness of the ordered medicine, dose, dilution method, administration route and schedule, premedication, and auxiliary medication to treat adverse effects associated with chemotherapy. These elements of the chemotherapy order are evaluated in the context of established protocols and the patient height, body weight, body surface area, and laboratory test results, which may reflect renal and liver impairment and the need to make dose reductions.

**Verification of proper medicine storage.** Proper temperature and lighting conditions for medicines and appropriate security measures to prevent access by unauthorized persons should be ensured during and after dispensing and preparing medicines. Most hospitals have policies and procedures for checking thermometers periodically and maintaining manual temperature logs for temperature-sensitive medicine storage areas. Policies and procedures also address the use of locks and alarm systems to ensure the security of storage areas. However, in some hospitals, refrigerators are not equipped properly with thermometers, locks, and alarms; therefore, substantial losses of costly medicines are incurred, although data are available to support the storage of some medicines labeled for refrigerated storage for brief periods at room temperature.

Some hospitals use automated medicine storage and dispensing devices (e.g., cabinets) to ensure secure medicine storage in patient care areas. However, some devices are equipped with an override function to allow access and administration by nursing staff before a pharmacist reviews the medication order, and the use of such override functions by nurses can result in medication errors.

**Preparation of medicines.** Many medicines are not commercially available in ready-to-use form because of limited stability or other factors. Some medicines are available only in bulk containers and must be repackaged for use in unit dose drug distribution systems. Most American hospitals repack the oral medicines but not injectable medicines. Repackaging is done manually for individual patients as needed at many hospitals, although some large hospitals prepare batches of commonly used unit doses using automated packaging equipment. Labeling of repackaged doses with bar codes or other machine-readable coding is performed at some hospitals.

Repackaging of sterile medicines in single unit-of-use syringes is sometimes performed as part of a unit dose drug distribution system. Compounding of i.v. admixtures and parenteral nutrient solutions is also commonly required to meet patient-specific needs when premixed solutions are not available commercially. In the Global Survey, only 14% of respondents indicated that the pharmacy department compacts all i.v. admixtures for every patient in most hospitals in their country, and 80% of respondents indicated that such compounding takes place in few hospitals in their country.

Some hospitals have standardized the concentrations of sterile products used in the institution to simplify preparation and reduce the risk for error in preparation and administration, especially for high-risk medicines. However, a wide variety of concentrations are used in other facilities. Inconsistencies in expressing concentrations have caused confusion among physicians and errors in pharmaceutical calculations.

Ideally, sterile medicines for parenteral administration should be prepared in a laminar airflow hood located in the pharmacy department using aseptic technique. However, in European hospitals, injectable medicines are commonly prepared in or near patient care areas because of insufficient resources. In the Global Survey, 33% of respondents indicated that a laminar airflow hood is used for compounding sterile products in most hospitals in their country, and 62% of respondents indicated that this equipment is used in few hospitals in their country.

Hazardous drugs (e.g., cytotoxic anticancer drugs) present unique concerns about the safety of hospital staff who handle the drugs as well as the need to maintain product sterility. In some hospitals, specialized biological safety cabinets located in the pharmacy department or chemotherapy room are used to protect staff during the preparation of hazardous drugs, although other hospitals lack these cabinets. In the Global Survey, 25% of respondents indicated that the pharmacy department prepares cancer chemotherapy doses in most hospitals in their country. In many hospitals, chemotherapy doses typically are prepared by physicians and nurses with or without pharmacist order review.

**Dispensing and distribution of medicines.** Some hospitals use unit dose drug distribution systems with
carts of drawers for each patient containing patient-specific doses. The carts usually contain enough doses for one day and are exchanged once a day. When a new medication is ordered, there is a mechanism to provide for the delivery of enough doses of the new medicine until the next cart exchange. The administration records listing the prescribed drug, dose, route of administration, and frequency are placed in the drawers in some hospitals.

Unit dose drug distribution systems are supplemented by crash carts and the stocked medicines for use in patient care emergencies. The use of stocked medicines in patient care areas varies among hospitals. Differences reflect efforts to weigh safety concerns associated with the use of stocked medicines without previous pharmacist order review and the perceived need for prompt access to medicines in urgent situations.

In the Global Survey, 26% of respondents indicated that most hospitals in their country distribute the majority of medicines to patients as unit doses, but a comparatively larger percentage (58%) of respondents indicated that few hospitals in their country do so.7 Some hospitals use automated medicine storage and distribution devices and bar-code technology to ensure the accurate filling of the machines and dispensing. However, in the Global Survey, only 8% of respondents indicated that medicines are picked via a process that is at least partially automated in most hospitals in their country, and 83% of respondents indicated that such automation was used in few hospitals in their country. A lack of computerization may explain these findings. Fifty-six percent of survey respondents indicated that the pharmacy department uses at least one computer for pharmaceutical service functions in most hospitals in their country, but 29% indicated that computers are used for these functions in few hospitals in their country.

**Use of patient's own medicines.** Hospitals vary in their policies for allowing the use of patient medicines brought from home.3 Roughly one in three respondents to the Global Survey suggested that most hospitals in their country have specific policies that address the use of patient’s own medicines, and approximately one in two respondents suggested that few hospitals in their country have such policies.7 The practice of allowing the use of patient’s own medicines tends to be widespread in some countries where hospitals are reimbursed under a fixed-payment system based on the diagnosis. In other countries, patient use of their own medicines is usually allowed only for unusual medicines that are not available in the hospital pharmacy, when suitable alternatives are not available, when the medicines can be accurately identified, and when the patient can reliably explain how he or she has been using them. The use of herbal or dietary supplements is permitted in some hospitals if concerns about interactions between supplements and prescribed medicines can be allayed. Allowing the use of patients’ own medicines did not appear to increase the risk for medication error in a teaching hospital in the United Kingdom.15

**After-hours dispensing and preparation of medicines.** The availability of 24-hour pharmacy services and mechanisms for providing dispensing and preparation services when the pharmacy is closed vary among hospitals. Some hospitals without 24-hour pharmacy services have a mechanism for retrospective review of new medication orders filled while the pharmacy was closed.

**Special hospital areas.** In many hospitals, the emergency department and operating suites are areas in which pharmacist oversight for medication is lacking. High-risk medication is common in these areas. In the Global Survey, 18% of respondents indicated that a pharmacist reviews medication orders for appropriateness of the drug, dose, frequency, and route of administration for patients during surgery in most hospitals in their country, but 76% of respondents indicated that such review takes place in few hospitals in their country.7 Only 10% of respondents indicated that the pharmacy department compounds i.v. admixtures for special units, such as intensive care units, but not for others in most hospitals in their country, and 81% of respondents indicated that such compounding takes place in few hospitals in their country. Clinical pharmacy services were introduced in the emergency department in a limited number of U.S. hospitals decades ago.16 However, most American pharmacists have struggled in recent years to meet new requirements of the Joint Commission for medication order review in the emergency department.

**Literature evaluation**

Various strategies and technologies have been developed to improve the accuracy and efficiency of the tasks involved in dispensing and preparing medicines, including CPOE, pharmacy-based i.v. admixture services with standardization of concentrations, unit dose drug distribution systems, bar-code technology, automated medicine storage and distribution devices, and automated prescription-filling systems. Authoritative guidelines and best practices have been developed to provide pharmacists with assistance in dispensing and preparing medicines.

CPOE. The use of CPOE systems expedites the transmittal of medication orders to the pharmacy department and eliminates the risk of transcribing error. It also facilitates the medication-order-review process if orders are selected by the prescriber from menus of standardized orders in the CPOE.17 These systems enhance the efficiency of dispensing and reduce the risk of medication er-
rers. In the pediatric nephrology ward, the use of CPOE in combination with a unit-dose drug distribution system significantly reduced prescribing and administration error rates compared with handwritten prescribing and a ward stock distribution system.

In a large, academic medical center, implementation of CPOE significantly reduced the turnaround time for medication (i.e., the time from ordering until administration). Minimizing turnaround time through the use of CPOE contributes to the efficient dispensing of medicines. The incorporation of cancer chemotherapy protocols into a CPOE system has been shown to reduce the risk of chemotherapy prescribing error. It also facilitates the review of chemotherapy orders for appropriateness.

**Pharmacy-based intravenous admixture services.** The use of pharmacy-based i.v. admixture services reduces the risk of error in performing pharmaceutical calculations and compounding i.v. admixtures. Many "high-alert" medicines are parenteral products for which caution in preparation is warranted. One in four medication incidents reported to the National Patient Safety Agency (NPSA) in the United Kingdom involved injectable medications. Centralizing and standardizing i.v. admixture compounding (ordering, concentrations used, and labeling) in the pharmacy department have been shown to improve efficiency in preparation and reduce costs.

A study of the concentrations of medicines in syringes used to prepare i.v. admixtures in a critical care unit in the United Kingdom revealed wide variability, suggesting the need to use prefilled syringes from a commercial source or standardized concentrations for i.v. admixture preparation. Standardizing i.v. concentrations has been shown to significantly reduce the incidence of wrong concentration and wrong dose errors.

Guidelines for the aseptic preparation of sterile products and the handling of hazardous drugs are available. The United States Pharmacopeia (USP) has issued requirements for pharmaceutical compounding of sterile preparations. The NPSA has issued recommendations for actions to improve the safety of injectable medicine use, including focusing efforts on high-risk medicines and ensuring that there are up-to-date protocols for prescribing, preparing, and administering injectable medicines in all clinical areas. In its Statement of Professional Standards on Medication Errors Associated with Prescribed Medication, FIP acknowledges the potential for safety problems with i.v. and other injectable medicines and suggests that special attention should be devoted to labeling these products. Requirements for compounding high-risk preparations are more stringent than those for other preparations, resulting in a reduction in compounding of high-risk preparations in American hospital pharmacies.

**Unit dose drug distribution systems.** Studies evaluating the effect of unit dose drug distribution systems on medication error rates consistently demonstrate a positive influence. In an Australian hospital, the use of a unit dose drug distribution system (instead of a conventional ward stock drug distribution system) increased pharmacy time requirements for drug distribution, but it reduced nursing time for medication-related activities and significantly reduced medication errors. However, missing doses commonly occur with unit dose drug distribution systems.

In many hospitals, unit-dose cart filling is performed by a pharmacy technician, and the accuracy of cart-filling is checked by a pharmacist. In studies in which the cart-checking step was performed by a second trained pharmacy technician with a pharmacist double checking a random sample of filled drawers, the cart-filling accuracy was not reduced compared with the conventional practice of having a pharmacist check all drawers. These findings suggest that pharmacy technicians with the proper training could assume responsibility for the accuracy of unit-dose cart filling, thereby freeing up pharmacist time without compromising patient safety.

A unit-of-use drug distribution system was developed for an emergency department with a limited formulary of medicines. This system improved pharmacy control of medicine use, reduced the inventory of medicines used in the emergency department, provided automatic restocking, improved security and labeling, and saved time for emergency department personnel.

**Bar-code technology.** The use of bar-code or other machine-readable technology at the bedside to reduce the risk of medication errors is well established. A bar-code medicine packaging and distribution system was shown to enhance inventory control as well as dispensing accuracy. A hospital pharmacy-based, bar-code repacking center was established to allow the scanning of bar codes on sterile and nonsterile medicines during the dispensing and administration processes. Quality control procedures for the repackaging process with oversight by a pharmacist were effective for detecting errors in repackaging.

At an academic tertiary medical center with a bar-code-assisted dispensing system, scanning all doses for dispensing error was compared with scanning only one of several identical doses in a batch. Both scanning strategies reduced the risk of dispensing error, but scanning every dose was preferable to scanning random samples from a batch. In one hospital pharmacy, implementation of bar-code technology for dispensing provided a positive financial return on investment with a 5-year net benefit of nearly $3.5 million because
of a reduction in dispensing errors and adverse drug events. A break-even point was reached after 1 year.

On February 25, 2004, the U.S. Food and Drug Administration (FDA) finalized a rule requiring bar codes on the labels of most human drugs and biological products to improve patient safety. The rule also requires machine-readable information on container labels of blood and blood components. FDA estimates that the rule will help prevent nearly 500,000 adverse events and transfusion errors while saving $93 billion in health costs over 20 years.

In its Statement of Professional Standards on Medication Errors Associated with Prescribed Medication, FIP calls for the use of machine-readable coding on all medicines and recognizes the importance of standardizing this coding. All unit-dose packages should be labeled with a machine-readable code (as well as human-readable identification) with a unique identifier for use with bar-code-medicine-administration systems, including pharmacy automation systems and automated medicine storage and dispensing devices.

Automated medicine storage and distribution devices and prescription-filling systems. Medicines may be stored in and dispensed from automated storage and distribution devices (e.g., Pyxis MedStation, Cardinal Health, Dublin, OH; AcuDose-Rx, McKesson Corp., San Francisco, CA) in patient care areas, which are particularly helpful in urgent care situations and facilities without 24-hour pharmacy services. The use of such devices for controlled substances can facilitate audits.

Automated medicine storage and distribution devices can reduce the rate of medication errors and increase the efficiency of drug administration. They also may free pharmacist time for clinical services. However, increases in pharmacy workload and pharmacy-related errors (incorrect loading of cabinets) have also been reported. Automated medicine storage and distribution systems should be fully integrated with the health care institution’s medication-use process to provide medicines in unit dose or single unit-of-use packages in ready-to-use form, make medicines available only near the time of administration, create an individualized patient medication profile, allow for pharmacist review of medication orders before dispensing, ensure proper storage conditions, prevent access by unauthorized personnel, allow access in emergencies, and meet applicable regulations and standards.

Automated prescription-filling systems can reduce the pharmacy staff time required for the direct and indirect activities related to the filling of prescriptions. These activities include receiving, order entry, filling, inspection, packaging, dispensing, telephone calls, and inventory management.

Continuum of dispensing and preparation practices

A wide continuum of dispensing and preparation practices is found among hospital pharmacies, depending on human and financial resources, safety considerations, local regulations, and priorities. In many hospitals, medicines are prepared in patient care areas or obtained in ready-to-use form from the ward stock by nursing staff immediately before administration without pharmacist review of the medication order or oversight of the drug preparation process to ensure appropriateness and patient safety. These practices are particularly dangerous when high-risk parenteral and hazardous medicines are involved. The stock of medicines on the wards should be minimized for safety reasons. At the most basic level, nonemergency medication orders should be accurately and efficiently transcribed and sent to the pharmacy department for review of appropriateness by a pharmacist. The review is preferably prospective, although a retrospective review of a random sample of orders to identify problems might be considered a basic practice. The use of CPOE represents an advanced practice for accurately and efficiently transmitting medication orders to the pharmacy and contributes to the accuracy of the order review process because of the standardized medication orders and automated screening functions inherent in the software.

Verification of proper medicine storage (temperature, lighting, and security) may be performed by checking thermometers and using conventional locks and keys, with the use of automated storage and dispensing cabinets considered an advanced practice to accomplish this task.

When medicines are not available commercially in ready-to-use form, preparation is required. Preparation of medicines for parenteral administration should be performed in a clean, low-traffic area using aseptic technique at a minimum. Pharmacy-based i.v. admixture services with sterile product preparation performed in a laminar airflow hood and preparation of hazardous medicines performed in a biological safety cabinet represent advanced practices.

The use of unit-dose drug distribution systems with limited stock of medicines represents a basic practice for accurately and efficiently dispensing medicine to inpatients. Repackaging of medicines for use in a unit dose drug distribution system might be considered an intermediate practice. The use of automated medicine storage and distribution devices and bar-code technology to ensure accurate dispensing represent advanced practices. The use of automated prescription-filling systems is another advanced practice for accurately and efficiently dispensing medicines.

Manually documenting outpatient medication profiles is a basic practice for accurately dispensing medicines...
to these patients. Creating electronic patient medication profiles and using software to screen for drug allergies, drug interactions, inappropriate dosing, and therapeutic duplication are more advanced practices on the continuum to accomplish the task.

### References


20. Food and Drug Administration. FDA rule requires bar codes on drugs and blood
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Literature review

The literature review was based on searches of knowledge-based resources, journals, and websites. Published studies, reports, conference proceedings, consensus statements, and abstracts published in English were evaluated. Approximately 3000 citations were reviewed.

On an international basis, the domain of administration of medications is primarily the responsibility of nurses, although nurse technicians are used in countries such as Brazil. Medication administration is often referred to as the “sharp edge” in the medication-use process because errors introduced at the prescribing, dispensing, or transcribing step, if not intercepted, will result in the patient receiving the medication in error.

The administration of medications consists of a series of complex, problem-prone processes. In a study of the origin of errors, 38% of preventable medication errors occurred at the administration step. It has been claimed that nurses spend up to 40% of their time administering medications. The frequency of administration errors ranges from 2.4% to 47.5%, depending on the drug distribution system in place. In the United Kingdom, a recent report by the National Patient Safety Agency (NPSA) indicated that 56.5% of reported errors associated with severe harm or death occurred at the administration step.

Medication orders require the drug, dose, rate, route, frequency, and, when appropriate, duration to be explicit and specific to the needs of the patient in order to achieve the desired outcome. In effect, medication orders are sentences where an error or lack of precision in any of the elements of the order can result in unintended consequences. Administration of the wrong medication, dose, dosage form, route, rate, or frequency are examples of consequences due to misinterpretation, ambiguity, or lack of knowledge or understanding of elements of the medication order sentence.

Principles of safe medication administration

A number of principles for safe medication administration can be gleaned from a review of the literature. The 5 rights (5 Rs) of medication administration (right patient, right drug, right dose, right route, and right time) are principles that nurses are taught as part of their nursing education; however, nurses may not always adhere to the 5 Rs and may also lack knowledge about the medication, including the indication, usual dose, route, actions, adverse effects, contraindications, and drug–drug or food–drug in...