

Pediatric medication safety considerations for pharmacists in an adult hospital setting

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Purpose. Risks and vulnerabilities of the medication-use process in nonpediatric institutions that also serve pediatric patients are reviewed, and guidance on risk mitigation strategies is provided.

Summary. There are many risks and vulnerabilities in the medication-use process as it relates to pharmacotherapy for pediatric patients admitted to adult institutions. Mitigation of these risks is critical and should encompass various available resources and strategies. Special emphasis should be placed on use of technology to improve overall safety. Available literature recommends optimization of technology and resource use, institutional support for pediatric pharmacists' involvement in managing pediatric medication use, and provision of early exposure to pediatric patients in pharmacist training programs as additional methods of mitigating risks associated with pediatric medication use in adult institutions. Adult hospitals that provide care for pediatric patients should assess their processes in order to identify hospital-specific interventions to promote pediatric medication safety.

Conclusion. Pediatric medication safety frameworks in U.S. adult institutions vary widely. Treating pediatric patients involves risks in all areas of the medication-use process. Optimizing technology, utilizing external resources, supporting a pediatric pharmacist, and providing early-career exposure to pediatric patients are methods to mitigate risks in institutions that primarily serve adult patients.

Keywords: adult, medication safety, nonpediatric, pediatric

Am J Health-Syst Pharm. 2019; 76:1481-91

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This article is part of a special *AJHP* theme issue on considerations in the management of pediatric patients. Contributions to this issue were coordinated by Peter N. Johnson, Pharm.D., BCPS, BCPPS, FPPAG, and Jamie L. Miller, Pharm.D., BCPS, BCPPS, FPPAG.

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DOI 10.1093/ajhp/zxz168

Pediatric patients are at increased risk for medication errors and are at increased risk for harm due to these errors. The rate of medication errors resulting in harm or death in children is higher than the rate in adults (31% and 13%, respectively).^{1,2} Additionally, medication errors not causing harm occur 3 times more frequently in children than in adults.³ Although most reported errors in pediatric patients are similar to those encountered in adults, errors occurring in general acute care hospitals tend to result in higher levels of harm than those occurring in pediatric hospitals.⁴ Commonly reported errors in children and adults include use of an inappropriate medication for a given disease state, an incorrect dose or treatment interval, a lack of drug

therapy monitoring, and an incorrect route of administration.¹ Specific medication errors most commonly reported in pediatrics involve dosing, with errors stemming from calculated doses and dosing intervals^{1-3,5}; this can be attributed to the need for individualized dosing calculations based on weight, age, or body surface area and clinical indication. A survey-based study of the use of various safety measures by pediatric practitioners in an adult hospital identified common gaps in aspects of care such as documentation of mg/kg dosing and maximum dosing, use of a pediatric pharmacist, use of a pediatric medication safety committee, and use of computerized provider order entry (CPOE) for weight-based dosing in the emergency department (ED).⁶

With over 200 pediatric hospitals in the United States and hundreds more in other countries, the numbers of medical care facilities for children have grown over the past several decades. However, many adult institutions still serve pediatric patients with acute care and surgical needs. These institutions may not have several of the safeguards available at pediatric institutions, such as providers trained in the complexities of pediatric patients, access to 24-hour pharmacy services, and pediatric-based order sets, policies, and protocols. The dual purpose of this article is to identify the risks and vulnerabilities of the medication-use process in adult institutions that serve pediatric patients and to provide advice on how to mitigate these risks, with a special emphasis on the use of technology. The article concludes with a listing of resources available to assist pharmacists in caring for pediatric patients in a primarily adult-focused setting.

Adult institutions that also serve pediatric patients should take extra precautions to meet the safety needs of pediatric patients. Consider the following example: You are the only pharmacist working in a small hospital when a mother arrives to the ED with a toddler in status epilepticus. The ED physician orders rectal diazepam, but this is a nonformulary medication and is not stocked in the pharmacy. The physician asks for an alternative, and you recommend a dose of i.v. lorazepam. The physician asks you to determine an appropriate dose and enter a (verbally approved) order in the CPOE system. You quickly look up the dose using an online reference and start to enter the order. However, there is only an adult order set available in the electronic medical record (EMR). You must enter the order by manipulating the adult order set or by entering a free-text order. You triple check the dose and preparation and take the dose to the ED. You check the dose and calculations with the nurse. She begins to administer the dose according to your recommendation, via a slow push, because no i.v. pumps that will

KEY POINTS

- Pediatric medication safety frameworks in U.S. adult institutions vary widely.
- Treating pediatric patients involves risks in all areas of the medication-use process.
- Optimizing technology, utilizing external resources, supporting a pediatric pharmacist, and providing early exposure to the pediatric population in pharmacist training are methods to mitigate risks in caring for the pediatric population in institutions that primarily serve adult patients.

accommodate the small dose and infusion rate are available. A few minutes later the seizure stops, and the patient is prepared for transfer to a pediatric hospital that is 75 miles away. This scenario may occur with some frequency, and each time there is a risk of errors in the care of a pediatric patient.

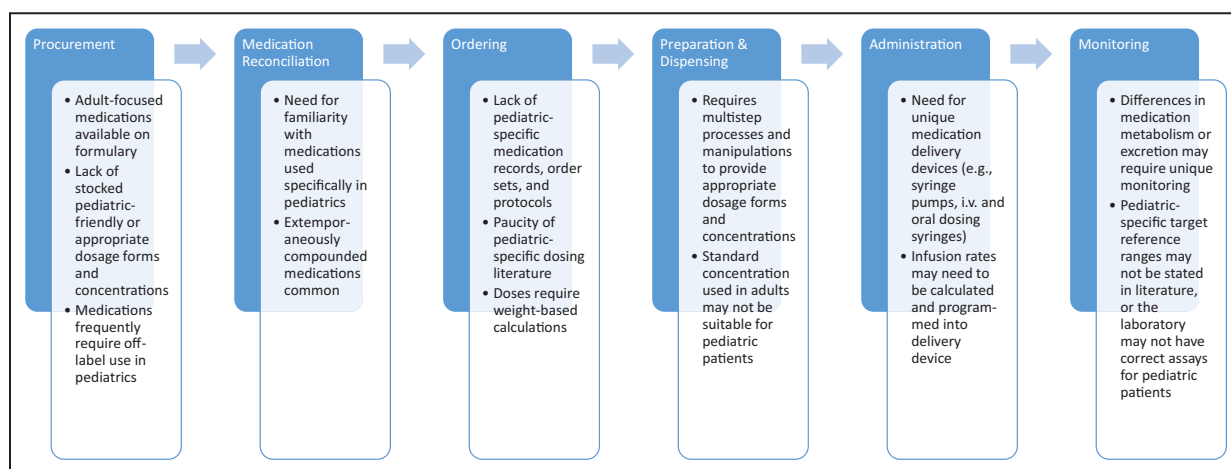
Risks and vulnerabilities of the pediatric medication-use process

From procurement to monitoring, the medication-use process as it applies to pediatric patients is unique due to the increased risks and vulnerabilities of this patient population (Figure 1). It has been shown that medication errors occur during all stages of the medication-use process.⁷ Pediatric patients have less tolerance for errors, and certain types of medications are more likely than others to be involved in errors in pediatric settings, specifically i.v. fluids, analgesics, and antibiotics.⁸ In 2015, the Institute for Safe Medication Practices (ISMP) highlighted safety concerns stemming from pediatric medication use in primarily adult institutions through the results of a survey assessing pediatric medication safety practices.⁹ This survey highlighted the increased compliance with

error prevention strategies in pediatric hospitals versus adult hospitals that care for pediatric patients, including differences in perceptions of compliance with these strategies by healthcare discipline. Creating a culture that focuses on patient safety for all patients is paramount to optimal care.

Procurement and formulary management. Adult hospitals may not have pediatric medications or supplies on the formulary or stocked in the pharmacy. Additionally, having a pediatric-trained pharmacist involved in formulary and drug policy decisions is not always possible. Both of these issues can present challenges, as pediatric patients often require specific medications and supplies.

The off-label use of medications in pediatric patients is necessary and can be challenging. The American Academy of Pediatrics (AAP) published a position statement on off-label medication use.¹⁰ Some institutions regard off-label use of medications as incorrect, illegal, or only for investigational purposes. However, off-label use of medications, especially in pediatrics, is not only appropriate but is often necessary. Clinical decision making guided by available evidence is of utmost importance in treating pediatric patients, because the labeling of most drugs does not specify pediatric indications and dosing guidance. Since large clinical drug trials are often not conducted in pediatric populations, practice is often guided by case reports and expert opinion. Off-label use of medications is not considered investigational and thus does not require informed consent documentation unless it is part of an investigational study. Therefore, while providers should inform patients and families of the general risks and benefits of off-label medication use, off-label use does not require formal informed consent. Additionally, formulary management decisions should not be based solely on whether an agent is to be used for FDA-approved versus off-label indications in pediatric patients. Likewise, medications considered first-line agents for treating adults should not instinctively

Figure 1. The medication-use process and pediatric risk considerations.

be considered first-line agents for pediatric indications. In times of drug shortages, the off-label use of medications in pediatric patients should be considered.

Drug shortages are a challenge for all institutions and patients but can pose specific challenges in treatment of pediatric patients. Some hospitals may use outsourced products, such as prefilled syringes, with extended dating and specific markings for pediatric use, which can be advantageous for these institutions. If pediatric preparations become unavailable, a pharmacy may need to begin compounding these products, leading to increased risks related to nonstandard processes and multistep dilutions and compounding.

Supplies can also pose a challenge for adult institutions providing care for pediatric patients. The Joint Commission, in conjunction with the National Pediatric Readiness Project, is developing requirements to include equipment and medications that may be necessary for proper resizing of resuscitation equipment and weight-based dosing for pediatric emergencies.¹¹ These requirements will allow an organization to determine the types of pediatric equipment and supplies needed for its ED on the basis of historical data and discussions with emergency medical services in the community. AAP published a policy statement with recommendations for ED care for pediatric patients to decrease medication-related

errors in this high-risk area.¹² These recommendations include implementing standardized formularies and concentrations; using an ED pharmacist; advocating for pediatric medication safety training in medical, nursing, and pharmacy curricula; and decreasing medication errors in the home.

Medication reconciliation. It has become a standard that medication reconciliation is completed for each patient at admission and discharge. In 2005, the Joint Commission identified inpatient medication reconciliation as a National Patient Safety Goal, stating that hospitals should be required to be compliant with medication reconciliation practices for each patient in order to resolve any discrepancies. These discrepancies can occur on admission, transfer, or discharge. A prospective chart review-based study focused on medication discrepancies in children that were caught by a pharmacist at the time of hospital discharge and the potential severity of the errors.¹³ Of the 501 discharge medication orders reviewed, 20% were found to have discrepancies, with the records of 33% of patients having at least 1 discrepancy. These discrepancies were classified as having minor to moderate harm potential, with the most common discrepancies involving directions for use, incorrect dosage form, omitted medications, and medications no longer being indicated. An observational study described the

rate, types, timing, and predictors of medication discrepancies in children and young adults with chronic disease at a pediatric hospital.¹⁴ Ten percent of the medication reconciliation errors had the potential for harm, and almost half were due to errors in obtaining a preadmission medication history. The most frequent errors were dosing-related errors on admission, including incorrect dose, incorrect frequency, and drug omission errors, which occurred in 45%, 40%, and 26% of admissions, respectively. The respiratory, metabolic, and endocrine drug classes were shown to pose the highest potential risk of causing harm. In addition, Kaushal et al.³ reviewed 10,778 pediatric inpatient medication orders and reported that 6% of orders contained errors, with 28% containing a dosing error. The drug classes most commonly involved in medication errors were antiinfectives, analgesics and sedatives, electrolytes and fluids, and bronchodilators.

The errors identified during or resulting from medication reconciliation for pediatric patients often result from challenges that may be unique to pediatrics. Oftentimes patients and families know their doses in volumes of liquids versus microgram or milligram doses. Additionally, if the patient receives a liquid formulation at home, the formulation and/or compounding information may not be available. Many outpatient pharmacies develop

individualized compounding recipes, and a lack of standard concentrations makes reconciliation of home medications and matching with formulary options difficult. Frequent dosing changes during use of certain medications, such as antiepileptics, present additional challenges.

In addition to medications, it is recommended that vaccination status be included in the reconciliation process. Access to this information is difficult even for adult patients, but many more vaccines are indicated over the long course of pediatric care, adding to the complexity of obtaining an accurate history. Furthermore, children's immunization histories often reside in the records of individual caregivers and may not appear in a consolidated medical record. A clear picture of the status of pediatric patients' stages of vaccination completion should be considered, especially in the face of specific disease states such as asplenia, sickle cell disease, and Kawasaki disease.

In many hospitals, both pediatric and adult facilities, pharmacists do not routinely perform medication histories upon admission. Commonly, nurses and providers are charged with completing medication histories with patients and caregivers; because nonpharmacist caregivers may not have a clear understanding of medication doses and formulations, this practice increases the risk of medication errors. It is a best practice to have members of the pharmacy workforce involved in medication reconciliation in adult care settings, and this practice should be extended to pediatric patients as well. If resources to enable pharmacist-initiated medication histories for all patients are not available, some hospitals ensure that all patients admitted through the ED have medication histories completed by a pharmacy technician, pharmacy intern, or pharmacist to improve history-taking accuracy.

Ordering. Selecting the correct dose—one of the quintessential steps in placing a medication order—is especially challenging in pediatrics. In the

treatment of pediatric disease states, appropriate doses of many medications are not known and special attention to detail is required to devise a dosing regimen based on limited available evidence. Common calculation errors, which can have more serious effects in pediatric versus adult patients, include unit conversion errors, miscalculation of body surface area, incorrect drip rate calculations, and weight-based errors (e.g., calculating on the basis of dry versus actual weight, expressing weight as pounds instead of kilograms, performing calculations in the absence of a documented weight value). It is a medication safety best practice to require that dose amounts always be specified in prescriptions and inpatient orders using a leading zero before a decimal point (e.g., 0.5 mg, *not* .5 mg), with no trailing zero after a decimal point (e.g. 5 mg, *not* 5.0 mg), as recommended by the National Council for Prescription Drug Programs.¹⁵ The use of tall-man lettering to prevent sound-alike, look-alike errors is also recommended. These practices have been supported for pediatric and adult medication safety by many professional and patient safety organizations, such as ISMP, FDA, the Joint Commission, and the National Coordinating Council for Medication Error Reporting and Prevention. In addition, many drugs lack FDA-approved pediatric indications and dosing guidelines, which presents an added layer of risk in ordering medication regimens and results in the significant difference in the frequency of ordering errors in pediatrics versus adult medicine; a study of error reports submitted to U.S. national databases indicated frequencies of 47% and 28%, respectively.¹

Use of a reputable pediatric dosing reference is important, as an incorrect dose could have serious adverse effects. One specific scenario in which appropriate use of dosing references is vital is treatment of patients with reduced kidney function. Commonly used equations for estimating glomerular filtration rate (GFR) in adults include the Cockcroft-Gault and Modification of Diet in Renal Disease study equations.

However, these equations should not be used in pediatrics due to their tendency to overestimate GFR. Commonly used formulas in pediatrics include the Schwartz, Leger, Bedside Chronic Kidney Disease in Children (CKiD), and Counahan-Barratt equations.¹⁶ Applying the correct formula for specific age ranges is necessary for implementation of renal dosing adjustments listed in a pediatric drug reference.

While dosing references are valuable, users of those references must know how pediatric patients are categorized by age and when a patient is no longer considered a pediatric patient. The child's age and stage of development may dictate appropriate dosing according to age-related pharmacokinetics.

Rounding of doses in pediatric patients is often necessary to ensure that the dose volume is measurable. For example, if the concentration of a suspension is 30 mg/mL and an order is written for 29 mg, the resulting dose volume is 0.967 mL. This dose should be rounded to 30 mg, resulting in a dose volume of 1 mL, which can easily be measured by pharmacy staff as well as caregivers at home. Pharmacists are well positioned to ensure that dose rounding is performed as necessary because they are the health professionals most familiar with drug formulations and concentrations.

With increasing numbers of overweight and obese pediatric patients, it is also important to take the patient's weight and puberty stage into account when selecting medication dosing regimens. It has been reported that approximately one-third of pediatric patients in the United States are considered overweight or obese, although the prevalence of obesity appears to be plateauing.¹⁷ The Pediatric Pharmacy Advocacy Group (PPAG) issued a position statement with recommendations for dosing of medications in overweight and obese children.¹⁸ Clinicians should continue to use weight-based dosing for patients weighing at least 40 kg unless the dose or dose per day exceeds the recommended adult dose for the indication. Pharmacists practicing in adult and

pediatric pharmacy should be familiar with dosing regimens for adult patients to ensure that maximum doses are not exceeded. Additionally, pharmacokinetic monitoring should be performed, when available, to guide dose adjustments in overweight or obese children in order to ensure safe and effective medication dosing. Considerations related to drug properties (e.g., lipophilic versus hydrophilic, volume of distribution) and recommendations on which weight value to use for weight-based dosing (i.e., total body weight, adjusted body weight, ideal body weight, or lean body weight) should be taken into account.¹⁹

Drug dosing references often recommend dosing regimens using different formats (e.g., “mg/kg/day divided into 3 doses” versus “mg/kg/dose every 8 hours,” “micrograms/kg/min” versus “micrograms/kg/hour”). Other common errors in misreading dosing recommendations can occur due to a lack of familiarity with drug product availability, including various concentrations, formulations, and strengths. If these details are overlooked by the ordering provider, dosing errors can occur.

The ordering and prescribing stage of the pediatric medication-use process has been shown to be the stage most vulnerable to medication errors.²⁰ Many pediatric professional organizations support the use of CPOE with clinical decision support to target ordering and/or prescribing errors. Use of CPOE has been shown to decrease medication-related errors in pediatric inpatients by up to 97%.^{21,22} However, there are reports of unintended consequences of CPOE, namely juxtaposition errors (e.g., choosing the incorrect medication from a drop-down list), delays in administration of appropriate therapy, and disruptions in workflow.²⁰ Additionally, there is conflicting information regarding whether there has been an increase or a decrease in medication error-associated mortality in pediatrics after CPOE implementation.²⁰ If CPOE is to be implemented at an institution, proper development and implementation, including pediatric applications, are paramount.

Preparation, dispensing, and administration. Another significant challenge in caring for pediatric patients in any institution is a lack of available dosage forms to allow for appropriate administration. Common alterations to current dosage forms include cutting tablets for partial doses, opening capsules and adding the contents to a food or beverage, and use of i.v. formulations for oral administration. However, there are several concerns when altering adult formulations for pediatric use, including insufficient data to support the practice, unknown bioavailability, extemporaneous compounding errors, and unclear beyond-use dating.

In recent years, manufacturers have begun marketing previously unavailable liquid dosage forms of medications whose use required pharmacies to compound oral liquid extemporaneous preparations. Examples of commercially available liquid formulations that were previously compounded for use in pediatrics include formulations of sildenafil, enalapril, and sotalol. Use of these newer commercial liquid drug products is generally accompanied by significant expense, which has left pharmacists wondering whether they should continue compounding the medication to reduce the cost burden. However, Section 503A of the Federal Food, Drug, and Cosmetic Act states that compounding a preparation that is “essentially a copy of a commercially available drug product” is generally not allowed.²³ The act states that exemptions can be made and that “drug products can be compounded as customized therapies for identified individual patients whose medical needs cannot be met by commercially available drug products.” This restriction ensures that drug products are not compounded for patients who could use a commercially available product. Criteria for deciding whether a drug product is “essentially a copy” include the following: the compounded drug has the same active pharmaceutical ingredient (API) or ingredients; the API(s) has the same, a similar, or an easily substitutable

dosage strength; and the commercially available drug product can be used by the same route of administration as that prescribed for use of the compounded drug. Additional criteria require that the change made for an individual patient produces a significant difference for that patient.

Adult hospitals may only have premixed manufacturer-supplied i.v. preparations available. Due to the concentrations of these premixed products, without dilution they provide a volume too high for a pediatric dose. For example, vancomycin injection is available as a premixed product with a concentration of 5 mg/mL. In order to deliver a standard 15-mg/kg dose to a 7-kg infant with heart failure, a volume of 21 mL would be used, but that volume may potentially be inappropriate for that infant. In this example, the total maintenance volume for 1 day would be around 700 mL, with vancomycin potentially constituting 84 mL of that volume. Total maintenance volumes for pediatric patients must be evaluated daily, much like maintenance volumes for adult patients with heart or kidney impairment. Additionally, insulin dosing in infants and young children can prove to be challenging. With commercially available fast-acting insulin formulated at 100 units/mL, the insulin dose for a 3-kg infant must be prepared by dilution to make a potential dose of 0.5 units measurable for safe administration. Other medications associated with a high risk of dilution or concentration errors include i.v. and enteral anticoagulants, antihypertensives, analgesics, and antibiotics.

Even if a pharmacy is equipped to prepare pediatric concentrations from commercially available concentrations, providing a clinically appropriate and measurable volume may require a multi-step process, introducing an opportunity for error at each step. For example, if a concentration requires a serial dilution, missing 1 step in the dilution may lead to an overdose.

Precise dose measurement using metric units and selection of an appropriate drug delivery device are crucial

for the safe preparation and administration of medications for pediatric patients in both inpatient and ambulatory care settings. Use of the smallest-sized syringe possible allows for accurate, safe dosing of medications. Some adult hospitals may not routinely stock 1-mL or 5-mL syringes, which may require inappropriate use of syringe markings or excessive rounding of doses using available supplies. Similarly, an i.v. syringe pump or syringe module may be needed to deliver infusions by syringe, but for some facilities the expenditure required to keep syringe pumps on hand may be difficult to justify.

Monitoring. Pediatric patients are also at increased risk for adverse drug reactions due to a lack of published dosing information and FDA-approved labeling to guide treatment regimens.²⁴ This lack of information on dosing, pharmacokinetics, safety, efficacy, and clinical use of drugs in pediatrics leads to medications being used off-label. The use of some medications (e.g., heparins) requires extrapolation from available adult data. If there is available literature describing the use of medications for pediatric indications, the evidence was generally obtained in small studies and may not be generalizable to all pediatric populations. Consequently, increased laboratory testing and drug monitoring may be required. In order to ensure safe use of medications in children, pharmacists practicing in adult facilities may have to do extensive literature searches or rely on drug information centers or other resources for guidance on drug regimens for some pediatric disease states. Table 1 lists some available resources for pharmacists caring for pediatric patients.

Strategies for mitigating risk

Ordering. One risk mitigation strategy to help reduce ordering errors was identified in a 2015 ISMP survey regarding pediatric medication safety practices.²⁵ The survey identified error prevention improvements associated with expression of calculated doses as mg/kg or mg/m² and having a pharmacist in clinical areas.

Use of EMR systems that allow for configuration of default medication doses or frequencies based on a patient's age, weight, or location is another risk mitigation strategy. These configurations can vastly improve the safety of medication ordering. For example, if an age-based configuration is built for a certain medication, the provider will only see weight-based dosing units when placing an order for a pediatric patient but will see non-weight-based doses when placing orders for adult patients. Similarly, medication records can be built such that ordering users will see different versions for patients located in a neonatal intensive care unit or pediatrics unit; this can assist in fostering a philosophy of "make it easy to do the right thing." Using pediatric-specific configurations can also allow for different concentrations to be available by patient age, which can prevent ordering of inappropriately large volumes for small patients.

Preparation and dispensing. ASHP is currently collaborating with the FDA and other professional organizations, including PPAG and ISMP, to implement national standardized concentrations for i.v. and oral liquid medications for adult and pediatric patients.²⁶ This initiative, Standardize 4 Safety, is a national, interprofessional effort to standardize medication concentrations and recipes in order to decrease medication errors and to increase the safety of transitions of care.

Many pediatric institutions prepare standard concentrations of i.v. medications that allow for an appropriate volume to be delivered to accommodate smaller doses and patient sizes. The Standardize 4 Safety initiative is also addressing concentrations and dosing units for i.v. continuous medications for adult and pediatric patients.

The use of compounding records within the EMR can provide standardized instruction, product selection, and barcode scanning to assist in preparing i.v. or oral pediatric compounds. Figure 2 displays an example of a compounding record for the preparation of oral

clonidine for NICU patients. The individual preparing the compound selects the record within the EMR and is provided with the ingredients, quantities, and instructions for preparation. Barcode scanning technology can also be used, which helps to ensure correct product selection. Alternative methods may include the use of a "recipe book" consisting of paper copies of compounding instructions. The use of the EMR to display compounding instructions allows for all users within the institution and/or health system to see the same information; updates are made centrally, eliminating the risk of outdated information that arises if multiple copies of hard-copy recipe books exist. Additional benefits of electronic instructions include the elimination of paper at the point of preparation; such documents can result in a cluttered workspace and are not permitted in an ISO class 5 environment.

Medication safety guidelines recommend dispensing medications in the most ready-to-administer form.²⁷ Sites with 24-hour pharmacy services may be better equipped to provide doses in that manner, but those without 24-hour pharmacy services may rely on nonpharmacy personnel to prepare medications. The use of EMR systems, in addition to barcode scanning and clear instructions for medication preparation, can assist in addressing these challenges. Figure 3 shows an example of an additional label that prints along with the product label that is affixed to a patient-specific medication preparation (e.g., an i.v. syringe). This additional label provides instruction to the individual preparing the medication on what ingredient concentrations and amounts to use. This label can be customized to include further information, such as desired dispensing apparatus (e.g., syringe type), any special tubing or filters required, and whether a compounding recipe is required to prepare the final product. Information included on this label can be especially useful if nonpharmacy staff prepare medications in hospitals without 24-hour pharmacy services.

Table 1. Commonly Used Resources for Pharmacists Caring for Pediatric Patients

Resource	Overview of Information Available
ASHP Pediatrics Resource Center www.ashp.org/Pharmacy-Practice/Resource-Centers/Pediatrics	Pediatric disease state-specific articles and guidelines
Resource Clinical www.resourceclinical.com	Guidance on medication administration via enteral feeding tube, tablet crushing/cutting, enteral administration of injectable medications
Standardize 4 Safety initiative www.standardize4safety.ashp.org	Interprofessional initiative to create national standard i.v. and oral liquid medication concentrations for adults and pediatric patients
<i>Pediatric Pharmacotherapy</i> ^a	Textbook of pediatric topics for students, residents, and entry-level pharmacists
<i>Nelson Textbook of Pediatrics</i> ^b	Textbook of common pediatric disease states and stages of development
<i>Pediatric and Neonatal Dosage Handbook</i> ^c	Complete reference for medication indications, dosing, administration, and monitoring in pediatric patients, including off-label dosing; recipes for extemporaneous compounds
<i>Pediatric Injectable Drugs</i> ^d	Comprehensive reference for i.v. medication preparation and administration
<i>Drugs in Pregnancy and Lactation</i> ^e	Evidence-based manual on drug use during pregnancy and lactation
Infectious Diseases Society of America www.idsociety.org	Evidence-based guidelines and information for common infectious disease states
Pediatric Infectious Diseases Society www.pids.org	Evidence-based guidelines and information for common pediatric infectious disease states
European Society of Paediatric Infectious Diseases www.espid.org	Evidence-based guidelines and information for common pediatric infectious disease states
<i>Principles and Practice of Pediatric Infectious Diseases</i> ^f	Comprehensive textbook of infectious diseases in children and adolescents
<i>Feigin and Cherry's Textbook of Pediatric Infectious Diseases</i> ^g	Comprehensive textbook of pediatric infectious diseases
American Academy of Pediatrics www.aap.org	Professional resources for pediatric practitioners, including clinical practice guidelines and Red Book recommendations for pediatric infectious diseases diagnosis, treatment, and prevention
Centers for Disease Control and Prevention www.cdc.gov	Information on seasonal health issues, immunization schedule (updated annually), reports of infectious diseases outbreaks
<i>Advanced Pediatric Therapeutics</i> ^h	Textbook organized by pharmacy practice setting, written for the advanced level pediatric practitioner

^aBenavides S, Nahata MC, eds. *Pediatric pharmacotherapy*. Lenexa, KS: American College of Clinical Pharmacy; 2013.^bKliegman RM, St. Geme JW III, Blum NY et al. *Nelson textbook of pediatrics*. 21st ed. Atlanta: Elsevier; 2019.^cTaketomo CK. *Pediatric and neonatal dosage handbook*. 25th ed. Hudson, OH: Lexicomp; 2018.^dPhelps SJ, Hagemann TM, Lee KR, Thompson AJ. *Pediatric injectable drugs*. 11th ed. Bethesda, MD: American Society of Health-System Pharmacists; 2018.^eBriggs GG, Freeman RK, Towers CV, Forinash AB. *Drugs in pregnancy and lactation*. 11th ed. Philadelphia: Wolters Kluwer; 2017.^fLong SS, Prober CG, Fischer M. *Principles and practice of pediatric infectious diseases*. 5th ed. Philadelphia: Elsevier; 2018.^gCherry JD, Harrison GJ, Kaplan SL et al. *Feigin and Cherry's textbook of pediatric infectious diseases*. 8th ed. Philadelphia: Elsevier; 2019.^hEiland L, Todd T, Luedtke S et al. *Advanced Pediatric Therapeutics*. Memphis, TN: Pediatric Pharmacy Advocacy Group; 2015.

Figure 2. Example of compounding record for preparation of a pediatric suspension in an electronic medical record.
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Choose medication to produce: CLONIDINE 20 MCG/ML ORAL SUSP (NICU) COMPOUND or Look up by control number:

Amount to produce: × = 30 mL Bottle Shelf life: 28 Days Expiration: 06/14/2019 2359

☐ Repackage to: Quantity:

Ingredients	Package	Manufacturer	Lot Number	Expiration Date	Quantity to Use	QS
CLONIDINE HCL 0.1 MG TABLET	❗	❗	❗	❗	0.6 mg	
WATER FOR INJECTION, STERILE INJECT	❗	❗	❗	❗	1 mL	
SIMPLE SYRUP	❗	❗	❗	❗	30 mL	Yes

Notes:

Label printer:

Number of labels:

Recipe

CLONIDINE 20 MCG/ML ORAL SUSPENSION

1. Crush 6 clonidine 0.1 mg tablets into a fine powder in glass mortar
2. Add 1 mL sterile water for injection and mix to a uniform paste
3. Add 15 mL simple syrup to mortar and transfer suspension to amber bottle
4. Rinse mortar with simple syrup and add to amber bottle
5. QS volume to 30 mL with simple syrup

FINAL PRODUCT: Total volume = 30 mL; Concentration = 20 mcg/mL
 EXPIRATION: 28 days
 LABELING: Shake Well; Refrigerate
 STORAGE: Refrigerate

Figure 3. Example of production label for a unit dose preparation.
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gentamicin (PF) (GARAMYCIN) injection 4.7 mg

Dose: 4.7 mg = 0.47 mL of 10 mg/mL

Ingredient	Dose	Dispense
gentamicin (PF) 20 mg/2 mL	4.7 mg	1 x 0.47 mL

Dispense in 3 mL syringe
 Due time: 5/15/19 2041
 [CF REPRINT] 5/17 1602

Even with these tools in place, complexities of pediatric care still make it difficult to achieve an ideal EMR configuration for each medication-use situation. For example, EMR configurations for patient age may not take into account patients with extremely high or low weights and their use can result in immeasurable doses or inappropriate volumes. Relying on the clinical and problem-solving expertise of the pharmacy and nursing teams is essential in these situations.

Administration. Use of infusion pumps with drug libraries and dose-error reduction systems can improve patient safety across the continuum. Medication doses that require very low administration rates present opportunities for errors in pediatric medication use. For example, some neonates may require administration rates less than 0.1 mL/hr, which may only be possible using a syringe pump. Steps to ensure that an adequate supply of syringe pumps is available within

an institution should be considered. Pharmacist awareness of this technological requirement will allow proactive assessment of not only the need for syringe pumps but also the availability of EMR data needed for safe pump use to pump users.

Using a pediatric and/or neonatal drug library allows for customized selection and delivery of pediatric i.v. medications. Syringe pumps allow administration at lower infusion rates, which is often necessary for smaller pediatric patients. Unfortunately, adult hospitals may not have an abundant supply of syringe pumps, which may require nurses to administer i.v. push or intermittent medications manually, resulting in inaccurate administration rates.

Infusion pump integration technology has provided an additional layer of safety for administration of i.v. medications. Institutions that have implemented this technology are able to wirelessly transmit information from the EMR to the infusion pump,

removing the risk of manual programming. Additionally, the pump can send information to the EMR to provide automatic documentation of administration information. Weight-based dosing may result in precise administration rates that are rounded differently in the pump versus the EMR (e.g., 2.79 mL/hr versus 2.8 mL/hr); in this case, a nurse integrating infusion data would receive an alert due to this mismatch. Such discrepancies in rounding and health professionals' desire to avoid alert fatigue create a barrier to wider implementation of this technology to help ensure safe medication use in one of the highest-risk populations.

Resources for the nonpediatric pharmacist

If medications are involved, it is almost guaranteed that pharmacists will be asked to provide recommendations

on doses, monitoring, order sets, and drug policy. This task will be especially challenging for pharmacists without specialized training in pediatrics. The resources listed in Table 1 provide information on various pediatric disease states and medication dosing along with administration guidance.

Pediatric learning opportunities for pharmacists and pharmacy students

In a survey of pediatric practitioners within adult hospitals, 57% reported access to a pharmacist trained in pediatrics.⁶ With increasing numbers of pharmacy graduates completing residency training, it is important to encourage exposure to pediatric patient populations to build a well-rounded foundation for their careers. Likewise, for students embarking on experiential rotations, selecting experiences

that will provide exposure to this population and some knowledge to facilitate their participation in appropriate care for pediatric patients in the future. Specialized training is not practical for all pharmacists, but gaining exposure to resources and building a network of colleagues can position those without specialized training to provide safer care for all of their patients.

Guidelines for meeting the needs of hospitalized pediatric patients are available to assist pharmacy departments and leaders in developing their ability to care for this patient population.²⁸ These guidelines encompass many topics pertinent to pediatric pharmacy practice, including education and training, technology standards, medication-use standards, and research. In addition, PPAG has published a position statement related to the minimum core competencies for providing pediatric

Table 2. Risk Mitigation Strategies for Adult Hospitals Serving Pediatric Patients^a

Medication-Use Process Step	Risk Mitigation Strategies
Procurement and formulary management	• Stock pediatric formulations, if possible • Consider pediatric formulations in drug shortage management • Assess historical data related to past pediatric patients who presented to the adult hospital and the needs of the community to better prepare for future patients
Medication reconciliation	• Utilize pharmacy personnel to conduct medication history taking • Provide training for those compiling medication histories on pediatric formulations and medication-use considerations
Ordering	• Use rule-based contexts in EMR • Implement published best practices in medication safety (e.g., eliminate use of trailing zeros, record measurements in metric units) • Continue to use weight-based dosing for patients ≥ 40 kg unless the dose or dose per day exceeds the recommended adult dose for the indication
Preparation, dispensing, and administration	• Utilize compounding records in EMR • Provide standardized preparation instructions in EMR • Dispense doses in most ready-to-administer form • Utilize smart infusion pumps, syringe pumps or modules, pediatric and/or neonatal drug libraries, and infusion pump integration technology
Miscellaneous	• Provide pharmacy students and residents with exposure to pediatric populations • Require basic pediatric competencies for pharmacy personnel • Provide access to pediatrics references • Facilitate pharmacist involvement in pediatric services and drug policy

^aEMR = electronic medical record.

pharmacy services in the hospital setting.²⁹ The PPAG skill and knowledge development recommendations include items such as weight-based dosing and calculations, medication additives and preservatives, pediatric references and dosage form selection, developmental pharmacokinetics, and common pediatric disease states and treatment guidelines. Additional recommendations pertain to parenteral nutrition, pharmacokinetic drug monitoring, medication dosing and preparation for resuscitative efforts, and communication with pediatric patients and families. Skills and knowledge in these areas are needed to understand and care for pediatric patients. A minimal competency level should be required for any healthcare workforce members who care for this population.

Pharmacist role in medication error prevention

A hallmark challenge in treating pediatric patients in an adult institution is the lack of a dedicated pediatrics service line and healthcare workers who specialize in the care of this patient population. Given the complexities of providing appropriate medication therapy mentioned earlier, pharmacy personnel are often requested to participate in each step of the medication-use process, which may require self-guided training for pharmacists to become familiar with proper dosing and delivery of pediatric medications. It is a common request that pharmacists be involved in overall operational planning for new pediatric services, as they are considered medication experts and often display the attention to detail that is needed for this planning.

ISMP has highlighted key safety principles for use in medication error prevention, several of which can be applied to designing processes for care of pediatric patients.³⁰ Pharmacists must assist in simplifying and reducing the number of steps or options to mitigate risks associated with preparing pediatric doses. Adding redundancies (e.g., double checks) and limiting access or use through patient-specific contexts

in the EMR can help overcome these challenges.

While general medication safety processes for adults also apply to pediatric patients, a summary of additional risk mitigation strategies to consider for pediatric patients in each stage of the medication-use process can be found in Table 2.

Conclusion

Pediatric medication safety frameworks in U.S. adult institutions vary widely. Treating pediatric patients involves risks in all areas of the medication-use process. Optimizing technology, utilizing external resources, supporting a pediatric pharmacist, and providing early-career exposure to pediatric patients are methods to mitigate risks in institutions that primarily care for adult patients.

Disclosures

The authors have declared no potential conflicts of interest.

References

1. Crowley E, Williams R, Cousins D. Medication errors in children: a descriptive summary of medication error reports submitted to the United States Pharmacopeia. *Curr Ther Res*. 2001; 26:627-40.
2. Joint Commission. Sentinel event alert: preventing pediatric medication errors (April 2008). www.jointcommission.org/sentinel_event_alert_issue_39_preventing_pediatric_medication_errors/ (accessed 2019 May 13).
3. Kaushal R, Bates DW, Landrigan C et al. Medication errors and adverse drug events in pediatric inpatients. *JAMA*. 2001; 285(16):2114-20.
4. Grissinger M. Medication errors affecting pediatric patients: unique challenges for this special population. *Pa Patient Saf Advis*. 2015; 12:96-102.
5. Leape LL, Bates DW, Cullen DJ et al. Systems analysis of adverse drug events. ADE prevention study group. *JAMA*. 1995; 274(1):35-43.
6. Alvarez F, Ismail L, Markowsky A. Pediatric medication safety in adult community hospital settings: a glimpse into nationwide practice. *Hosp Pediatr*. 2016; 6(12):744-9.
7. Miller MR, Robinson KA, Lubomski LH et al. Medication errors in paediatric care: a systematic review of epidemiology and an evaluation of evidence supporting reduction strategy recommendations. *Qual Saf Health Care*. 2007; 16(2):116-26.
8. McPhillips HA, Stille CJ, Smith D et al. Potential medication dosing errors in outpatient pediatrics. *J Pediatr*. 2005; 147(6):761-7.
9. Institute for Safe Medication Practices. Results of pediatric medication safety survey (part 2): comparing data subsets points out areas for improvement (July 2015). www.ismp.org/resources/results-pediatric-medication-safety-survey-part-2-comparing-data-subsets-points-out-areas (accessed 2019 May 13).
10. Frattarelli DA, Galinkin JL, Green TP et al.; American Academy of Pediatrics Committee on Drugs. Off-label use of drugs in children. *Pediatrics*. 2014; 133(3):563-7.
11. Joint Commission. Leading hospital improvement. Right-sizing pediatric ED equipment (November 2018). www.jointcommission.org/the_view_from_the_joint_commission/right-sizing_pediatric_ed_equipment%E2%80%94your_opinion_needed/ (accessed 2019 May 13).
12. Benjamin L, Frush K, Shaw K et al., for the American Academy of Pediatrics, Committee on Pediatric Emergency Medicine; American College of Emergency Physicians, Pediatric Emergency Medicine Committee; Emergency Nurses Association, Pediatric Emergency Medicine Committee. Pediatric medication safety in the emergency department. *Pediatrics*. 2018; 141:e20174066.
13. Huynh C, Wong IC, Tomlin S et al. An evaluation of paediatric medicines reconciliation at hospital discharge into the community. *Int J Pharm Pract*. 2016; 24(3):196-202.
14. DeCoursey DD, Silverman M, Chang E et al. Medication reconciliation failures in children and young adults with chronic disease during intensive and intermediate care. *Pediatr Crit Care Med*. 2017; 18(4):370-7.
15. National Council for Prescription Drug Programs, Inc. Recommendations and guidance for standardizing the dosing designations on prescription container labels of oral liquid medications: white paper version 1.0 (February 2014). www.NCPDP/media/pdf/wp/DosingDesignations-OralLiquid-MedicationLabels.pdf (accessed 2019 Jan 11).
16. Rodieux F, Wilbaux M, van den Anker JN, Pfister M. Effect of kidney function on drug kinetics and dosing in neonates, infants, and

- children. *Clin Pharmacokinet*. 2015; 54(12):1183-204.
17. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA*. 2014; 311(8):806-14.
 18. Matson KL, Horton ER, Capino AC; Advocacy Committee for the Pediatric Pharmacy Advocacy Group. Medication dosage in overweight and obese children. *J Pediatr Pharmacol Ther*. 2017; 22(1):81-3.
 19. Kendrick JG, Carr RR, Ensom MH. Pediatric obesity: pharmacokinetics and implications for drug dosing. *Clin Ther*. 2015; 37(9):1897-923.
 20. Abramson EL, Kaushal R. Computerized provider order entry and patient safety. *Pediatr Clin North Am*. 2012; 59(6):1247-55.
 21. King WJ, Paice N, Rangrej J et al. The effect of computerized physician order entry on medication errors and adverse drug events in pediatric inpatients. *Pediatrics*. 2003; 112(3 Pt 1):506-9.
 22. Potts AL, Barr FE, Gregory DF et al. Computerized physician order entry and medication errors in a pediatric critical care unit. *Pediatrics*. 2004; 113(1 Pt 1):59-63.
 23. Food and Drug Administration. Compounded drug products that are essentially copies of a commercially available drug product under section 503A of the Federal Food, Drug, and Cosmetic Act: guidance for industry (January 2018). www.fda.gov/media/98973/download (accessed 2019 Jan 12).
 24. Napoleone E. Children and adverse drug reactions). *Ital J Pediatr*. 2010; 36:4.
 25. Institute for Safe Medication Practices. Results of survey on pediatric medication safety (part 1): more is needed to protect hospitalized children from medication errors (June 2015). www.ismp.org/resources/results-survey-pediatric-medication-safety-part-1-more-needed-protect-hospitalized#footnote3_81jyh5r (accessed 2019 May 15).
 26. Standardize 4 Safety initiative overview. <https://ashp.org/Pharmacy-Practice/Standardize-4-Safety-Initiative/Initiative-Overview> (accessed 2019 Jan 8).
 27. Billstein-Leber M, Carrillo CJD, Cassano AT et al. ASHP guidelines on preventing medication errors in hospitals. *Am J Health Syst Pharm*. 2018; 75(19):1493-517.
 28. Eiland LS, Benner K, Gumpfer KF et al. ASHP-PPAG guidelines for providing pediatric pharmacy services in hospitals and health systems. *J Pediatr Pharmacol Ther*. 2018; 23(3):177-91.
 29. Boucher EA, Burke MM, Johnson PN et al; Advocacy Committee for the Pediatric Pharmacy Advocacy Group. Minimum requirements for core competency in pediatric pharmacy practice. *J Pediatr Pharmacol Ther*. 2015; 20(6):481-4.
 30. Paperella S. System design and error-reduction strategies for high-alert medications. Paper presented at ISMP Medication Safety Intensive Workshop. Boston, MA; 2016 May 5-6.

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