

This series brings you up-to-date information about medication safety and strategies to prevent medication errors. It draws on Australian incidents and US experience, including (with permission) material from ISMP Medication Safety Alert! a bulletin published by the Institute for Safe Medication Practices, USA <www.ismp.org>. This series is coordinated through the Committee of Specialty Practice in Medication Safety (Chair, Rosemary Burke, Director of Pharmacy, Concord Hospital, NSW). Australian incidents are collated and recommendations made by Penny Thornton (Federal Councillor, SHPA, and Pharmacy Services Manager, The Children's Hospital, NSW; e-mail: pennyt2@chw.edu.au).

AUSTRALIAN INCIDENTS

Good news on the anticoagulant front from Queensland!

In line with national and international priorities, Queensland Health (QH) has been working towards a system for prescribing, administration and monitoring of IV unfractionated heparin. Consequently, reference and therapeutic ranges of activated partial thromboplastin time (aPTT) have been standardised across all QH sites following consultation by the QH Safe Medication Practice Unit with QH Pathology Services. This will simplify the implementation and utilisation of the statewide 'Heparin Intravenous Infusion Order and Administration Form' which incorporates the prescribing, decision support, monitoring and administration of heparin. A standard prefilled syringe of sodium heparin 25 000 units diluted to 50 mL with normal saline has also been introduced to reduce administration of non-standard concentration. The system changes aim to increase the safety and efficacy of anticoagulation by:

- recommending evidence-based dosing which achieves a therapeutic aPTT as quickly as possible;
- prompting a timely change in dose in response to an aPTT out of range;
- standardising communication of orders; and
- standardising the concentration of the infusion.

The 'Heparin Intravenous Infusion Order and Administration Form' has been trialled, together with the standard prefilled heparin syringe in two tertiary hospitals with improvement in documentation and management of heparin therapy.

[*Australian Safety Message 55, January 2007*]

Oral syringes to prepare doses of nebulised medication?

A patient was due for a normal saline flush and IV antibiotics plus salbutamol and ipratropium via nebuliser. All items were drawn up in individual syringes in a kidney dish. They were unlabelled. It is assumed the patient administered nebulised items IV. Patient was reported to have become agitated, tachycardic and have palpitations. It is recognised that medication for nebulisation in adults now comes in containers which can be regarded as unit dose and a syringe is generally not needed for dose preparation, however, when combinations or fractional doses are required, as in paediatrics, the potential for confusion with an IV dose still exists. It might be wise to extend the recommendation to use oral syringes to this group of drugs. As IV drugs are sometimes used for nebulisation, the syringe type should be chosen to match the route of administration.

[*Australian Safety Message 56, February 2007*]

US SAFETY BRIEFS

Pharmaceutical industry, medical device companies part of the solution?

Numerous fatal errors have been recently reported; one involved infants who died from heparin overdoses, which is believed may have been avoided if the pharmaceutical company had provided distinctive labelling and packaging of various strengths of heparin; another involved a young mother who died after receiving an epidural analgesic intravenously, which may have been avoided if containers, tubing, and connectors for epidural drugs were different than IV drugs. Looking back on the causes of fatal medication errors that have happened in



the last decade, many can be traced to labelling and packaging issues, and problems with medical devices and how humans interact with them. This is not to say that poor system design, environmental challenges, and miscommunication within facilities have not played a role in medication errors. We repeatedly see evidence of new and existing products and devices that contribute to repeated medication errors. Both Lantus (insulin glargine) and Apidra (insulin glulisine) injection are available in a 3 mL cartridge to be used with the new OptiClik device. The dose is displayed digitally in a small window near the dial used to set the dose. While the dose is clearly visible in the window, the pen could be dialled to the wrong dose if it is oriented in the wrong direction, just like a left-handed practitioner or patient might hold it—upside down, with the needle to the right, away from the hand (20% of people are left handed). For instance, when the pen is oriented incorrectly, a '52' units dose looks like '25' units. Many other doses can also be confused: what appears to be a dose of '10' units is actually '1' unit (01); a dose of '50' units is actually '5' units (05); a dose of '21' units is actually '12' units; a dose of '62' units is actually '29' units; and so on. The design of this pen is potentially dangerous, as the patient could receive a significant overdose or a subtherapeutic dose of insulin, a high-alert drug. Thus, we believe the device is unacceptable for use under any circumstances unless these safety issues are resolved. To their credit, many hospitals and pharmacies have been taking steps to reduce the risk of errors with products and devices. Whether employing failure mode and effects analysis when bringing new devices into the facility or implementing the Joint Commission National Patient Safety Goals related to infusion pumps and look-alike and sound-alike drug names, improvements at the user end are ongoing, to the extent possible. But many of these strategies are really just a stopgap measure until pharmaceutical and medical device companies respond with equal accountability through expert pre-market testing and a willingness to act quickly when a new problem surfaces through post-marketing surveillance. As we noted 2 years ago, FDA has yet to issue new labelling or packaging guidance documents or to require pharmaceutical and medical device companies to test new devices and proposed drug names and packaging using front-line practitioners and safety experts. We need to get all key stakeholders to work together toward the lasting changes needed to prevent harm from medication errors. We all need to be part of the solution.

[*ISMP Medication Safety Alert! 16 November 2006*]

PEN injectors: technology is not without imPENDING risks

Interest in self-administration of medications, especially among the elderly with chronic diseases has propelled the use of pen injectors as a drug delivery method. As with any new technology, ISMP has received numerous reports of errors that have occurred when using pen injectors. Since the use of these devices will continue to expand in the future, we are working to establish safe practice guidelines to reduce the risk of serious errors.

Using pens like vials. In response to the rising costs of medications, some facilities have replaced insulin vials with insulin pen injectors (or just the pen cartridges) from which nurses withdraw doses using insulin syringes and needles. In some cases, the pens/cartridges are used as multidose vials for a single patient, and each dose is removed with a sterile needle and syringe; in other cases, the pens/cartridges are used as floor stock from which insulin doses are removed for multiple patients using a new sterile needle and insulin syringe for each puncture into the cartridge membrane. Manufacturers do not recommend the withdrawal of medication from the pen, except in an emergency with a malfunctioning pen. In these instances, the pen should then be discarded, even if insulin remains in the pen. Similar to withdrawing medication from a vial, these practices may also result in unlabelled syringes of insulin. Large pockets of 'air' have been observed in cartridges of insulin pens after aspirating some of the drug with a needle. If the pen/cartridge is not discarded, and the air is not eliminated before delivering a subsequent dose, patients could receive less than the desired dose as well as an injection of air. **Error-prone device design.**

Users have injected adrenaline into their thumbs when attempting to remove the black cap on an EpiPen (adrenaline). Although the cap looks like it should be removed, it actually houses the needle and activates the injection when pressed against the patient's thigh. Failure to activate the device has also occurred when the device has not been properly pressed against the thigh to cause injection of the drug. **Dispensing errors.** Insulin products with look-alike and sound-alike names have contributed to errors in which the wrong pen injectors have been dispensed. For example, a Novolog Mix 70/30 (70% insulin aspart protamine, 30% insulin aspart) FlexPen was dispensed instead of a Novolog (human insulin aspart) FlexPen; the patient experienced unexpected fluctuations of blood sugar levels until the error was noticed. Adult and junior strengths of EpiPen have been confused leading to dispensing errors and unfavourable responses to this emergency drug. Confusing volume and dose, health professionals and patients have mistakenly confused the dose with the volume to be administered from pen injectors. With Apokyn (apomorphine) the design of the pen injector may also contribute to an error as the pen is marked in mL and the drug is dosed in mg and, e.g. confusion could arise and 1 mL (10 mg/mL) could be administered if the prescribed dose is 1 mg. Treating the available dose as a single dose, the entire dose in a multidose pen injector has been administered, believing it was a single-use device. For example, a nurse administered the full contents of a pen containing Forteo (teriparatide) 750 µg to an inpatient to treat osteoporosis. The pen contained enough teriparatide for 28 daily doses (typically 20 µg/daily) at which time it should be discarded even if drug remains in the pen. The manufacturer clearly lists the full contents (750 µg/3 mL) on the carton label and pen injector, but notation that the pen contains a 28-day supply is small and may be overlooked. Based on the label, the patient thought she was giving herself 750 µg each day, which she prepared by turning the pen dial once until it clicked. Thus, she told her nurse and physician that she took this dose at home, which was subsequently prescribed. At home, she was actually receiving 20 µg with each daily dose. Since the pen had been dispensed accidentally without a needle, the nurse drew its entire contents

into a syringe and administered it. **Inadequate patient education.** Patient education before discharge might not correspond with how the medication will be administered at home. Patients who are educated about using a device, but then cannot afford to purchase the medication in this fashion, will not be prepared to draw doses from a vial. Conversely, patient education before discharge might not be with the actual pen that will be used at home. Many patients do not tip and roll their insulin suspension pens adequately to assure proper mixing. This may result in large clumps of aggregated insulin flowing from the pen during the first injection, leading to hypoglycaemia followed by subtherapeutic doses. **Additional concerns.** If pens are dispensed for each inpatient, space may be limited, and labels with the patient's name, location, and identification number could cover important information. If patients find, after initial injection, that a multidose pen contains less drug than needed for a single dose, they will be required to rearm the device, or use a new device, to inject the remaining amount. Memory of how much was already given may be inaccurate, leading to dosing errors. The wide variety of pen injector designs makes it difficult to learn how to use them properly and maintain competence.

[ISMP Medication Safety Alert! 30 November 2006]

Compounded topical anaesthetics

FDA sent warning letters to several compounding pharmacies and posted information about serious risks related to certain compounded topical anaesthetic creams. The pharmacies were warned to stop compounding and distributing local anaesthetic products with concentrations higher than available commercially. Exposure can cause grave reactions, including seizures, cardiac arrhythmias, and death. The creams are often used to lessen pain in outpatient procedures such as laser hair removal, tattoos, and skin treatments. We have highlighted two events involving women who died after receiving pharmacy-compounded topical lignocaine and tetracaine creams prior to laser hair removal. In one case, the cream had been applied from groin to ankles and used with an occlusive dressing, which is known to increase absorption. One cream contained 10% lignocaine and 10% tetracaine, while the other woman's cream contained 6% of each. Failure to consider the high concentrations of topical anaesthetics prescribed, how they are used, and the extent of absorption has contributed to other topical anaesthesia deaths.

[ISMP Medication Safety Alert! 14 December 2006]

IV lipid emulsion for bupivacaine toxicity

We previously mentioned the tragic death of a healthy 16-year-old woman in labour after an epidural analgesic (presumably bupivacaine) was inadvertently infused intravenously instead of penicillin. Bupivacaine is cardiotoxic and cardiac arrest has occurred after convulsions resulting from systemic toxicity. In performing blocks, unintended IV injection is possible and may result in cardiac arrhythmia or cardiac arrest. A Black Box Warning mentions that resuscitation has often been difficult or impossible. Successful resuscitation using a 20% lipid emulsion following cardiac arrest was recently reported. Although anecdotal in nature, lipid emulsion has been shown to increase the cardiotoxic threshold of bupivacaine in rats and dogs. Thus, in addition to the standard American Heart Association Advanced Cardiac Life Support protocol, lipid emulsion may be a novel treatment for bupivacaine-induced cardiotoxicity. Because lipid emulsion is not readily available, it has been suggested stocking a 20% lipid emulsion solution in sites where regional anaesthesia is performed. The side effects of lipid emulsion used in these circumstances have not been studied, nor can a specific dose be recommended. However, in the successfully treated case mentioned above, 100 mL of 20%

Intralipid was given peripherally. Propofol, for which 10% lipid emulsion serves as a vehicle, is not a substitute for lipid emulsion because a large dose would be required in a situation where its cardiodepressant effects may be detrimental.

[ISMP Medication Safety Alert! 14 December 2006]

High-alert medication 2007—Anticoagulants

High-alert medication for 2007 is anticoagulants (unfractionated heparin, warfarin, low-molecular-weight heparin {LMWH}). When used or omitted in error, they can cause life-threatening or fatal bleeding, or thrombosis. ISMP recommends conducting an interdisciplinary failure mode and effects analysis within your facility to identify sources of failure with the use of anticoagulants, and to individualise the key improvements needed to reduce the risk of harmful errors with these medications <www.ismp.org/Tools/FMEAofAnticoagulants.pdf>.

Common risks associated with anticoagulants

Duplicate or concurrent therapy. Unrecognised concomitant use of anticoagulants, particularly unfractionated heparin prescribed upon admission and LMWH prescribed in the ED and continued upon admission. Patient confusion about generic and brand names of warfarin, leading to self-administration of both warfarin and Coumadin. **Accidental stoppage of therapy.** Forgetting to resume an anticoagulant after holding a dose; forgetting to resume an anticoagulant upon discharge.

Look-alike vials/syringes. Mix-ups among various concentrations of heparin packaged in vials or bags; mix-ups between heparin and other look-alike vials; mix-ups between heparin flush syringes and other look-alike syringes. **Dosing errors.** Administering the wrong dose because the barrel of Clexane (enoxaparin) prefilled syringes lack sufficient mL gradations. Patient self-administration errors due to confusion if required to take different warfarin doses on alternate days or if frequent dose adjustments are required, especially if the dose differs from the label on the bottle. Incorrect dosing when resuming warfarin after reversing its effects, failing to recognise that phytonadione continues to block the effects of warfarin for about a week. Failure to reduce the standard starting dose of warfarin for elderly patients. Failure to consider renal function when using LMWH. Abbreviating units as ‘U’ resulting in 10-fold overdoses. Infusion pump setting errors with IV heparin—concentration or rate of infusion, or forgetting to reset the pump after delivering a bolus dose from the continuous infusion bag. Mix-ups between kilogram and pounds or not using a current measured weight when calculating doses. IV heparin admixture errors if a standard, pre-mixed solution is not in use.

Calculation errors. Mathematical errors in determining the volume of heparin to administer. Miscalculation of the volume of heparin to be added to TPN or other electrolyte solutions.

Monitoring problems. Failure to obtain baseline lab tests and/or verify the most recent lab values before prescribing and administering an anticoagulant. Adjusting warfarin doses too often without assessing overall trends in international normalised ratio (INR) values. Erroneous INR/activated partial thromboplastin time (aPTT) results. Patient failure to comply with outpatient testing. **Drug and food interactions.** Lack of effective electronic alerts for drug, herbal, and food interactions with warfarin. **Spinal haematoma.** When used concurrently with spinal puncture, increased risk of epidural or spinal haematoma. **Adverse drug reactions.** Failure to detect and quickly treat heparin-induced thrombocytopenia.

Recommendations

Standardisation. Develop and implement interdisciplinary treatment and monitoring guidelines. Use a standard weight-based heparin protocol for each indicated use of a heparin infusion. Use standard order sets or pre-printed orders. Do not abbreviate units as ‘U’ on handwritten, typed, or

computerised materials. Standardise the concentration of therapeutic heparin infusion; require pharmacy to prepare and dispense any approved use of a non-standard concentration. Administer warfarin at a standard time that allows for thorough review of daily lab results and necessary dose adjustments before administration. Establish and follow a strategy for handling ‘hold’ orders. Establish protocols for standard and rapid reversal of anticoagulation. **Simplification.** Administer bolus doses from a pharmacy-prepared syringe. Dispense warfarin in exact patient doses. Dispense heparin flush solutions from the pharmacy in the exact concentration required for the patient population and/or parenteral access device in use. Provide single use or unit-dose packages to patient care units.

Externalise error-prone processes. Use commercially prepared, pre-mixed IV heparin solutions for infusion and unit-dose syringes. **Improved access to information.** Employ smart pumps, bar coding, and computerised physician order entry. Use the patient’s actual weight in kg (or ideal body weight) to determine heparin doses. Affix infusion rate charts (pre-printed labels) to heparin infusion bags. Improve access to prior/current drug therapy by sending all ED and cardiac catheterisation orders to the pharmacy if patients are admitted to the hospital. Use anticoagulation flow sheets designed for use during the inpatient stay, and provide them to patients/transfer facility upon discharge. Teach patients self-monitoring and administration of prescribed anticoagulants.

Differentiation or constraints. Safely select, procure, and store anticoagulants away from other drugs with look-alike names or packaging. Require pharmacy to dispense all inpatient anticoagulants or verify all orders for therapeutic use of anticoagulants before removal from automated dispensing cabinets. Restrict access to multiple concentrations of heparin in both the pharmacy and patient care units. When unit stock of heparin is appropriate, provide the smallest size packages and the fewest doses necessary to meet the needs of patients between each restocking period. Eliminate heparin flushes for peripheral venous access catheters; use saline flushes only.

Reminders. Maintain functional drug interaction alerts for anticoagulants in computer order entry systems.

Redundancies. Employ strategically placed independent double checks, e.g. pharmacist checks stock drugs before leaving pharmacy; second nurse checks drug, line attachment, and pump settings before IV heparin is given. **Patient monitoring.** Obtain baseline lab tests before prescribing anticoagulants. Make coagulation lab test results available in 2 hours or less. Use a protocol and/or pre-printed orders for evaluation and treatment of heparin-induced thrombocytopenia. Establish inpatient pharmacy anticoagulation services and outpatient warfarin services for dosing, monitoring, and teaching patients about their therapy. Use process control charts to display trends in INR values and to assist with dosing.

[ISMP Medication Safety Alert! 11 January 2007]

Seasonal mix-ups

In reviewing medication errors, it’s clear that mix-ups between the antihistamine Zyrtec (cetirizine) and antipsychotic Zyprexa (olanzapine) seem to spike in the winter months. We have noticed a similar spike during the spring allergy season. Patients who receive Zyprexa in error have reported dizziness, sometimes leading to fall-related injuries, and patients on Zyprexa for a behavioural illness have relapsed when given Zyrtec in error. Including the purpose of the drug on prescriptions would help avoid mix-ups, as would storing the containers of these products apart from one another and adding reminders on containers and computer screens about the potential for error.

[ISMP Medication Safety Alert! 11 January 2007]

'e-Rx' errors in the drug selection process

Electronic prescribing (e-Rx) has great potential for reducing medication errors. It eliminates illegible prescriptions and reduces reliance on memory of drug interactions, allergies, and excessive dosing. Flawed e-prescriptions risk misinterpretation and cause workflow interruptions if clarifications are needed. One recurring problem is when doctors inadvertently choose the wrong item from a drug selection database, e.g. we received a copy of a prescription in which a doctor accidentally selected U-500 instead of U-100 insulin. Since the pharmacy had already encountered this type of mix-up, U-500 insulin was targeted as a high-alert medication. This alert required the pharmacist to perform a drug use review and fax a request for clarification before dispensing. The clarification confirmed that U-100 was the intended concentration. While e-Rx will undoubtedly improve medication safety, do not let your guard down when processing e-prescriptions.

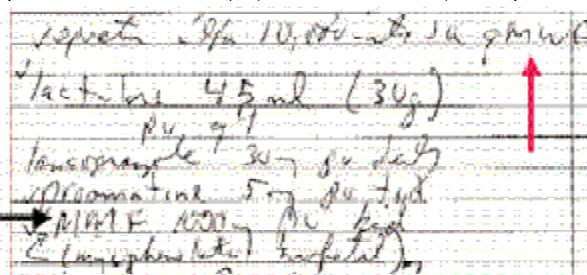
[ISMP Medication Safety Alert! 25 January 2007]

Five rights: a destination without a map

We have stressed previously that the 5 rights are merely broad goals or desired outcomes of safe medication practices that offer no guidance on how to achieve these goals. Thus, simply holding health practitioners accountable for giving the *right drug* to the *right patient* in the *right dose* by the *right route* at the *right time* fails to ensure medication safety. Adding a sixth, or seventh *right* (e.g. right reason, right drug form) is not the answer, either. We also pointed out that the 5 rights fail to acknowledge that human factors and system weaknesses contribute to errors, and that the focus of the 5 rights on individual performance does little to reflect that safe medication practices are a culmination of interdisciplinary efforts of many individuals and reliable systems. Despite these shortcomings, 'failure to follow the 5 rights' is still often cited as a performance deficit when a medication error occurs. Health practitioners cannot be held accountable for achieving the 5 rights, they can only be held accountable for following the processes that their organisations have designed and held out as the best way to verify the 5 rights. For example, nurses cannot really verify the *right patient* if they have no way of knowing whether the patient is who they say they are, whether the name on the arm band is accurate, and so on. They can only verify two unique patient identifiers assigned to the patient upon admission—a process the organisation deems to be 'enough' to satisfy that this is the right patient. Likewise, nurses and pharmacists cannot really verify that the *right drug* is provided in a given tablet, or that it contains the *right dose/strength*. But they can be held accountable for reading the label, requesting an independent double-check, questioning orders for drugs/doses that are illegible or appear unsafe, and using bar code technology. These are procedural steps the organisation has deemed sufficient to verify the *right drug* and the *right dose*. Thus, the health practitioner's duty is not so much to achieve the 5 rights, but to follow the procedural steps designed by the facility to produce these outcomes. If the procedural steps cannot be followed because of system issues, health practitioners have a duty to report the problem so it can be remedied. This distinction is not minor because if we hold individuals accountable for achieving the 5 rights, we should give them the authority to design their own systems for achieving these outcomes. After all, how can we hold them accountable for things that are not under their control? However, since facilities decide the processes that are necessary for achieving the 5 rights, individuals who follow these processes should not be held accountable for an undesirable outcome. Improvements must be made in the systems designed to achieve the 5 rights, not in the individual's practice or

behaviour. The 5 rights are not a behavioural model for achieving medication safety, but goals for which organisations must accept responsibility and design fail-safe ways that they can be achieved.

[ISMP Medication Safety Alert! 25 January 2007]



Don't abbreviate drug names

A 44-year-old man was admitted to hospital with hypotension. His medical history was orthotopic liver transplant with chronic rejection, possible alcoholic hepatitis, and end-stage chronic kidney disease. He was prescribed the immunosuppressant mycophenolate mofetil (Cellcept) using an abbreviation 'MMF 1000 mg po BID'. The physician then decided to write out the name of the drug below this entry. The pharmacist and nurse misinterpreted the MMF as M-W-F (every Monday, Wednesday, Friday). Liver transplants were not performed at the hospital, thus staff were not familiar with the proper dosing of this drug. The error was not noticed until the next day, after the patient had missed two doses. The error could have led to a rejected organ if it had been recognised much later. Unauthorised abbreviations of any drug name are potentially dangerous. In this case, the abbreviation was misunderstood as days of the week; in other cases, abbreviations have been misunderstood as a different drug.

[ISMP Medication Safety Alert! 25 January 2007]

NSW TAG has released 'Recommendations for terminology, abbreviations and symbols used in the prescribing and administration of medicines October 2006' for Australian use. Contact nswtag@stvincents.com.au for copies.

No cough and cold medicines for little ones, please

Morbidity and Mortality Weekly Report 12 January 2007 published a notice about infant deaths associated with cough and cold medicines. Three infants between 1 to 6 months old were found dead in their homes. A postmortem determined that cough and cold medicines were the underlying causes of the deaths. No abnormalities in cardiac pathology were revealed. On autopsy, two of the infants had evidence of respiratory infection. All three had high levels of pseudoephedrine (PSE) in postmortem blood samples. One infant had received a prescription and an OTC cough and cold medicine, both containing PSE. The other two also had received PSE-containing medications (one prescription and the other OTC). The federal Combat Methamphetamine Epidemic Act, has moved 9 products to behind the pharmacy counter and allowed their purchase only in limited amounts. No FDA-approved dosing recommendations exist for administering OTC cough and cold medicines to children under 2 years. Proper dosing for children in this age group has not been studied. Instructions on OTC medicines advise consumers to consult with their physicians. As an alternative to PSE and other nasal decongestants in children under 2, advise carers to consider clearing nasal congestion with a rubber suction bulb; secretions can be softened with saline nose drops and/or a cool-mist humidifier.

[ISMP Medication Safety Alert! 25 January 2007]