

Nurse AdviseERR®

Educating the Healthcare Community About Safe Medication Practices

Unrealized exposure to heparin leads to missed HIT diagnosis and subsequent limb thrombosis

Certain medical devices may be manually or commercially coated with heparin to negate the aggressive biological response that occurs when blood contacts a foreign surface. These biological responses, which can have an adverse effect on device performance and the patient's well-being, include platelet adhesion, platelet activation, fibrin production, thrombus formation, and other inflammatory responses. Examples of heparin-coated devices that help negate these responses include certain vascular access catheters and guidewires; drainage, retransfusion, or thermodilution catheters; devices used during cardiopulmonary bypass procedures; oximetry probes; and some vascular stents and grafts.

While heparin coating on devices and catheters may improve patency, reduce infection, and prevent clotting, even small exposures to heparin can lead to heparin-induced thrombocytopenia (HIT). HIT occurs in up to 5% of patients exposed to heparin,¹ particularly in therapeutic doses or when used for systemic prophylaxis.² However, HIT is an immune-mediated response and can develop from any large or small heparin source, including heparin flushes and heparin-coated catheters.³ Thrombotic events, such as deep vein thrombosis, pulmonary embolism, myocardial infarction, thrombotic stroke, and limb occlusion, occur in about 30-70% of patients with HIT.¹ Thrombosis caused by HIT has led to death in 20-30% of the cases, with a similar percentage of patients becoming permanently disabled by amputation, stroke, or other causes.⁴ Although the risk of thrombosis can be linked to the degree of thrombocytopenia, in 33.5% of HIT patients, thrombosis occurs several days before the onset of thrombocytopenia.⁵

One complicating factor with HIT is that the heparin source may be hidden in medical devices and undocumented in the patient's health record, making diagnosis difficult. When a patient is exposed to less obvious sources of heparin, such as heparin-coated catheters or devices, the development of thrombocytopenia may not be readily linked to the heparin exposure. Such an event was recently reported to ISMP.

Adverse Event

In an interventional radiology unit, a heparin solution diluted in saline had been prepared and placed on the sterile field for the radiologist to use during a procedure. Before the radiologist inserted a wire and catheter into the patient's venous access site, he dipped the end of it in the heparin solution. This process was repeated several times during the procedure. About 6 days after the procedure, the hospitalized patient developed thrombocytopenia, with the platelet count dropping about 50% below the patient's baseline. A laboratory test for HIT was ordered, and the result was reported as positive. However, the patient's primary physician could not find documentation that the patient had ever received heparin or been exposed to the drug. The physician concluded that the test result was a false positive and discharged the patient with an order for follow-up laboratory testing. Once home, the patient promptly suffered a thrombosis in his left arm, which later required partial amputation.

continued on page 2—HIT >

check *it* out

Consider the following recommendations to reduce the risk of patient harm due to unrecognized reactions to unnoticed allergens.

✓ **Identify hidden products.** Compile a list of drug-eluting stents and commercially available and/or user-applied medication-coated catheters and devices used in the facility that expose patients to heparin or other medications. Many of these devices and catheters will be used during interventional procedures or surgery, so involve clinicians in these areas as a resource.

✓ **Update the list.** Since pharmacy will not be dispensing many of the medication-coated medical devices and catheters, establish a system of widespread notification when new products are purchased so the list can be updated as needed. Identify an "owner" of the list who is responsible for keeping it updated. Ensure there is a contact with supply chain management to inform the "owner" of the list as well as a list of clinical groups that should be provided updates.

✓ **Obtain history before use.** Prior to initiating the use of medication-coated or drug-eluting catheters or devices, the practitioners who will be inserting the catheters or using the devices should ask patients if they have any allergies or a history of HIT. Document positive responses, and for a history of HIT, work with information technology staff to build an alert that is generated if heparin is subsequently prescribed (e.g., therapeutic or prophylactic doses).

✓ **Enable documentation of the exposure.** Work with your pharmacy and/or electronic health record (EHR) vendor to establish a system to document in the patient's medical record any exposure to heparin-dipped

continued on page 2—check *it* out >

> **HIT**—continued from page 1**Event Investigation**

Investigation of this event confirmed the patient's diagnosis of HIT and identified the patient's undocumented source of heparin—the catheter and wire dipped in the heparin solution during the interventional radiology procedure. The radiologist who had performed the procedure had not “prescribed” the heparin, so it was not recorded as an order; the heparin was just used to coat the wire and catheter to reduce the risk of clotting. Also, the use of diluted heparin was not documented on the procedural record, nor was it usual practice to document its use on the medication administration record (MAR), as the patient had not received a typical heparin dose that could be measured. Thus, the fact that the patient had been exposed to heparin was unknown to the patient's primary physician when thrombocytopenia developed a few days later.

The investigation also uncovered a plethora of commercially available heparin-coated stents, guidewires, and catheters that were in use in the health system, along with drug-eluting stents (e.g., **PACLitaxel**, everolimus), antibiotic-coated catheters, and other medical devices coated with potential allergens (e.g., triclosan). The hospital found that exposures to these products, which were not dispensed by the pharmacy, also might not be documented in the patient's medical record. Furthermore, patients were not consistently being asked about potential allergies or sensitivities to these products prior to use. Although small exposures to some of these products may result in little systemic effect, an allergic reaction (whose source might be hidden) could be significant.

HIT is associated with significant morbidity and mortality, especially if it goes unrecognized. A reaction to an unnoticed allergen could also cause harm. To reduce the risk of patient harm, consider the recommendations listed in the **check it out!** column, starting on page 1 in the right column.

References

- 1) Sakr Y. Heparin-induced thrombocytopenia in the ICU: an overview. *Crit Care*. 2011;15(2):211.
- 2) Schmutz M, Risch L, Huber AR, Benn A, Fischer JE. Heparin-induced thrombocytopenia-associated thrombosis in pediatric intensive care patients. *Pediatrics*. 2002;109(1):1-4.
- 3) Laster JL, Nichols WK, Silver D. Thrombocytopenia associated with heparin-coated catheters in patients with heparin-associated antiplatelet antibodies. *Arch Intern Med*. 1989;149(10):2285-7.
- 4) Ahmed I, Majeed A, Powell R. Heparin induced thrombocytopenia: diagnosis and management update. *Postgrad Med J*. 2007;83(983):575-82.
- 5) Greinacher A, Farner B, Kroll H, Kohlmann T, Warkentin TE, Eichler P. Clinical features of heparin-induced thrombocytopenia including risk factors for thrombosis. A retrospective analysis of 408 patients. *Thromb Haemost*. 2005;94(1):132-5.

Patient ingested cardboard “tablets” in demonstration pack!

In our November 2015 newsletter, we published a **Safety Wire** about the accidental dispensing of a demonstration starter pack of **XARELTO** (rivaroxaban) to a patient being discharged from the hospital. The demonstration pack is designed to look exactly like a Xarelto starter pack, but it only contains pictures of each tablet printed on a cardboard insert (**Figure 1**, on page 3). This demonstration pack is supposed to be used to teach patients to take the 15 mg tablets twice a day for the first 21 days and then transition to the 20 mg tablets once daily starting on day 22. But, the demonstration pack looks very similar to the starter pack, even listing the drug's national drug code and, upon opening the pack, instructions for the patient to find the correct day and press out and take the correct dose. The pack also has a tamper-proof locking mechanism where you would expect to find the drugs, and a place on the back of the package for a pharmacy label. The labeling does not identify that the product is for demonstration purposes.

continued on page 3—**Demonstration pack** >> **check it out** continued from page 1

catheters or guidewires, and/or medication-coated or drug-eluting devices and catheters. For example, pharmacy dispensing of a heparin vial or diluted heparin solution intended to manually coat a device during a procedure can be linked to the pharmacy system and the electronic medication administration record for documentation, even without a specific dose. Automated capture of the product dispensed or used, or a system of documentation that is seamless with the workflow, is desirable to improve documentation reliability.

✓ **Educate staff.** Be sure practitioners who care for patients exposed to medication-coated or drug-eluting devices know the symptoms to monitor to detect an allergic response or possible HIT. Ensure this information is included in the discharge summary or during any transition of care.

✓ **Seek out sources when symptoms arise.** It is imperative that practitioners look for hidden sources of medications when symptoms arise in patients suggesting possible HIT, an allergic reaction, or other potential drug reaction. Patients with exposure to heparin-coated or -dipped catheters who have thrombocytopenia and other risk factors (e.g., decreased platelet count 5-10 days after initiation of heparin or sooner if prior [within 30 days] heparin exposure, thrombosis) should be worked up for HIT.

✓ **Discontinue all sources.** If HIT is suspected or diagnosed, discontinue all sources of heparin (including less obvious sources such as heparin-coated catheters and heparin flushes), and initiate appropriate treatment.

✓ **Document adverse responses.** Place a prominent entry in the patient's medical record to alert staff to avoid the administration of, or exposure to, the medication (e.g., heparin, if HIT is diagnosed) in any form and through any route of exposure.

✓ **Reassess use.** Develop a diverse clinical team, including staff in the operating room and procedural care areas (interventional radiology) to regularly assess the need for medication-coated devices and catheters, with a goal of reducing unnecessary exposure.

> **Demonstration pack**—continued from page 2

Although the problem in the 2015 incident was resolved before the patient was discharged, we suggested that the patient could have “eaten the cardboard tablets, believing the medicine was imbedded in the cardboard (stranger things have happened).” Well, according to a letter published in the *American Journal of Health-System Pharmacy*, there’s at least one documented case where this did happen (Nguyen TT, MacLasco A, Vitto MJ.

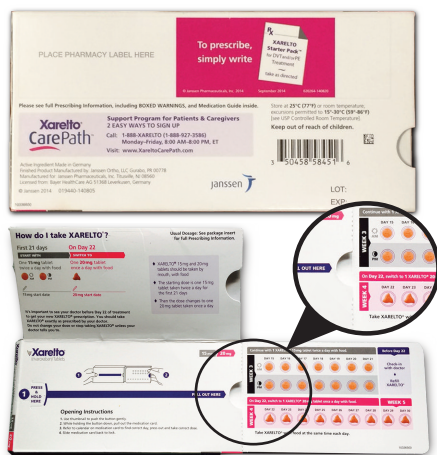


Figure 1. The demonstration starter pack of Xarelto contains pictures of the pills but no actual medication.

images of the tablets. A computed tomography (CT) scan showed progression of the previous embolus and a new, acute embolus in another lobe of the lung.

In 2015, ISMP contacted Janssen, the manufacturer, to ask the company to properly and prominently identify that the demonstration pack does not contain medication. The authors of the letter describing the more recent event also contacted the manufacturer about the medication error. These and other errors associated with “demonstration” products, including the administration of imitation intravenous (IV) solutions intended for simulation only, indicate the need for an industry-wide regulation requiring clear and prominent labeling of these products. For now, if you use any demonstration or simulation products, be sure to add an auxiliary label stating, “For Demonstration Only” or “For Simulation Only,” and keep these products away from actual medications or solutions.

Anaphylaxis readiness warrants **EPINEPHrine** auto-injectors

A patient with colon cancer presented to an emergency department (ED) after developing anaphylaxis while receiving a platelet infusion in the hospital’s outpatient infusion suite. The dose of **EPINEPHrine** for anaphylaxis is 0.2-0.5 mg (0.2-0.5 mL) of a 1 mg/mL solution, given subcutaneously or intramuscularly (IM), repeated every 5-15 minutes as necessary. But an ED physician ordered **EPINEPHrine** 1 mg IM as the initial dose, which was prepared in a syringe and given. Fortunately, the patient only experienced hypertension, tachycardia, and agitation, all of which soon resolved. But this episode reminded us once again of more serious dosing and wrong route errors that have been reported to ISMP over the years, as reviewed in our January 2016 newsletter (www.ismp.org/sc?id=3006), some of which have been fatal. Besides prescribing too high of a dose, we have also received reports of administering the full contents of a 1 mg/mL ampul or vial that has been drawn into a syringe and given by the IV route, which has proven harmful to some patients as well.

continued on page 4—**Anaphylaxis** >

SAFETY wires

⚡ Drug shortages and single-dose vials.

With a recent increasing number of drug shortages, it’s a good idea to pay even more attention to how drugs might be stored on patient care units, especially single-dose vials of drugs in short supply. In a desire to conserve supply, and without recognizing potential problems, some practitioners have been saving any content remaining in single-dose vials after withdrawing the dose needed for a patient. As an example, promethazine injection has recently been in short supply. In a facility without 24-hour pharmacy service, a nurse received an order for the drug after pharmacy hours. Because nurses had been made aware of the shortage, the vial was labeled with that patient’s room number, the date of opening, and the amount used (**Figure 1**). In the morning, the nurse told the pharmacist that the vial was saved for future doses since the medication was



Figure 1. Partially used vial of promethazine injection.

in short supply. In the nurse’s defense, there was nothing on the promethazine vial label to indicate it is a single-dose vial, which is not a requirement of manufacturers when small vial labels have insufficient space. Educational efforts about proper use of single-dose vials can help. But, when possible, it would be safest to have pharmacy prepare and dispense patient-specific doses.

Incidentally, concerning the use of promethazine injection, ISMP led an effort over 10 years ago to call attention to the hazards related to IV use and extravasation or accidental intra-arterial injection of promethazine, sometimes resulting in amputations. Many health professionals who use promethazine are unaware of the tissue damage that accidental intra-arterial use or IV extravasation may cause (www.ismp.org/sc?id=3004). The shortage of promethazine injection might present an opportunity to remove the drug entirely from the hospital formulary.

⚡ “Ellipta”—it’s not a drug. A pharmacist misread a prescription for INCRUSE ELLIPTA

continued on page 4—**SAFETY wires** >

> **Anaphylaxis**—continued from page 3

One way to prevent dosing errors during treatment of anaphylaxis is to use **EPI-NEPH**rine auto-injectors. If your organization has made a decision, for cost reasons, to replace the **EPIPEN** auto-injector this past year with ampuls and/or vials, or if your organization never stocked auto-injectors, please reconsider their use now as more generic **EPINEPH**rine auto-injectors are available, and their prices are decreasing.

If continuing to use vials or ampuls, it is important for the pharmacy to provide patient care areas with an anaphylaxis kit containing 1 mL (1 mg) vials of **EPINEPH**rine, syringes, and clear instructions for dosing, preparation, and administration. Although we recently heard from a pharmacist who was advocating the use of 30 or 50 unit capacity insulin syringes in **EPINEPH**rine anaphylaxis kits, only syringes marked in mL, not units, should be included. The pharmacist suggested that the insulin syringes would reduce the possibility of accidentally drawing up a full 1 mL (1 mg) amount of **EPINEPH**rine from a 1 mg/mL ampul or vial. We are concerned, though, that this practice could lead to problems.

First, intramuscular **EPINEPH**rine is the preferred route of administration for anaphylaxis. Insulin syringes have a subcutaneous needle already attached. (**EPINEPH**rine auto-injectors also have a relatively short needle, but there is evidence that the pressure exerted during the forceful injection is adequate to drive the drug into the muscle.) Also, insulin syringes are not volumetric (mL), so there are no 0.3 mL or 0.5 mL markings, which may be confusing during a medical emergency. Since insulin syringes measure only in units, some healthcare practitioners may not understand that 30 units measures 0.3 mL, or 50 units measures 0.5 mL. Also, if the **EPINEPH**rine is not injected right away and is set down, another practitioner could think the syringe contains insulin and not **EPINEPH**rine, even if the syringe is labeled.

The safest way to prevent **EPINEPH**rine errors is to incorporate the use of **EPI-NEPH**rine prefilled syringes (auto-injectors) into your emergency response process for anaphylaxis.



Influenza vaccine for healthcare workers

The Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP) recommend that all healthcare professionals get an annual influenza (flu) vaccine. By getting vaccinated, you can help protect your family, your patients, and your co-workers from getting sick. Influenza outbreaks in hospitals and long-term care facilities have been attributed to low vaccination rates among healthcare professionals. One of the easiest ways to prevent outbreaks is by getting an annual flu vaccine. That's right...it's time to roll up your sleeve and get a flu shot!

To subscribe: www.ismp.org/sc?id=384



ISMP Nurse AdviseERR (ISSN 1550-6304) © 2017 Institute for Safe Medication Practices (ISMP). Subscribers are granted permission to redistribute the newsletter or reproduce its contents within their practice site or facility only. Other reproduction, including posting on a public-access website, is prohibited without written permission from ISMP. This is a peer reviewed publication.

Report medication and vaccine errors to ISMP: Call 1-800-FAIL-SAF(E), or visit www.ismp.org/MERP or www.ismp.org/VERP. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

Editors: Ann Shastay, MSN, RN, AOCN; Judy Smetzer, BSN, RN, FISMP; Michael Cohen, RPh, MS, ScD (hon), DPS (hon); Russell Jenkins, MD; Ronald S. Litman, DO. ISMP, 200 Lakeside Drive, Suite 200, Horsham, PA 19044. Email: ismpinfo@ismp.org; Tel: 215-947-7797; Fax: 215-914-1492.

> **SAFETYwires** continued from page 3

(umeclidinium), which was a new prescription for a patient upon discharge from a hospital, as "Increase Ellipta." The pharmacist was only familiar with **BREO ELLIPTA** (fluticasone and vilanterol). Because the patient had not been taking an "Ellipta" inhaler previously, the pharmacist called the prescriber's office to clarify the dose of what he thought must be a prescription for Breo Ellipta. The prescriber confirmed the dose for Breo Ellipta as 100/25 mcg per inhalation, evidently overlooking the fact that he had prescribed Incruse Ellipta for this patient. When the patient was readmitted to the hospital several weeks later for an unrelated diagnosis, a pharmacist discovered the error while collecting a medication history from the patient and investigating why he was taking both **ADVAIR** (fluticasone propionate and salmeterol) and Breo Ellipta.

GlaxoSmithKline has marketed several inhalers for asthma or chronic obstructive pulmonary disease (COPD) using the "Ellipta" trademark to identify the inhalation delivery device. Breo Ellipta, used for asthma or COPD, was the first, becoming available in 2013. Since then, several other "Ellipta" products have been marketed, including **ANORO ELLIPTA** (umeclidinium and vilanterol) and Incruse Ellipta (umeclidinium), both for COPD, and **ARNUITY ELLIPTA** (fluticasone furoate), for asthma.

We have received reports about "Ellipta," the inhaler delivery system trademark, contributing to confusion and errors when patients or health professionals refer to these products only by that name and not the associated drug brand name. This increases the risk of an incorrect medication being added to the patient's medication history, which propagates errors further downstream during the ordering and dispensing process. We mentioned such confusion in our review article on inhalers in 2016 (www.ismp.org/sc?id=3005). Perhaps over time, practitioners will become more familiar with the various products using the Ellipta delivery system and realize that it is a device, not a drug. For now, educate staff about the various products that use the Ellipta inhaler as the delivery device, and discourage staff and patients from referring to these new inhalers by the name "Ellipta."