



## Action needed to prevent serious tissue injury with IV promethazine

Promethazine (PHENERGAN) injection is a commonly used product that possesses antihistamine, sedative, anti-motion sickness, and antiemetic effects. The drug is also a known vesicant which is highly caustic to the intima of blood vessels and surrounding tissue. Formulated with phenol, promethazine has a pH between 4 and 5.5. Although deep intramuscular injection into a large muscle is the preferred parenteral route of administration, product labeling states that the drug may also be given by slow IV push, which is how it is typically given in most hospitals. However, due to the frequency of severe, tragic, local injuries after infiltration or inadvertent intra-arterial injection, ISMP recommends that the FDA reexamine the product labeling and consider eliminating the IV route of administration.

Severe tissue damage can occur regardless of the route of parenteral administration, although intravenous and inadvertent intra-arterial or subcutaneous administration results in more significant complications, including: pain, burning, swelling, erythema, severe spasm of vessels, thrombophlebitis, nerve damage, paralysis, phlebitis, abscess, venous thrombosis, tissue necrosis, and gangrene. Sometimes surgical intervention has been required, including fasciotomy, skin graft, and amputation.

The true extent of this problem may be unknown. However, scores of reports submitted to ISMP, USP, and the Pennsylvania Patient Safety Reporting System; articles in profes-

sional literature; news of lawsuits in the media; and communications on various Internet listservs and message boards (ISMP, National Patient Safety Foundation, allnurses.com, and others) suggest that patient harm may be occurring more frequently than recognized. A few examples follow.

*In 2005, a 19-year-old woman went to the emergency department with flu-like symptoms and received the branded drug Phenergan IV. During the injection, she yelled out in pain and was tempted to pull out her IV line. After the injection, she told the nurse that her arm was still in significant pain and that she felt "something was wrong." The nurse reassured the patient and left the room. The patient's arm and fingers became purple and blotchy. The patient remained in the hospital for 30 days, during which she watched her previously healthy fingers turn black and shrivel*



Phenergan extravasation caused gangrene in a young woman's fingers. (Courtesy of *The Daily World*, Aberdeen, WA)

*(see photo). Her thumb, index finger, and top of her middle finger had to be amputated.<sup>1</sup>*

*In 2005, a patient received 12.5 mg of promethazine IV into an IV site in the hand. During the injection, the patient complained of extreme burning, but the nurse continued administering the medication. The patient developed an area*

*of necrosis on his hand, which eventually required skin grafting and physical rehabilitation.*

*In 2005, a physician intern posted the following request on the ISMP message board: "I am hoping by posting this message I might get some immediate feedback...I am currently doing a rheumatology consult and saw a patient who presented with a*

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### check it out! ✓✓✓✓

Along with manufacturer recommendations, consider the following strategies to prevent or minimize tissue damage when giving IV promethazine.

✓ **Dilute the drug.** Require further dilution of the 25 mg/mL strength to reduce vesicant effects and enable slow administration. For example, dilute the drug in 10 to 20 mL of normal saline if it will be administered via a running IV, or prepare the medication in minibags containing normal saline if there is time for pharmacy to dispense them for individual patients. Extravasation can also be recognized more quickly when promethazine is diluted than if the drug is given in a smaller volume.

✓ **Use large patent veins.** Give the medication only through a large-bore vein (preferably via a central venous access site, but absolutely no hand or wrist veins). Check patency of the access site before administration. Note: according to the package insert, aspiration of dark blood does not preclude intra-arterial placement of the needle because blood can become discolored upon contact with promethazine. Use of syringes with rigid plungers or small bore needles might obscure typical arterial backflow if this is relied upon alone.

✓ **Inject into the furthest port.** Administer IV promethazine through a running IV line at the port furthest from the patient's vein.

✓ **Administer slowly.** Administer over 10-15 minutes and remain with the patient to continuously observe the venous access site if administering the drug via a peripheral vein.

✓ **Limit concentration.** Since 25 mg/mL is the highest concentration of promethazine that can be given IV, stock

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Promethazine continued

*history of an intra-arterial injection of Phenergan at another hospital, likely causing the extreme pain throughout her arm and gangrenous first two digits, which will most likely be amputated. I am hoping anyone who reads this with experience handling this problem or knows of a possible reversal will please contact me ASAP. From what I have been able to gather, there is no current published treatment protocol. The patient will likely have her two fingers amputated soon, and in my opinion, could require more and suffer from lifelong chronic pain. This is a relatively young individual which makes everything more tragic."*

*In 2004, a professional guitar player was awarded \$2.4 million for her past and future medical expenses and \$5 million for her pain and suffering after she endured two amputation surgeries following accidental arterial administration of the branded drug Phenergan. Suffering from a migraine, the woman had gone to the emergency department, where she received the Phenergan, intended for IV administration. She developed circulatory problems and then progressive gangrene which led to amputation of her arm in stages.<sup>2</sup>*

According to the package insert, "Proper IV administration of this product is well tolerated, but use of this route is not without some hazards." To reduce the risk of these hazards, manufacturer labeling recommends to: give the drug in concentrations no greater than 25 mg/mL; administer the drug at a

rate no greater than 25 mg/minute; inject the drug through the tubing of an infusion set that is running and known to be functioning satisfactorily; and to stop the injection immediately if the patient reports burning to evaluate possible arterial placement or perivascular extravasation.

Nonetheless, ISMP believes these long-standing hazards require further action on the part of healthcare providers, FDA, and promethazine manufacturers. In the 1970s, after numerous reports of harmful infiltrations and inadvertent intra-arterial injections of hydroxyzine, FDA asked the manufacturer to revise the label and remove IV as an approved route. Today the drug is only indicated for IM or oral administration. Similarly, FDA should carefully investigate adverse events with promethazine to determine if labeling changes are warranted, including removal of FDA approval for IV administration.

See **checkitout!** in the right column, starting on page 1, for actions you can take to help prevent patient harm when administering IV promethazine.

**References:** (1) Friederich S. Malpractice allegations spotlight anti-nausea medication. *The Daily World*, Aberdeen, WA; December 7, 2005. Available: [www.thedailyworld.com/articles/2005/12/07/local\\_news/02news.txt](http://www.thedailyworld.com/articles/2005/12/07/local_news/02news.txt). (2) Patrick J. Marshfield woman wins 7.4 million jury award after she loses arm. *The Barre Montpelier Times Argus*; Barre, VT; March 19, 2004.

## pearls for patients



**Unauthorized medications.** An ICU patient was seen taking medications from her purse. When the nurse investigated, prescription bottles containing **VICODIN** (hydrocodone and acetaminophen) and **PERCOCET** (oxycodone and acetaminophen) were found. The patient told the nurse she was in pain and preferred to take her own medications. We've received similar reports of hospitalized patients who've taken their own vitamins, herbal products, birth control pills, metered-dose inhalers, antacids, and other drugs without telling their healthcare providers. With medication reconciliation a top priority in 2006, healthcare providers are clearly asking patients about the medications they've been taking at home. However, they might forget to remind patients that they should not take their home supply of medications while hospitalized, unless a nurse or physician specifically instructs them to do so. Extra doses or unrecognized drug interactions may occur. During the admission process and throughout the hospitalization, patients and families should be reminded about this. A directive to avoid taking unauthorized home medications, including over-the-counter products, should also appear in patient brochures or instructional materials.

## checkitout! continued

only this concentration (not the 50 mg/mL concentration).

✓ **Limit the dose.** Consider 6.25 to 12.5 mg of promethazine as the starting IV dose. Hospitals have reported effectiveness with these smaller doses.

✓ **Revise orders.** Revise preprinted order forms to ensure orders for promethazine reflect the safety measures listed above.

✓ **Educate patients.** Before administration of the drug, tell patients to let you know immediately if burning or pain occurs during or after the injection.

✓ **Create alerts.** Build an alert to appear on medication administration records (MARs) and on automated dispensing cabinet screens for nurses to view each time they access and administer a dose of promethazine, reminding them that the drug is a vesicant and should be diluted and administered slowly through a running IV.

✓ **Treat.** The manufacturer notes there is no proven successful management of unintentional intra-arterial injection or perivascular extravasation. However, sympathetic block and heparinization have been employed during acute management of promethazine extravasations.

✓ **Ask for alternatives.** Talk to pharmacy about safer alternatives that can be used for the conditions treated with IV promethazine. For example, 5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptor antagonists may be used for both prophylaxis and as rescue antiemetics. This drug class includes dolasetron (**ANZEMET**), granisetron (**KYTRIL**), and ondansetron (**ZOFRAN**).

✓ **Remove from formulary.** Some hospitals that have continued to experience adverse events despite safety measures have removed promethazine from their formulary or banned its IV use.

## Piggybacked insulin infusion leads to overdose

A diabetic patient was admitted to the emergency department with gastrointestinal bleeding. Upon assessment, a fingerstick glucose level of 762 mg/dL was discovered. An IV infusion of normal saline was started, running initially at 150 mL/hour, and the patient received an IV bolus dose of regular insulin (10 units). The physician also prescribed an insulin infusion (125 units/250 mL normal saline) to run at 8 units/hour (16 mL/hour), which was started after receipt from the pharmacy. The patient was then sent to radiology for a CT scan.

When he returned almost 2 hours later, the insulin infusion was empty. Bedside glucose monitoring every 30 minutes over the next 6 hours showed a drop in his glucose from 762 to 160 mg/dL. Fortunately, the patient did not suffer more severe hypoglycemia or other side effects.

## Liquid oral medication given IV

An order was written for "TUS-SIONEX suspension" (hydrocodone and chlorpheniramine), but the oral route of administration was not specified. Pharmacy dispensed the cough medicine in unit-dose oral syringes. The patient's nurse had recently joined the staff after working in a long-term care facility and was unfamiliar with oral syringes. Since the liquid was in a syringe and the patient had IV access, the nurse assumed the drug should be given IV. Unfortunately, a pharmacy label covered the manufacturer's words, "For oral use only," that were printed on the oral syringe. Noting that the drug was thick, the nurse transferred it from the oral syringe into a regular syringe, diluted it with saline, and injected it. Afterwards, she commented to another nurse that the drug was quite sticky. Further queries led to recognition that

The insulin infusion had been piggybacked into the primary IV line, not infused via a separate infusion pump. Although two nurses had double checked the insulin drip at the nurses' station, the reporting hospital believes the nurse who hung the insulin did not reset the pump to the correct rate. Thus, the insulin solution infused at 150 mL/hour, the rate previously set for the primary IV solution.

In addition to purchasing smart pumps with dosage error-reduction software, this hospital has made several changes to prevent errors: nurses must administer all IV solutions with high-alert drugs using a separate pump; an ED nurse must accompany patients to radiology if they have a high-alert drug infusing; and a verbal handoff between the accompanying nurse and the radiology staff, including verification of infusing IV therapy, must occur.

the drug had been given by an incorrect route. The IV site was quickly removed, the patient was monitored, and fortunately, no harm occurred.

Some nurses are not familiar with oral syringes and, thus, may mistake a liquid medication in an oral syringe as a parenteral product. Awareness of oral syringes and how they protect against inadvertent IV administration should be included in new staff orientation. Pharmacy labels should not cover important information, such as "For oral use only" warnings. Auxiliary labels with this caution are also available, which can be affixed (like a flag) to the syringe plunger of an oral syringe. Incomplete orders that do not express a route of administration also should be clarified before transcription of the orders and administration.

## safetywire



### Mixing up monitoring results.

Medications are often prescribed based upon recent diagnostic or patient monitoring results. However, we've received numerous reports of prescribing medications for the wrong patient after laboratory or other diagnostic/monitoring results were mixed up. In one event, a physician prescribed **CARDIZEM** (diltiazem) 20 mg IV followed by 30 mg orally for a patient in bed A after a telemetry unit nurse called to report that his cardiac monitor showed atrial fibrillation and flutter with a heart rate of 140. When the patient exhibited no change in his heart rate or rhythm after receiving the medication, the nurse called the physician again and received an order to administer 150 mg of amiodarone IV push followed by a 60 mg per hour infusion. A short time later, the nurse realized that the rhythm she was viewing on the monitor at the nursing station was for the patient in bed B. The names of the patients in bed A and bed B had been mixed up and posted on the wrong channel of the central monitoring unit at the nursing station. Cardiac monitors that display multiple patients' rhythms should be labeled with patients' names using a verification process involving two individuals (one at the bedside, one at the nursing station). In these settings, patients' lives could very well depend on rapid and accurate patient identification and treatment.

## ► Special Announcement

► **ISMP Teleconference.** Join us for our next teleconference, **Improving Medication Safety with Antithrombotic Agents**, to be held **September 13, 2006**. Continuing education credit will be available for pharmacists and nurses. Visit [www.ismp.org/educational/teleconferences.asp](http://www.ismp.org/educational/teleconferences.asp) for additional information and to register.

The 2006 ISMP Cheers Awards: Looking for Medication Safety Leaders

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**\*Nominations Deadline Extended\*  
to August 24, 2006**

*Tuesday Evening, December 5, 2006*

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This year's keynote speaker is **Charles R. Denham, MD**,  
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The *ISMP Cheers Awards* are one of the most prestigious ways to recognize true leaders in the field of patient safety. They honor individuals, hospitals, health systems, or companies that have made extraordinary advances in medication safety in the past year. Nominations are also being accepted for the 2006 *ISMP Medication Safety Alert*! **Subscriber Award**, which honors an organization that widely distributes one or more of the ISMP newsletters (Acute Care edition, Community/Ambulatory Care edition, *Nurse Advise-ERR*®, and *Safe Medicine*®) and uses the information to improve medication safety.

Award recipients will be recognized for their outstanding contributions at the annual Cheers dinner banquet. They will receive an award, travel stipend to attend the banquet, and national recognition for their work.

The nominations deadline has been extended to **August 24, 2006**.  
(See directions at the bottom of the page.)

## Support Appreciated

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For more information, to submit a nomination (self-nominations are encouraged), or to make a tax deductible donation to support the *Cheers Awards*, please visit ISMP online at [www.ismp.org/Cheers/default.asp](http://www.ismp.org/Cheers/default.asp) or call ISMP at 215-947-7797.