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Educating the healthcare community about safe medication practices

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## Safety Briefs

**Vaccine with two components.** **PENTACEL** is indicated for active immunization against diphtheria, tetanus, pertussis, poliomyelitis, and invasive disease due to *Haemophilus influenzae* type b. It is for use in children 6 weeks through 4 years of age and provides the convenience of multiple vaccines in one shot. However, it is a 2-vial vaccine product that requires mixing of the two components before administration to children (Figure 1). A medication error was reported in which only one component of the vaccine product, the DTaP/IPV (diphtheria and tetanus toxoids, acellular pertussis adsorbed, inactivated poliovirus) portion, was administered to the child, not the Hib (*Haemophilus b* conjugate) portion. The provider later continued the series and the child did not experience any harm. The error was discovered during an inventory of the vaccines. One reason


**Figure 1.** Pentacel vaccine requires mixing of two components. One component (vial on right) lists the brand name on the label, so staff may think it contains the entire product.

this may have happened is that the DTaP/IPV component carries the brand name Pentacel while the Hib component does not. Unless the person administering the vaccine is familiar with the product and takes the time to read the labeling, which indicates the two must be mixed, the person could easily think the vial labeled Pentacel is all that is needed. We contacted the company about this and also suggested enhancing the labeling to call attention to the need to mix the two components. Staff at the clinic have also been instructed to make sure the NDC number for each component has been documented in the vaccine log. This will help confirm administration of both portions of the vaccine.

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Lessons for us all

## Plain D5W or hypotonic saline solutions post-op could result in acute hyponatremia and death in healthy children

ISMP recently learned about the tragic deaths of two 6-year-old children stemming from severe postoperative hyponatremia. The fatal events occurred at two different hospitals. In at least one of these cases, it is clear that the rapid administration of plain D5W (dextrose 5% in water) postoperatively resulted in acute hyponatremia secondary to free water retention (also called *water intoxication*, which is described below). Postoperative children are at high risk for developing hyponatremia, and many fatalities from this disorder have been reported in the literature.[1-14] When the serum sodium concentration rapidly falls below 120 mEq/L over 24 to 48 hours—as in the two events described below—the body's compensatory mechanism is often overwhelmed and severe cerebral edema ensues, resulting in brainstem herniation, mechanical compression of vital midbrain structures, and death.[15]

### Case 1

In the first case, the child underwent an outpatient tonsillectomy and adenoidectomy. Postoperative orders included IV fluids of "1000 cc D5W – 600 cc q8h." An experienced pharmacist accidently calculated the infusion rate incorrectly and entered 200 mL/hour instead of 75 mL/hour on the child's electronic medication administration record (eMAR). He used a calculator and performed the calculation twice but had set up the mathematical problem incorrectly. Thinking in terms of how many 600 mL "doses" would be needed, he set up the calculation as follows: 600 mL (the volume to infuse over 8 hours) divided by 3 (the number of 600 mL "doses" he thought would be needed for 24 hours) and arrived at a 200 mL/hour infusion rate.

The nurse who started the infusion did not detect the pharmacist's error. She had quickly looked at the surgeon's postoperative orders and had obtained a bag of D5W to hang. But she felt rushed by the hectic pace of the unit and was distracted during the verification process because she had to find an infusion pump to administer the IV solution. The nurse thought her memory of the written order was sufficient for verification of the pharmacist's entry on the eMAR. This was not her usual practice; however, like other nurses on the unit, she had come to rely on the accuracy of their pharmacists who "never made mistakes." When the first 1,000 mL bag of D5W was empty, the nurse hung a second bag to infuse at 200 mL/hour.

Several times throughout the day, the child vomited small amounts of dark, bloody secretions, as expected from the surgery. Near the anticipated time of discharge that afternoon, the child's mother asked a nurse to administer an antiemetic before she took her daughter home. About 40 minutes after receiving promethazine 12.5 mg IV, the child became lethargic and began experiencing jerking movements, rigid extremities, and rolled-back eyes. The surgeon attributed this to a dystonic reaction from promethazine, administered a dose of IV diphenhydr**AMINE**, and admitted the child to a medical-surgical unit.

During the next few hours, the child's vomiting worsened, she became more unresponsive, and the seizure-like activity became much more pronounced and frequent. The nurses called the child's surgeon multiple times to report the seizure-like activity, during which additional doses of IV diphenhydr**AMINE** were prescribed and subsequently administered. Several nurses also told the surgeon that the seizure-like activity appeared to be more than a dystonic reaction to promethazine, although none of the nurses had ever witnessed such a reaction. Unfortunately, during this time the nurses failed to notice the infusion rate error or recognize that an infusion of plain D5W alone or an infusion rate of

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**Lab test, not medication.** When a pharmacist was reconciling medication orders on one of the nursing units, he was met with a transcription on the MAR that caused him to pause (Figure 1). After trying to figure out what was intended, he went back to the original order (Figure 2). The original order was also confusing except for some additional clues. The pharmacist recognized the signature (not shown) as one of the infectious diseases (ID) physicians and then checked the chart for a progress note or consultation. There he found that the physician suspected mycoplasma pneumonia, and to make the diagnosis, he appropriately ordered a


**Figure 1:** Transcription on nurse's MAR.


**Figure 2:** Original physician order.

mycoplasma IgM titer, which is found in 80% of *M. pneumoniae* cases within 1 week of infection. Mystery solved, but it does point out potential dangers of incomplete nomenclature. Had the ID physician written "mycoplasma IgM titer," the order would have been less confusing. There is also danger in allowing use of improper abbreviations because people get used to them, which could eventually lead to confusion, as happened here. Although "gm" is commonly seen as an abbreviation for grams, the USP-approved abbreviation for gram is a lower case letter "g" only. Besides the rather unusual situation described above, "gm" can also look like "gr," the abbreviation for the apothecary measurement, grains (which still appears now and then, such as with nitroglycerin dosing). In our June 30, 1999, issue we wrote about a serious **PHEN**obarbital overdose that started with a pharmacist typing "0.5 gr" on the prescription label. Later, during the patient's hospitalization, a physician took this to mean 0.5 grams (500 mg), not 0.5 grains (30 mg). Pharmacists and nurses failed to recognize the overdose and gave the patient **PHEN**obarbital 500 mg IV daily for three days. After the patient suffered respiratory difficulties, the dose was withheld and the error was soon discovered.

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## Hyponatremia

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200 mL/hour was unsafe for a 6-year-old child. Subsequently, a third 1,000 mL bag of D5W was hung after the second bag had infused.

After the child developed significant bradycardia that necessitated calling a code, the surgeon came into the hospital, observed the child having a grand mal seizure, and consulted a pediatrician to help manage the seizures. The consulting pediatrician finally recognized that the child was experiencing hyponatremia and water intoxication due to the erroneous infusion rate of 200 mL/hour during the previous 12 hours and the lack of sodium chloride in the infusate. The child had nonreactive pupils and exhibited decerebrate posturing. Stat lab studies showed a critically low concentration of sodium of 107 mEq/L. A CT scan of the brain revealed cerebral edema and, despite treatment, the child subsequently died.

### Case 2

In the second case, the child underwent surgery for coarctation of the aorta, a condition that had been identified in this otherwise asymptomatic, healthy child during a school physical. The child's postoperative course seemed to be progressing well, but later on post-op day 1, his physician prescribed a furosemide infusion (1 mg/hour) because the child's urinary output was less than expected despite several doses of **EDECRIN** (ethacrynic acid). By post-op day 2, the child's serum sodium level had dropped, so his physician prescribed an infusion of sodium chloride. It is uncertain whether the sodium chloride was ever administered, as the child's sodium level continued to drop and administration of the prescribed infusion was never documented on the MAR.

The child became less responsive throughout the morning of post-op day 2, and his parents expressed concern to several nurses when they could not awaken their son. The nurses assured the parents that deep sleep was expected due to the pain medication—**HYDRO**morphone—that the child was receiving. Despite ongoing, repeated concerns expressed by the parents, the nurses failed to recognize that the child was not simply sleeping soundly but exhibiting signs of severe, life-threatening hyponatremia.

When the child began experiencing seizure-like activity in the early afternoon, nurses attributed the movements to the child being "fidgety" from pain. The child also began vomiting. Unfortunately, the physician was not kept informed regarding the child's change in cognition, continued oliguria, vomiting, and seizure-like activity. When the critical care intensivist visited the child in the early evening for a routine assessment, he quickly recognized the problem. By then the child exhibited no reflexes or response to painful stimuli. Despite intubation and ventilation support, and aggressive treatment of hyponatremia and cerebral edema, the child died the following day.

Although many of the contributing factors and deeply seated root causes of these events differ, two common causes are clear: 1) lack of professional staff knowledge regarding the causes and signs of hyponatremia, and 2) the failure of professional staff to respond to concerns expressed by several nurses in Case 1, and by the parents in Case 2, regarding the rapidly deteriorating condition of these children.

### Hyponatremia and water intoxication

Hyponatremia is the most common electrolyte disorder,[15] particularly among hospitalized patients. Studies suggest that more than 4% of post-op patients develop clinically significant hyponatremia within 1 week of surgery, as do 30% of patients treated in intensive care units (ICUs).[15-18] In general, the causes of hyponatremia are varied, ranging from certain medications (e.g., diuretics, heparin, opiates, desmopressin, proton pump inhibitors) and disease states (e.g., renal and liver impairment, hypothyroidism or cortisol deficiency) to outpatient environmental conditions (e.g., prolonged exercise in a hot environment) and self-imposed conditions (e.g., psychogenic polydipsia, feeding infants tap water or formula that is too dilute). However, the causes of hospital-acquired hyponatremia most relevant to

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**Kapidex-Casodex confusion.** There have been reported instances of medication errors due to name confusion between **KAPIDEX** (dexlansoprazole) and **CASODEX** (bicalutamide). Both written and verbal prescriptions have been dispensed in error. Kapidex is indicated for healing of erosive esophagitis, maintenance of healed erosive esophagitis, and treatment of symptomatic nonerosive gastroesophageal reflux disease (GERD). It is available as 30 mg and 60 mg delayed-release capsules for oral administration. Casodex is indicated for use in combination therapy with a luteinizing hormone-releasing hormone (LHRH) analog for the treatment of stage D2 metastatic carcinoma of the prostate. Casodex is available as 50 mg tablets for oral administration. Patients who receive either drug in error could be unnecessarily subjected to unintended effects and/or adverse events. Specifically, Casodex is contraindicated in women. To reduce the potential for medication errors, please take time to verify written or verbal orders and build an alert in your computer system. If you are a prescriber, please include the drug's purpose on prescriptions.

### Editors' note

■ **No link to patient death established in ON-Q incident.** In the July 16, 2009, article on safety issues when using elastomeric pumps, we wrote about an incident involving a patient who was sent home with an ON-Q pump to treat postoperative pain. According to the reporter, on the second day of the planned 5-day infusion, the patient was brought to the emergency department in cardiac arrest. Staff noticed the pump was empty but were unable to identify the infusate since the pump was not labeled. When staff later learned that local anesthetic had been infusing, a blood level was drawn, which was determined to be elevated but not alarmingly so. The reporter mentioned that there was probably no link between the patient's death and the infusion rate or drug level. For clarification purposes, we would like to restate the fact that no such link was determined. Our reasons for mentioning the event were related to possible premature emptying of the pump in 2 days instead of 5 days, for which no causes were identified, and absent labeling on the pump to identify the drug.

## Hyponatremia continued from page 2

the events described above are twofold: administration of plain D5W or hypotonic saline parenteral solutions post-op, and failure to recognize the compromised ability of children to maintain water balance.[15]

Review of the literature suggests that administration of hypotonic saline or parenteral fluids without saline is physiologically unsound and potentially dangerous for hospitalized children.[1] A 2003 analysis[1] found more than 50 reported cases of neurologic morbidity and mortality, including 26 deaths, during a 10-year period resulting from hospital-acquired hyponatremia in children who were receiving hypotonic saline parenteral fluids.[1-14] More than half of these cases occurred in the postoperative setting in previously healthy children who underwent minor surgeries. Children are particularly vulnerable to water intoxication because they are prone to developing a syndrome of inappropriate antidiuretic hormone (SIADH).[1] Common childhood conditions requiring IV fluids, such as pulmonary and central nervous system infections, dehydration, and the postoperative state, are associated with a nonosmotic—and therefore inappropriate—stimulus for antidiuretic hormone (ADH) production.[1,14] The postoperative nonosmotic stimulus for ADH release typically resolves by the third postoperative day but can last until the fifth postoperative day.[1,18] Pain, nausea, stress, opiates, inhaled anesthetics, and the administration of hypotonic saline or solutions without saline also stimulate the excessive release of ADH in children.[1,14]

Children are also more vulnerable to the effects of cerebral swelling due to hyponatremia because they develop encephalopathy at less significant decreases in normal serum sodium levels than adults and have a poor prognosis if timely therapy is not instituted. In children, there is little room for brain expansion due to a higher brain-to-skull size ratio.[1,17,19] Children achieve adult brain size by 6 years of age, whereas full skull size is not achieved until 16 years of age.

Hyponatremic encephalopathy can be difficult to recognize in children, as the symptoms may be variable.[2,18] The most consistent symptoms include headache, nausea, vomiting, weakness, mental confusion, and lethargy. Advanced symptoms show signs of cerebral herniation, including seizures, respiratory arrest, noncardiogenic pulmonary edema, dilated pupils, and decorticate or decerebrate posturing.[1]

Irreparable harm can happen when low serum sodium levels are corrected too quickly or too slowly. Once the source of free water has been eliminated, the sodium level is typically increased by 4-6 mEq over the first 1-2 hours using an isotonic or near isotonic sodium chloride infusate.[15] Patients with seizures, severe confusion, coma, or signs of brainstem herniation may need hypertonic (3%) saline to correct sodium levels, but only enough to arrest the progression of symptoms. Formulas exist for determining the dose of hypertonic saline during replacement therapy.[14] Some clinicians believe that, in serious cases, treatment of hyponatremia should be rapid since the risk of treating too slowly—cerebral herniation—is felt to be greater than the risk of treating too quickly—osmotic demyelination syndrome, which has been associated with lesions in the white matter of the brainstem.[14] These lesions are more common in adults. (**Please note:** The preceding information is in no way sufficient to guide the treatment of hyponatremia or suggested as an evidence-based standard of care. It was provided only to convey that expert opinions vary regarding prevention and treatment of hyponatremia and to encourage discussion among an interdisciplinary clinical team charged with developing electrolyte replacement protocols.)

### Conclusions

Standards of practice should be established for postoperative IV solutions used to hydrate patients—particularly children. The standards should acknowledge that the administration of solutions with saline in maintenance parenteral fluids is an

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*Special Announcements...*

## ISMP October teleconferences

### October 6 - Beyond the 5 Rights: A Safety Bolus for Nursing Leadership

Are nurse leaders in your organization worried about the risk of drug administration errors? Are they concerned that the "5 Rights" alone will not keep patients safe? Don't let a medication-related sentinel event be your wake-up call! Learn where risk is present but "hidden" in your medication administration system, and discover the high-leverage error-reduction strategies that can reduce the risk of harmful errors. Speakers will also discuss common at-risk behaviors that lead to errors during medication administration and the nurse leader's role in establishing a learning culture.

### October 15 - Preventing Errors with Insulin: A Multidisciplinary Approach

While the number of people with diabetes mellitus rises at alarming rates, insulin use and the risk of errors are also increasing. ISMP invites practitioners to join us for this important presentation during which we will explore the current trends in insulin therapy, barriers to optimal therapy and safety, and common errors that occur with insulin. Error prevention strategies will be presented, including improved communication of insulin orders as well as safe preparation, storage, delivery, and administration of insulin, including the use of insulin pens.

For details on both programs, please visit: www.ismp.org/educational/teleconferences.asp.

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important prophylactic measure that can be taken to prevent hyponatremia in children, who are prone to an increase in ADH production.[15] If appropriate, criteria should include when lab studies need to be drawn to determine electrolyte levels in patients receiving IV fluids for hydration over an extended period of time.

Protocols should be established to identify, treat, and monitor patients with hyponatremia, water intoxication, and/or SIADH. Clinically significant hyponatremia may be nonspecific in its presentation; thus, professional staff must include this in the differential diagnoses in patients presenting with early symptoms or an altered level of consciousness. All physicians, pharmacists, and nurses need a thorough understanding of fluid and electrolyte balance and the pathophysiology of hyponatremia, water intoxication, and SIADH to increase their index of suspicion when symptoms appear, and to become more responsive to voiced concerns regarding the patient's condition.

All hospitals should also consider establishing a rapid-response team (RRT) that allows any healthcare worker to summon an interdisciplinary team to a patient's bedside for a full evaluation when they fear something is seriously wrong with the patient and have expressed their concerns without an adequate response. The RRT provides an opportunity to step in *before* a tragedy occurs. Once the RRT has been formed and is functioning well, consider inviting patients and families to call the RRT to address unresolved concerns about their safety and health; subtle changes may be more readily identified as abnormal by family members than by healthcare providers. For more on RRTs, please see our June 1, 2006 newsletter (www.ismp.org/Newsletters/acutecare/articles/20060601.asp). ISMP Canada also published a Safety Bulletin (www.ismp-canada.org/download/safetyBulletins/ISMPCSB2008-01DDAVP.pdf) regarding the death of a young patient who developed hyponatremia in response to desmopressin and post-op hypotonic IV solutions used to initially treat hypernatremia and central diabetes insipidus.

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