Note: All dosages given are for adults unless otherwise stated. The information on medications contained in this course is not meant to be prescriptive or all-encompassing. You are encouraged to consult with physicians and pharmacists about all medication issues for your patients.

Acknowledgements

RN.com acknowledges the valuable contributions of...

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Purpose and Objectives

The purpose of High-Alert Medications: Safe Practices is to identify several high-alert medications that are considered to present the highest risk to patients and recommend ways to improve safety in administering these medications.

After successful completion of this course, you will be able to:

1. Explain why certain medications and classifications of medications are designated as high-alert medications.
2. Give examples of recommendations to improve safety with high-alert medications.
3. Give examples of nurses’, pharmacists’ and others’ perceptions of high-alert medications as reported in a 2007 Institute for Safe Medicine Practices study.
4. Identify important safety precautions when administering heparin.
5. Identify important safety precautions when administering warfarin.
6. Identify important safety precautions when administering digoxin.
7. Identify important safety precautions when administering electrolytes.
8. Identify important safety precautions when administering insulin.
9. Identify important safety precautions when administering narcotics.
10. Identify important safety precautions when administering sedatives, specifically midazolam.
11. Identify important safety precautions when using patient-controlled intravenous analgesia and patient-controlled epidural analgesia.

Note:

This course contains many recommendations for the safe use of high-alert medications. As a nurse, you are responsible for knowing which medications your organization has identified as high-alert medications and for following scrupulously your organization’s policies and procedures.
**Introduction**

Why are certain medications identified as high-alert medications?

High-alert medications have the highest risk for causing injury when misused. These medications have narrow therapeutic indexes or small margins of safety – that is, there is a small difference between a therapeutic dose and a harmful dose.

Data collected and analyzed by the Joint Commission (TJC), the Institute for Safe Medical Practices (ISMP), the Institute for Healthcare Improvement (IHI), and the United States Pharmacopoeia (USP) have identified the medications most often involved in medication errors that result in injury or death. Their findings identify high-risk, or high-alert, medications which have a heightened risk of patient harm when they are used in error.

High-alert medications include medications that nurses have administered frequently and for many years, such as insulin, heparin, warfarin, narcotics, and sedatives. In fact, researchers have reported that 2/3 of emergency admissions for adverse medication reactions were related to warfarin, insulin, oral antiplatelet agents and oral hypoglycemic agents (Budnitz et al, 2011).

Certainly less commonly used medications fit the criteria for high-alert medications also. For example, chemotherapeutic agents present safety threats to both patients and staff members. Nurses need special training for administering chemotherapy. This course does not include chemotherapeutic agents.

To protect patient safety, it is important that nurses and other healthcare professionals remain alert to the dangers of these medications and not allow familiarity to breed complacency. Protect your patients from harm by communicating clearly and complying strictly with policy related to high-alert medications.

**High-Alert Medications Can Harm Patients**

The Institute for Healthcare Improvement (5 Million Lives Campaign, 2008) has collected data indicating that:

- 40 harm events occur per 100 hospital admissions
- 50% of these harm events are medication-related
- Common types of harm resulting from medications:
  - Bleeding
  - Hypotension
  - Hypoglycemia
  - Delirium
  - Lethargy
  - Bradycardia

**Joint Commission standards require healthcare organizations to:**

- Identify high-alert medications used in the organization.
- Develop and implement processes for procuring, storing, ordering, transcribing, preparing, dispensing, administering, and/or monitoring high-risk or high-alert medications.

TJC, 2011b
High-Alert Medications Addressed in This Course

<table>
<thead>
<tr>
<th>Medication or Classification</th>
<th>Reason Designated as High-Alert Medication: Improper dose, administration, or monitoring can lead to...</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticoagulants:</strong> Heparin and Warfarin</td>
<td>Fatal bleeding from overdose. Thrombotic events from inadequate dose.</td>
</tr>
<tr>
<td><strong>Digoxin</strong></td>
<td>Extremely narrow therapeutic index. Toxicity or subtherapeutic effect can be fatal.</td>
</tr>
<tr>
<td><strong>Electrolytes</strong></td>
<td>Renal dysfunction or failure, cardiac arrest, coma, respiratory arrest, seizures, rhabdomyolosis*, and death.</td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
<td>Cardiac changes, electrolyte disturbances, seizures, coma, and death.</td>
</tr>
<tr>
<td><strong>Narcotics and Sedatives Sample medication:</strong> Midazolam</td>
<td>Injury due to falling, respiratory depression, coma, and death from overdose. Uncontrolled pain and anxiety from inadequate dose: Midazolam is frequently used to produce conscious sedation for procedures. Significant risk of respiratory depression during and following a procedure.</td>
</tr>
</tbody>
</table>

*Rhabdomyolosis is an acute, sometimes fatal disease characterized by destruction of muscle tissue.

Lists of High-Alert Medications

ISMP creates and periodically updates a list of high-alert medications. The list is lengthy and includes categories of medications that are used only in specialized settings, such as anesthetics, chemotherapeutic agents, dialysis solutions, neuromuscular blocking agents, and radiocontrast agents. Some of the specific medications listed are for the most part limited to use in specialties, such as magnesium sulfate and oxytocin in Labor & Delivery.

As a part of its 5 Million Lives safety campaign, IHI focuses on four categories of high-alert medications which represent areas of greatest harm and greatest opportunity for improvement (5 Million Lives Campaign, 2008):

- Anticoagulants
- Insulin
- Narcotics and opiates
- Sedatives

Know the list of high-alert medications which your organization has developed. Pay particular attention to policies and procedures related to the high-alert medications used in your practice area. You may be very familiar with the specific medications, but your organization may have established more stringent safety-oriented policies and procedures than you have used in the past. Policies may include independent double-checks or the use of specialized supplies.
Differing Views: Nurses, Pharmacists, and Administrators

ISMP periodically surveys nurses, pharmacists, and risk/quality/safety managers concerning high-alert medications. The survey asks which medications the respondents think should be high-alert medications and which medications the respondents' facilities have designated as high-alert medications (ISMP, 2007a).

Comparing the 2007 survey results with results obtained in 2003, there was a sizable decrease in the number of respondents who considered warfarin a high-alert medication. Yet, risk/quality/safety managers placed warfarin among the top 10 medications they believed should be designated high-alert. The Joint Commission’s National Patient Safety Goals (NPSG) make specific safety recommendations for anticoagulant therapy.

In general, nurses identified specific medications as high-alert with greater frequency than pharmacists, for example 73% of nurses identified oxytocin as a high-alert medication, as compared with only 38% of the pharmacists.

Survey respondents identified more specific medications as high-alert than their facilities had designated. For example:

- Epidural or intrathecal medications: 93% of respondents, 79% of respondents' facilities
- Inotropic medications, IV, such as digoxin, 67% of respondents, 50% of respondents’ facilities (ISMP, 2007a)

**ISMP's Top Ten-Ranked High-Alert Medications**

The top ten-ranked high-alert medications ranked by the 2007 ISMP survey were:

<table>
<thead>
<tr>
<th>Medication</th>
<th>% of Respondents Identifying as High-Alert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapeutic agents, parenteral</td>
<td>97%</td>
</tr>
<tr>
<td>Neuromuscular blocking agents, such as succinylcholine</td>
<td>94%</td>
</tr>
<tr>
<td>Epidural or intrathecal medications</td>
<td>93%</td>
</tr>
<tr>
<td>Insulin, IV</td>
<td>93%</td>
</tr>
<tr>
<td>Potassium chloride for injection</td>
<td>93%</td>
</tr>
<tr>
<td>Potassium phosphates injection</td>
<td>87%</td>
</tr>
<tr>
<td>Anesthetic agents, general, inhaled and IV, such as propofol</td>
<td>86%</td>
</tr>
<tr>
<td>Heparin, unfractionated, IV</td>
<td>85%</td>
</tr>
<tr>
<td>Adrenergic agonists, IV, such as epinephrine</td>
<td>84%</td>
</tr>
<tr>
<td>Sodium chloride injection, hypertonic, more than 0.9% concentration</td>
<td>83%</td>
</tr>
<tr>
<td>Thrombolytics/fibrinolytics, such as tenecteplase</td>
<td>83%</td>
</tr>
</tbody>
</table>

Survey findings indicate that practitioners identify more medications as high-alert than their organizations designate.
High Alert Meds as Designated Most Often by Healthcare Facilities

The MOST highly-ranked high-alert medications as designated by the facilities of the respondents to the 2007 ISMP survey were:

<table>
<thead>
<tr>
<th>Medication</th>
<th>% of Respondents’ Facilities Identifying as High-Alert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapeutic agents, parenteral</td>
<td>90%</td>
</tr>
<tr>
<td>Insulin, IV</td>
<td>88%</td>
</tr>
<tr>
<td>Potassium chloride for injection</td>
<td>86%</td>
</tr>
<tr>
<td>Heparin, unfractionated, IV</td>
<td>80%</td>
</tr>
<tr>
<td>Epidural or intrathecal medications</td>
<td>79%</td>
</tr>
<tr>
<td>Neuromuscular blocking agents, such as succinylcholine</td>
<td>78%</td>
</tr>
<tr>
<td>Potassium phosphates injection</td>
<td>77%</td>
</tr>
</tbody>
</table>

Although respondents (nurses, pharmacists, and risk/quality/safety managers) identified more medications than their healthcare facilities considered high-alert, both respondents and their facilities frequently identified many of the same medications as high-alert, including:
- Parenteral chemotherapeutic agents
- IV Insulin
- Parenteral KCl
- IV Heparin, unfractionated
- Epidural or intrathecal medications
- Neuromuscular blocking agents such as succinylcholine
- Potassium phosphates injection

High Alert Meds as Designated Least Often by Healthcare Facilities

The LEAST common high-alert medications as designated by the facilities of the respondents to the 2007 ISMP survey were:

<table>
<thead>
<tr>
<th>Medication</th>
<th>% of Respondents’ Facilities Identifying as High-Alert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral hypoglycemics</td>
<td>21%</td>
</tr>
<tr>
<td>Colchicine injection</td>
<td>29%</td>
</tr>
<tr>
<td>Epoprostenol (Flonan®)</td>
<td>39%</td>
</tr>
<tr>
<td>Dialysis solutions, peritoneal and hemodialysis</td>
<td>40%</td>
</tr>
<tr>
<td>IV adrenergic antagonists</td>
<td>41%</td>
</tr>
<tr>
<td>IV radiocontrast agents</td>
<td>43%</td>
</tr>
<tr>
<td>Liposomal forms of drugs</td>
<td>44%</td>
</tr>
</tbody>
</table>
Organizational Safety Precautions

Authorities recommend that healthcare organizations implement general strategies to prevent harm related to high-alert medications, such as:

- Limit the concentrations of these medications that are available in the organization and/or in the automatic dispensing cabinets of particular nursing units.
- Stock only small vials of high-alert medications.
- Differentiate high-alert medications with warnings, including warnings on automatic dispensing cabinet screens and medication labels, such as NOTE CONCENTRATION on high concentration preparations.
- Standardize orders that permit use of a limited number of concentrations. Using a limited number of concentrations allows for developing dosage charts that can be laminated and kept readily available for nurses. Standardize protocols for use of reversal agents.
- Limit the possibility of error related to decimal places by requiring rounding off whenever possible.
- Institute forcing functions. Forcing functions impose requirements that prevent errors. For example, by stopping an order entry or programming of a pump when preset limits are exceeded, or by requiring use of a preprinted height/weight/body surface area chart for ordering chemotherapy.
- Include reminders and information about appropriate monitoring parameters in the order sets, protocols, and flow sheets.
- Eliminate the need for calculation through use of tables.
- Reduce the number of steps in processes.
- Alert staff members to look-alike/sound-alike medications, that is medications which have generic or trade names that look alike when written or sound alike when spoken.

Nursing Practice Precautions

- Inform patients and, with their permission, their family members about their medications. A well-informed patient serves as a final safety check. Encourage patients to question changes in the medications they receive.
- Question any medication order which seems to require an unusual volume, number of tablets, syringe size, or other deviation from usual amounts.
- Monitor patients closely, including vital signs, neuro checks and relevant lab results.
- Heed alarms on automatic medication dispensing cabinets, pumps, or other devices equipped with alarms. Resist the temptation to work around or bypass alerts.
- If using bar-code technology, always scan medications at the patient’s bedside.
- Assure that reversal agents and resuscitation equipment are readily available.
- Call the rapid response team at the first indication of a serious adverse drug event.
Root Causes of Sentinel Events

What are the top 5 root causes of sentinel events involving medication errors or medication delivery equipment?

Medication Error Events
1. Human Factors
2. Physical Environment
3. Leadership
4. Communication
5. Assessment

Medical Equipment-related Events (including but not limited to IV pumps)
1. Medication Use
2. Leadership
3. Communication
4. Human Factors
5. Assessment

(TJC, 2011c)

Usually multiple root causes contribute to a single sentinel event. Nurses can have a direct impact on three of the 5 root causes frequently identified in medication-related sentinel events: human factors, communication, and assessment.

Additional Nursing Practice Precautions
- Institute independent double-checks prior to administering selected high-alert medications. Double-check the infusion pump setting against the order before beginning the infusion and every time you change the rate or replace a bag or cassette.
- Match high-alert medication orders to the patient’s diagnosis, the medication’s indication, and vital patient information to confirm that the medication and dose are appropriate.
- Limit verbal orders to true emergencies. Never take verbal orders for chemotherapy medications. Write the order in the patient’s record and then read back to the prescriber: patient name, order as written, spelling of the medication (Cohen, 2007).
- Keep informed with resources such as Nurse Advise-ERR and ISMP Medication Safety Alert! You can subscribe to these newsletters at http://www.ismp.org.

Independent double-check
- Verify medication, dose, and programming with most recent order.
- Document according to policy.
- Policy should reserve double-checks for a limited number of high-alert medications. Too much double-checking can increase frustration, decrease efficiency, and lead to complacency and work-arounds (Cohen, 2007).
**Anticoagulants**

TJC has established and continues to update a National Patient Safety Goal specific to improving safe administration of anticoagulants (TJC, 2011d).

The most commonly used anticoagulants are also the ones most frequently cited in error reports: unfractionated heparin, warfarin, and enoxaparin, a low molecular weight heparin (LMWH). The entire classification of anti-thrombotic medications is considered high-alert, including:

- Direct thrombin inhibitors such as argatroban and lepirudin.
- Factor Xa inhibitors, such as fondaparinux (Arixtra®).
- Glycoprotein IIb-IIIa inhibitors, such as abciximab (ReoPro®).
- Thrombolytics, such as alteplase (Activase®).

Concurrent use of heparin and enoxaparin with argatroban and lepirudin has led to errors.

**General guidelines for safe anticoagulant therapy include:**

- Improving staff communication and access to information.
- Implementing close pharmacy oversight and involvement, such as a pharmacist-managed anticoagulation service.
- Enhancing patient education.
- Managing anticoagulant therapy with a multidisciplinary team.
- Using evidence-based protocols and best practices.

**TJC Recommendations for Anticoagulant Safety**

TJC NPSG require that healthcare organizations:

- Use only oral unit-dose, prefilled syringes and pre-mixed IV preparations. For children, use only products specifically designed for children.
- Use approved protocols for initiation and maintenance of anticoagulation therapy.
- Assess baseline coagulation status before beginning therapy. For warfarin, include INR in the assessment.
- Document baseline status and current INR in the medical record.
- Address baseline and ongoing laboratory tests required in a written policy.
- Manage potential medication and food interactions with warfarin using authoritative sources.
- Use programmable infusion pumps to administer IV heparin.
- Educate providers, staff, patient, and family regarding anticoagulant therapy.
- Provide patient and family education that includes:
  - The importance of follow-up monitoring
  - Compliance
  - Drug-food interactions
  - The potential for adverse drug reactions and interactions
  - Measure and improve anticoagulation safety and effectiveness

(TJC, 2011d)
Institute for Healthcare Improvements (IHI) Recommendations

IHI recommendations:

- Calculation and dosing errors, due to errors in calculating the dose based upon the patient’s weight in kilograms
- Use Guidelines or Pre-Printed Orders for Vitamin K
- Implement Weight-Based Heparin Protocols
- Use Programmable Pumps and Independent Double-Checks for IV Anticoagulants
- Develop a Warfarin Dosing Service or Clinic
- Use Alarm Devices to Ensure Consistent Anticoagulant Dosing
- Use Pre-Mixed Heparin Solutions
- Provide Coagulation Test Results Within Two Hours or at Bedside
- Use Dosing Charts for Heparin
- Prepare All Heparin Doses and Solutions in the Hospital Pharmacy
- Continue to Use Anticoagulation Flowsheets after Discharge
- Implement Patient-Directed Administration of Warfarin
- Educate Patients to Manage Warfarin Therapy at Home
- Develop Weekly Dosing Regimens for Anticoagulants
- Titrate Anticoagulant Doses
- Eliminate Heparin Flush of Peripheral Intravenous Lines
- Standardize International Normalized Ratio Testing Equipment
- Adjust Anticoagulants with Thrombolytics and G2b/3A Inhibitors
- Use Anticoagulation Flowsheets
- Use Low Molecular Weight Heparin (LMWH)
- Eliminate the Use of Heparin Solution with Arterial Lines
- Allow Pharmacists to Manage an Anticoagulant Service

http://www.ihi.org/

Look-alike/Sound-alike Issues:

Heparin may be confused with Hespan®

Heparin: Most Common Errors

- Calculation and dosing errors, due to errors in calculating the dose based upon the patient’s weight in kilograms.
- Vials of insulin and heparin have been stored in close proximity and mistaken for one another.
- Infusion pump programming errors, such as setting a bolus rate and neglecting to reset the pump for a continuous infusion rate.
- Heparin lock flush solution is sometimes mistakenly used for heparin therapy.
- Patients who have heparin-induced thrombocytopenia (HIT) have received heparin, leading to serious consequences.
Heparin and LMWH are commonly administered to prevent and to treat DVT. Because of common usage, some staff occasionally fail to check orders and labels carefully.

Abbreviations:
- “U” for units has been mistaken for a zero, leading to a ten-fold overdose.
- “cc” (cubic centimeter) has led to overdoses when mistaken for zeros.

**Heparin: TJC Recommendations**

- Require prescribers to include the calculated dose and the dose per weight in milligrams per kilogram or body surface area. Since heparin is ordered in units, the order should state the units per kilogram required. This facilitates an independent double-check of the calculation. For morbidly obese patients, the standard nomograms may not be accurate.
- Consolidate and limit the number of institutional unfractionated heparin dosing nomograms. Before the start of a heparin infusion and with each change of the container or rate of infusion, require an independent double-check of the medication, concentration, dose calculation, rate of infusion, pump settings, line attachment and patient identity.
- Use heparin flush only for central lines, and eliminate heparin flush of peripheral intravenous lines. Stock and use only pre-filled syringes commercially prepared at set unit doses for flush solutions.
- Identify patients who have heparin-induced thrombocytopenia (HIT) to avoid life-threatening events from heparin exposure.
- TJC recommends dispensing only preservative-free heparin to neonates and build an alert to pharmacists with this directive into order entry systems.
- Write out the word units and use mL rather than cc. ISMP and the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) advise this as well.

**Look-alike/Sound-alike Issues:**

* Lovenox® may be confused with Lasix®, Levaquin®, Lotronex®, Protonix®

**LMWH Risks**

Low molecular weight heparins (LMWH):
- Peak in 3 – 5 hours
- Remain effective for 12 hours
- Have a half-life elimination 2 – 3 times longer than heparin

Serious adverse effects have occurred when heparin was administered to patients who still had active enoxaparin (Lovenox®) in their systems.

**Enoxaparin is measured in milligrams. Milligrams of enoxaparin are not equivalent to units of unfractionated heparin. Other LMWH medications, dalteparin and tanzaparin are measured in international units. LMWH units are not interchangeable with units of heparin. Not all LMWH units are interchangeable.**

The effects of LMWH are not evident in aPTT (activated Partial Thromboplastin Time) since LMWH acts differently than heparin. LMWH strongly inhibits clotting factor Xa and has only a small effect on aPTT.

LMWH is to be administered only via deep subcutaneous injection.
Administering Heparin

- Assure that protamine sulfate, the antidote for heparin, is available.
- Assure that heparin protocols, policy, and procedure are standardized and clear.
- Do not stock heparin on the unit.
- Initially assess: height, weight, allergies, diagnosis, and indication for heparin.
- Assure that orders are complete and conform to organizational policy.
- Base the dose on a recent and accurate body weight.
- Assure that the patient is not receiving medications that affect blood clotting or the action of heparin, such as LMW heparin.
- Always use an infusion pump for IV administration.
- Use independent double-checks to assure accuracy of both dosage calculation and pump programming. Double-check patient identifiers, medication, concentration, rate, channel selection, and line attachment.
- Label the distal end of the heparin line.
- When a bolus is ordered, administer from a vial and not by adjusting the IV rate.
- When withdrawing blood from a heparinized central line in an adult, withdraw and discard at least 10 mL of blood before obtaining a sample for clotting studies.
- Before adjusting doses on a sliding scale, assure accuracy of the latest aPTT. If the result deviates greatly from previous results without explanation, an error may exist due to timing of the draw or other issues.
- Require bold labeling of the medical record when a patient receives heparin off the nursing unit – such as in the cardiac catheterization lab.

Adding Heparin to an IV

Do NOT add heparin to a container of IV fluid that is hanging. Doing so may result in 97% of the medication being infused in only 1/3 of the solution.

After removing the container and adding the heparin, agitate the container repeatedly to assure that the medication is thoroughly dispersed (Hadaway, 2000).

Safe Storage of Heparin

Errors have resulted when insulin and heparin were stored in close proximity and one was mistaken for the other. Heparin flush solutions and therapeutic doses of heparin should be stored separately. Limiting the number of heparin concentrations is recommended.

Monitoring Heparin Therapy

- Assure that aPTT blood draws occur at the appropriate times, 4 – 6 hours after initial dose or dose change. Usual therapeutic range is 1.5 – 2.5.
- Monitor aPTT and platelets throughout heparin therapy.
  - Monitor aPTT to evaluate/adjust therapy.
  - Monitor platelets to identify heparin-induced thrombocytopenia (HIT).
- Monitor for obvious bleeding and for subtle signs of bleeding, including shortness of breath, headache, decrease in blood pressure, weakness, and dizziness.
• Report to the provider:
  • Signs of bleeding.
  • Gross hematuria.
  • Hematoma formation or extension.
  • Excessive bleeding or oozing at incision or IV site.
  • Hemoglobin decrease of > 2 grams per deciliter (g/dL) or total hemoglobin of < 8 g/dL.
  • Platelets less than 100,000/mm$^3$, a decrease of 50,000/mm$^3$, or a decrease of 50% of baseline. These findings indicate HIT.

**Heparin Flush**

Numerous medications and categories of medications are incompatible with heparin, including:

- Aminoglycosides
- Ampicillin
- Antiemetics
- Antineoplastic agents
- Several cephalosporins
- Ciprofloxacin
- Steroids
- Vancomycin

When these drugs are administered via an IV catheter, the SASH (saline, administer, saline, heparin) method is recommended:

- Flush saline through the catheter
- Administer the medication
- Flush with saline again
- Flush heparin into the line

The saline flushes prevent possible precipitation and occlusion of the catheter (Hadaway, 2000).

**Warfarin: Most Common Drug Interactions**

More than 150 medications and numerous other substances, including many over-the-counter medications and food substances are known to interact with warfarin (Coumadin®). The most commonly reported interactions involve:

- Acetaminophen (Tylenol®).
- Aspirin.
- Cimetadine (Tagamet®, Pepcid®).
- Ciprofloxacin/levofloxacin (Cipro®).
- Erythromycin/clarithromycin (Biaxin®).
- Fluconazole (Diflucan®).
- Levothyroxine (Synthroid®).
- Metronidazole (Flagyl®).
- Nonsteroidal anti-inflammatory drugs (NSAIDs), such as celecoxib (Celebrex®) and naproxen

Material protected by copyright
(Naprosyn®). (These medications also increase risk of GI irritation).

- Sulfamethoxazole/trimethoprim (Bactrim®, Septra®).

All of these medications potentiate warfarin, creating increased bleeding tendency.

**Warfarin: Additional Drug Interactions**

Additional medications that increase the anticoagulation effects of warfarin include:

- Allopurinol (Zyloprim®)
- Influenza vaccine
- Isoniazid (INH®)
- Phenytoin (Dilantin®) – may increase or decrease effect
- Propranolol (Inderal®)
- Ranitidine (Zantac®)
- Selective Seratonin Reuptake Inhibitors (SSRIs), such as fluoxetine (Prozac®), sertraline (Zoloft®), and paroxetine (Paxil®)

**Medications that decrease the anticoagulation effects include:**

- Aluminum Hydroxide (AlternaGEL®) – by causing decreased absorption
- Barbiturates, such as sodium amobarbital (Amytal®), secobarbital (Seconal®), phenobarbital (Luminal®), pentobarbital (Nembutal®), and secobarbital sodium and amobarbital sodium (Tuinal®)
- Carbamazepine (Tegretol®)
- Estrogens (Premarin®)
- Phenytoin (Dilantin®) – may increase or decrease effect

Activated Partial Thromboplastin Time (aPTT), a blood test which is used to monitor heparin therapy is increased by warfarin. This is a test interaction. However aPTT is NOT used to monitor warfarin therapy.

**Warfarin: Interactions With Other Substances**

- **Vitamins.** Vitamin K is the antidote for warfarin. Vitamin E increases the effect of warfarin. The patient who takes warfarin should maintain a consistent intake of vitamins K and E.
- **Ethanol.** Acute alcohol ingestion decreases metabolism of warfarin which increases the effect of the medication. Chronic daily alcohol use increases the metabolism of warfarin which decreases the effect of the medication.
- **Herbs and Nutraceuticals.**
  - Decreased response to warfarin – St. John’s wort, Coenzyme Q10, alfalfa (large vitamin K content).
  - Increased response to warfarin – cat’s claw, dong quai, evening primrose, feverfew, red clover, horse chestnut, garlic, green tea, ginseng, and ginkgo.

There are many potential and somewhat unpredictable interactions with warfarin. Encourage patients
to notify their prescribers of changes in diet or medications. Alert patients particularly to the risks of bleeding with use of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs). Doses are adjusted regularly based on laboratory studies: INR and PT. Changes in these values as a result of interactions may indicate a need to adjust the dose of warfarin.

**Warfarin: Laboratory Monitoring**
Prothrombin time (PT) and International Normalized Ratio (INR) values are used to adjust warfarin doses.

INR is a standardized PT value generated from the PT ratio and the International Sensitivity Index (ISI).

Hemoglobin is also monitored to detect bleeding that is not otherwise evident.

- Normal PT = 10.9 – 12.9 seconds
- Therapeutic PT = 1.5 – 2 times the control
- Therapeutic INR = 2 – 3 depending upon the indication for anticoagulation

An increase in INR may be observed 36 – 72 hours after administration of warfarin.

A reduced initial dose in the range of 2.5 – 5 mg is recommended for patients aged 65 years and older, or patients who have co-morbidities which could affect response to warfarin, such as thyroid disease (Lacy, et al, 2010).

**TJC recommends that organizations consider reports of INRs greater than three and episodes of vitamin K administration as possible indicators of warfarin-associated adverse drug events and take immediate steps to address these events.**

**Look alike/Sound-alike Issues:**
- Coumadin® may be confused with Avandia®, Cardura®, Compazine®, Kemadrin®
- Jantoven® may be confused with Janumet®, Januvia®

**Warfarin: Assessment and Planning**
- Be alert for the affects of the patient’s disease condition, treatment, or changes in medications or diet during hospitalization. The elderly and patients who have congestive heart failure or liver disease experience more pronounced effects of warfarin. Events during hospitalization can greatly alter a patient’s response to warfarin.
- Assess carefully for evidence of bleeding – especially when the patient’s condition may produce bleeding, such as peptic ulcer disease, cancer, and other conditions that produce a heightened risk for internal bleeding.
- Assure that warfarin is discontinued in advance of invasive procedures. Call this need to the attention of the provider when the patient is receiving warfarin. Depending upon the patient’s situation, discontinuation of warfarin may be recommended from 3 – 5 days in advance of an invasive procedure.
- When warfarin is initiated in active thrombosis usually heparin or LMW heparin is continued for 4 days and until the INR is therapeutic for 2 days.
- Any change in medication profile or food intake (including NPO) may affect the patient’s response
to warfarin and may require an adjustment of the dose.

- INR should be measured at the time a change is initiated and a few days later, since interaction effects may not develop immediately.
- The onset of anticoagulation effects occurs 36 – 72 hours after administration and full therapeutic effect is evident in 5 – 7 days.

TJC recommends that warfarin NOT be discontinued according to automatic stop policies without verifying the medication’s indication and contacting the prescriber.

Test Yourself:
Which is the correct pairing of medication and lab test used to monitor therapy?
A. Warfarin – aPTT  
B. Warfarin – INR - Correct  
C. Heparin – PT  
D. Heparin – INR

Administering Warfarin
- Assure that the warfarin antidote, vitamin K (phytonadione®) is available.
- Maintain consistency:
  - Administer warfarin at the same time each day.
  - Do NOT administer warfarin with food.
  - Administer warfarin at a separate time from other medications. Other medications may decrease absorption of warfarin.
- Administer warfarin 1 – 2 hours before or 6 hours after cholestyramine or sucralfate, because these medications bind warfarin.
- Avoid intramuscular injections.
- Verify the strength of tablets – tablets of different strength may look alike.
- Inform the patient of the INR result and warfarin dose before administering warfarin.
- Be especially cautious in creating a safe environment, since minor injuries can lead to bleeding and bruising.

Test Yourself:
What is the antidote for warfarin?
Answer: Vitamin K
Warfarin: Patient Teaching

Advise the patient to:

- Consult his provider for any indications of bleeding, severe diarrhea (which alters vitamin K absorption), and in advance of any dental or surgical procedures.
  - Warfarin is usually discontinued 3 days prior to intrusive procedures. In some situations, 4 – 5 days in advance of a procedure may be recommended.
- Be alert for subtle signs of bleeding, such as:
  - Dark tarry stools
  - Dizziness
  - Weakness
  - Shortness of breath
  - Decreased urine output
  - Headache
  - Mental status changes
- Adhere to prescribed doses. And, if a dose is missed, simply resume the next dose, rather than "making it up."
- Take warfarin at the same time each day.
- Adhere to the schedule for PT, INR testing.
- Maintain a consistent diet, particularly vitamin K intake.
- Maintain a safe environment to decrease the risk for falls and other injuries.
- Wear a MedicAlert ID bracelet or necklace.

Test Yourself:

Which symptom is a possible indicator of bleeding?

A. Clay-colored stools
B. Shortness of breath - Correct
C. Increased urinary output
D. Diaphoresis

Keep Abreast of Safety Alerts

The FDA, ISMP, and other safety-oriented organizations periodically release important safety alerts. Safety alerts often involve high-alert medications. For example, at the FDA’s request, the maker of warfarin (Coumadin®) added a black-box warning to the label.

The previous label included risk of bleeding. The strengthened black-box warning states that warfarin can cause major or fatal bleeding and cautions that:

- Bleeding is more likely to occur during the starting period and with a higher dose (resulting in a higher INR).
- Risk factors include: high intensity of anticoagulation (INR greater than 4.0), age 65 or over, highly variable INRs, history of gastrointestinal bleeding, hypertension, cerebrovascular disease, serious heart disease, anemia, malignancy, trauma, renal insufficiency, concomitant medications, and long duration of warfarin therapy.

The black box contains specific recommendations regarding INR monitoring.
FDA regulations require that patient medication guides be distributed with each prescription that is dispensed for products that the FDA has determined pose a serious and significant public health risk (Hughes, 2006).

**Digoxin**

Digoxin (Lanoxin®) has an extremely narrow therapeutic index. Therapeutic dose is highly individualized. The desired therapeutic dose is difficult to ascertain by serum levels alone. The clinical picture is also significant in establishing a patient’s therapeutic dose.

Because the therapeutic dose may be difficult to establish and because digoxin toxicity may be life-threatening, careful monitoring of serum levels, electrolyte levels, and clinical symptoms is of great importance.

In addition to the look-alike/sound-alike issues associated with digoxin, patients who travel internationally or procure medications from sources outside the U.S. must be vigilant. There is no worldwide oversight of brand names of medications. A given brand name may be associated with a different medication from one country to another. For example, Dilacor® is a brand name for diltiazem in the U.S., digoxin in Serbia, barnidipine in Argentina, and verapamil in Brazil. Lanoxin® may be confused with Lemoxin®, the brand name for cefuroxime in Mexico, or Limoxin®, the brand name for amoxicillin in Mexico. (Lacy, et al, 2010, p. 443).

**Look-alike/Sound-alike**

- Digoxin may be confused with Desoxyn®, doxepin
- Lanoxin® may be confused with Lasix®, levothyroxine, Levoxyl®, Levsinex®, Lomotil®, Lonox®, Mefoxin®, naloxone, Xanax®.

**Digoxin in Wide Use**

Digoxin is widely prescribed and used by more than one million people in the U.S. Indications include:

- Congestive Heart Failure (CHF)
- Atrial Fibrillation and Atrial Flutter
- Sinus Tachycardia
- Paroxysmal Supraventricular Tachycardia (PSVT)
- Myocardial Infarction (MI), though use is controversial due to the increased O2 demand to support strengthened cardiac function
- Occasional use in Cardiogenic Shock and Angina Pectoris
- Prophylaxis to prevent arrhythmia in persons who have heart disease and experience stressors such as serious illness, surgery, or pregnancy

In 2008, the Digitek® brand of digoxin was packaged and distributed in double the labeled strength. More than 1,000 patient deaths resulted (ISMP, 2009).
A Digoxin Error
A provider ordered 0.0625 mg IV daily for a patient. The pharmacist dispensed an ampoule containing 0.5 mg with instructions on the outer plastic bag to administer 0.25 mL. The nurse mistook the prescribed dose for 0.625 mg, administered the entire ampoule, and called the pharmacy for a second ampoule to administer the additional 0.125 mg.

The pharmacist went to the unit, clarified the error with the nurse and explained the additional monitoring that the patient would require. The nurse was comfortable reporting the error to the patient’s provider, but did not report it to the charge nurse or per organizational policy.

The patient, who had already been on telemetry showed no signs of digoxin toxicity over the next several days.

The lack of error reporting deprived team members of the opportunity to learn from this error, and identify and implement safeguards (ISMP, 2006).

Digoxin Toxicity
Because digoxin toxicity can be lethal, it is important to recognize early warning signs: anorexia, nausea, vomiting, and diarrhea. Other manifestations of digoxin toxicity include life-threatening ventricular arrhythmias, progressive bradycardia, 2nd- or 3rd-degree heart block unresponsive to atropine, serum potassium greater than 5 mEq/L.

Patients who have severe, acute toxicity exhibit hyperkalemia, whereas patients who have chronic toxicity exhibit hypokalemia or normokalemia.

Dehydration, hypokalemia, and hypomagnesemia increase the risk of toxicity. Patients who also take diuretics, often prescribed concurrently with digoxin, are at increased risk for toxicity. Hypercalcemia increases the risk of toxicity. Fluid and electrolyte imbalances may lead to toxicity even when serum levels of digoxin are within therapeutic limits.

Digoxin Immune Fab (Digibind®) is the antidote for digoxin and is used to treat severe, acute toxicity.

Adverse Effects of Digoxin
Additional adverse effects include:

- Allergic reaction, including laryngeal edema
- Arrhythmia
- Confusion, hallucinations, unusual thoughts or behavior
- Dizziness or lightheadedness
- Drowsiness
- Gynecomastia
- Headache
- Rash
- Vision changes (blurred or yellow)
**Digoxin: Monitoring in the Acute Care Setting**

Monitoring is of utmost importance for patient safety – especially when the patient is undergoing initial digitalization or stabilization on a new dose. However, even for the patient who may have a long history of effective digoxin therapy, the additional stress of illness or surgery and addition of medications that potentially interact with digoxin places the patient at risk for toxicity or subtherapeutic dosage.

With the patient who is receiving digoxin, monitor:

- Heart rate and rhythm.
- Apical pulse for one full minute before administering. Hold digoxin for heart rate less than 60 beats per minute, or as ordered or required by organizational policy.
- For clinical signs of toxicity and for signs of exacerbation of the condition for which digoxin is prescribed.
- Serum electrolytes with special attention to potassium, magnesium, and calcium.
- Serum creatinine. Because digoxin is excreted in the urine 50-70% unchanged, patients with compromised kidney function are at risk for digoxin toxicity (Lacy, et al, 2010, p. 444).
- Serum concentrations of digoxin must be closely monitored during stabilization and during illness or additional medications that potentially interact with digoxin. Levels should be drawn 6 – 8 hours after last dose, regardless of route of administration, optimally 12 - 24 hours after a dose. Serum concentrations decrease in response to exercise, therefore a rest is recommended 2 hours before the blood draw.

**Digoxin: Precautions in the Acute Care Setting**

If a digitalized patient is receiving IV calcium salts, rapid administration may create a risk of serious arrhythmias.

For IV administration, digoxin injection may be diluted (4-fold or more) with normal saline, dextrose 5% in water, or sterile water for injection. Infuse slowly, 5 min or longer.

IM injection can lead to severe pain at the injection site. If the medication must be administered IM, inject it deeply into the muscle and follow with massage. Do not inject more than 2 mL into a single site (Drugs.com, 2011a).

When switching from the oral to the IV or IM route, a reduction in dose of 20-25% is recommended.

Digoxin is on the list of Medications Potentially Inappropriate for Elderly Patients (RN.com, 2009). The maximum safe dose recommended for elderly persons is 0.125 mg daily.

**Patient Teaching: Taking Digoxin**

Thorough patient teaching is essential to protect patient safety. Most patients receive digoxin on a long-term basis and so are at risk for toxicity or subtherapeutic dosing.

Advise the patient about how to take digoxin:

- If you miss a dose, do not double dose. Skip the dose if the next dose is due in less than 12 hours. If the next dose is due in more than 12 hours, take the dose as soon as remembered.
- Take your digoxin regularly even when you are feeling well.
• Maintain adequate hydration. Toxicity is more likely when dehydrated. This is especially important if you are also taking diuretic medications.
• Maintain a supply of the medication so that you do not run out and miss a dose.
• Antacids delay absorption.
• It is best to take digoxin without food. Peak concentration is reduced if taken with food. Meals containing increased fiber or foods high in pectin may decrease absorption. Maintain adequate potassium in diet.
• Ephedra creates a risk of cardiac stimulation; natural licorice causes sodium and water retention and increases potassium loss.


Because digoxin and other medications also are known by different trade names in countries outside the U.S., ISMP recommends that patients who are traveling abroad carry an adequate supply of their medications along with a list of the medications they are taking by both generic and brand name, so that they will be able to confirm that the correct medication has been dispensed if they require a prescription refill.

Patient-Provider Communication Related to Digoxin
Advise the patient about communicating with the provider who prescribes digoxin:
• Follow your provider’s advice concerning laboratory tests. Serum electrolytes, serum levels of digoxin, and serum creatinine should be monitored at intervals and especially at times when:
  • Digoxin has not been taken as prescribed for whatever reason
  • Cardiac symptoms recur despite an initial positive response to digoxin
  • Symptoms of toxicity are experienced
• Keep your provider informed of your use of all medications, including over-the-counter medications, and nutritional supplements such as herbal products and vitamins. MANY medications interact with digoxin, particularly amiodarone, quinidine, and verapamil.
• Assure that the provider who prescribes your digoxin is aware of any newly identified medical conditions, especially thyroid disease.
• If you are pregnant, or think you may be pregnant, notify your provider immediately, digoxin is classified as FDA pregnancy category C, indicating a risk to the fetus.

(Drugs.com, 2011a; Lacy et al., 2010; Mayo Clinic, 2011a; MedlinePlus, 2010a)

Provide written instructions to the patient, including food sources of potassium.

Electrolytes
For all electrolytes:
• Check serum electrolyte values regularly for any patient who is receiving electrolyte replacement or experiencing loss of electrolytes, due to vomiting, nasogastric drainage, or diarrhea.
• Pay careful attention to route – especially to distinguish between IV infusion, IV piggyback, and IV push.
• Pay careful attention to dosage. Clarify any confusion re: milligrams (mg) and millequivalent
• Verify both the electrolyte dosage and amount and composition of diluents.
• Use an IV infusion pump. Adhere to maximum hourly dosage limits. Double-check programming of the pump.
• Monitor for the symptoms of hyper-and hypo-states of electrolytes. Remember that imbalance of one electrolyte may affect another. Serious imbalances can develop quickly.
• Electrolytes are administered as salts – a combination of two electrolytes – which creates a potential for imbalance of two electrolytes. The order must name a salt and not only an electrolyte, such as “sodium phosphate” rather than “phosphate.” “Phosphate” could mean either sodium phosphate or potassium phosphate.
• If you find an unexplained difference comparing latest serum electrolyte results with previous results, it may be advisable to repeat the test before taking action.

Look-alike/Sound-alike Issues:
The salts of the electrolytes are a look-alike/sound-alike issue peculiar to the electrolytes. Assure that you accurately identify the salt which has been ordered – both in the order and when preparing the medication.

Test Yourself:
Which lab value is especially important to monitor when the patient is receiving diuretics?
A. Serum albumin
B. Total cholesterol
C. Serum electrolytes — Correct!
D. Serum glucose

Calcium: Administration
• Clarify any order that fails to specify the calcium salt.
• Orders should specify the dose in mEq, and NOT in amps or vials.
• Administer only orally or IV. Tissue sloughing and necrosis can result from IM or subcutaneous administration, or injection into a small vein. Severe necrosis and sloughing may result from improper administration.
• IV administration:
  • IV push at a rate of 0.7 mEq/min – 1.8 mEq/min, except in cardiac arrest. Cardiac arrhythmias, sinus bradycardia, and cardiac arrest may result from too rapid administration – especially if the patient is also receiving digoxin (Lanoxin®).
  • Do NOT infuse a calcium salt in the same IV line as solutions containing phosphate, such as TPN. Interactions between calcium and phosphorus can produce calcium phosphate which precipitates and injures organs.
• Calcium content of different calcium salts varies greatly. Calcium chloride is three times as potent as calcium gluconate (Lacy, et al, 2010).
Look-alike/Sound-alike Issues:

Distinguishing the correct salt is critical. Calcium carbonate may be confused with calcitriol; Florical® may be confused with Fiorinal®, Mylanta® may be confused with Mynatal®. Nephro-calci may be confused with Nephrocaps®. Remegel® (Great Britain, Ireland, Italy) may be confused with Renagel®, the trade name for sevelamer in the U.S.

Test Yourself:

Which routes are appropriate for administering calcium?

A. Oral and IV into a large vein - Correct
B. Oral and Subcut
C. Subcut and IM
D. IV and IM

Calcium: Monitoring

- If the patient who is receiving oral calcium has diarrhea, monitor calcium levels carefully as malabsorption may result.
- Assess serum phosphorus level. If elevated, calcium phosphate may form and precipitate into the vasculature causing organ injury.
- Assess serum albumin level. Low albumin levels cause calcium levels to appear falsely low. Direct measurement of ionized calcium, or estimate of total serum calcium using a formula is recommended (Lacy, et al, 2010).
- For the patient who is receiving a calcium channel blocker along with a preparation of calcium, assess blood pressure frequently. Calcium will antagonize the effect of the calcium channel blocker.
- Monitor for hypotension, dizziness, syncope, flushing, nausea, or vomiting.
- Assess the IV site frequently. Local irritation and necrosis can occur. Administer via a small needle into a large vein.

Magnesium

- Infuse IV at a maximum rate of 150mg/min and per organizational policy and procedure (Lacy et al., 2010; American Society of Health-System Pharmacists [AHSP], 2006b).
- Continuous IV infusion:
  - 2g/hr is the recommended maximum rate.
  - The usual dose in cardiac situations is a rate of 1 gram or less per hour.
  - For preeclampsia, 2-4 grams per hour can be administered by specially trained personnel (Lacy et al., 2010).
- Oral doses:
• Administer with a full glass of water.
• Oral magnesium can cause diarrhea.
• Oral magnesium salts interact with oral quinolone antibiotics and with tetracyclines, causing decreased absorption of these antibiotics. Allow one to three hours between doses of oral magnesium and doses of these medications, such as ciprofloxacin and doxycycline.

• Intramuscular doses:
  • Administer into a large muscle mass, preferably gluteal.
• Replacement of magnesium may take three to seven days.
• Monitor renal function.

Look-alike/Sound-alike Issues:
• MgSO4 is a “Do not use abbreviation” as is MS for morphine sulfate since those abbreviations may be mistaken for one another.
• Magnesium sulfate may be confused with manganese sulfate, morphine sulfate.

Potassium Chloride (KCl) IV Administration
ALWAYS FOLLOW YOUR ORGANIZATION’S POLICIES regarding specific parameters. The following guidelines are evidence-based recommendations.

• Always dilute KCl, never give a bolus or IV push. Your organization’s policy may limit the concentration on KCl in IV fluids to 60 mEq – 80 mEq per liter.
• Always use an infusion pump.
• Administer at a rate of no more than 10 mEq per hour peripherally; administer at a rate of no more than 20 mEq per hour via central line.*
• Administer IV riders of 40 mEq/100mL via central line as the concentration can cause vein irritation.*
• Do NOT inject KCl into a container on IV pole. Remove the container, inject the KCl, and agitate thoroughly to avoid a dangerously high concentration (Hadaway, 2000).
• Follow guidelines for recommended maximum concentrations of KCl:
  • 60 mEq/L – maintenance fluids
  • 20 mEq/100 mL or 40 mEq/250 mL – peripheral line
  • 40 mEq/100mL – central line
  • 20 – 60 mEq/24 hr as a usual dose, should not exceed 200mEq/24 hr

Look-alike/Sound-alike Issues:
  KCl may be confused with HCl; KaonCL10® may be confused with Kaolin; Klor-Con® may be confused with Klaron®; microK® may be confused with Macrobid®, Micronase®

Potassium Chloride (KCl) Oral Administration
Oral Administration:
• Oral products differ in their action. For example, K-Dur® tablets are long-acting, but K-Lor® powder is immediately absorbed for rapid effect.
• Administer oral preparations with a full glass of water to avoid gastric irritation.
• Do NOT crush PO tablets. Instruct the patient to swallow tablets whole, without chewing.
Always follow your organization’s policy and procedure regarding any medication administration.

**Potassium Chloride (KCl) Monitoring**

- Monitor laboratory values:
  - Renal function tests, impaired renal function requires a reduced dose.
  - Electrolyte levels for both potassium and magnesium:
    - Serum potassium levels every four hours. Desired level 3.5 mEq/L – 5 mEq/L.
    - Serum magnesium. Desired level 1.6 mg/dL – 2.5 mg/dL. Adequate magnesium levels are necessary to correct hypokalemia.
- Assess cardiac status. Monitoring may be indicated and is usually required per policy for patients who receive more than 10 mEq/hr.
- Assess IV site for infiltration and phlebitis, as KCl irritates the vein.
- Assess for signs and symptoms of elevated potassium.

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms of Elevated Potassium:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Bradycardia</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
</tr>
<tr>
<td>Diarrhea</td>
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<tr>
<td>Dysphagia</td>
</tr>
</tbody>
</table>

**Sodium Chloride (NaCl) 3% (Hypertonic Saline)**

Any NaCl solution of a concentration greater than 0.9% is hypertonic. TJC recommends that hypertonic saline (HTS) should not be available in patient care areas.

Acute head trauma patients sometimes receive intravenous (HTS) via continuous IV infusion to reduce cerebral edema. Use should be restricted to specific indications such as initial treatment of acute, serious, and symptomatic hyponatremia, or acute head trauma.

**Special precautions are required, because HTS:**

- Is incompatible with many medications that can be safely mixed with saline.
- Is incompatible with blood.
- In concentrations greater than 3% causes local vascular irritation and infiltration could harm tissues. When HTS infiltrates into the tissues, the high concentration of NaCl pulls more fluid and creates significant edema which can further harm tissues and cause necrosis.

**When administering HTS:**

- Monitor electrolyte levels and fluid status.
- Administer only via central line for concentrations greater than 2%.
- Always use an infusion pump.
- Monitor the rate carefully, recommended maximum = 1 mEq/kg/hr (Lacy et al., 2010).
- Dedicate the HTS line to HTS only and clearly label it (Mortimer & Jancik, 2006).
HTS Toxicity

Toxicity is directly related to both the rate and magnitude of change in serum sodium levels. Symptoms are primarily neurologic. Osmotic demyelination syndrome is a rare but dangerous adverse effect.

Insulin: A Problem-Prone MEDICATION

In addition to disease processes or surgical intervention, the stress of hospitalization, and changes in nutritional intake and physical activity all threaten glycemic control for the hospitalized patient.

Hypoglycemia is the most frequent complication of insulin therapy and is an extremely frequent adverse event in hospitals worldwide (5 Million Lives Campaign, 2008). Authorities recommend using standardized protocols for glycemic control (ASHP, 2006).

Errors with insulin most commonly result from:
- Improper monitoring
- Timing and assessment of blood glucose results
- Failure to adjust therapy in response to assessment findings

Frequently reported errors in administering insulin include:
- Wrong patient
- Wrong dose
- Wrong type
- Wrong route
- Improper timing
- Omission of dose

Look-alike/Sound-alike Issues

Because of the large number of insulin products and insulin combination products, vigilance is critical for patient safety. Double-checks help to assure identification of the correct insulin product. Examples include Humalog® mix 50/50 may be confused with Humalog® and Humulin® 50/50; Novolin® 70/30 may be confused with Novolog® Mix 70/30; Insulin glulisine may be confused with insulin glargine; Humalog® may be confused with Humalog® Mix 50/50; Humira®, Humulin®N, Humulin®R, Novolog®, Lantus® may be confused with latanoprost (Xalatan®).

High-Risk for Hypoglycemia

20% of hospitalized patients are at risk for problems related to glycemic control (American Society of Health-System Pharmacists, 2006a).
Insulin: A Case Situation

Your patient has two insulin orders:

- An order for the long-acting insulin ultralente (Humulin®) U 14 units subcut every evening at 1900, and
- An order for the rapid-acting insulin lispro (Humalog®) on a sliding scale depending upon blood glucose.

You have come on duty for the 1900 – 0700 shift. The patient’s daily insulin dose is charted as having been given on schedule and blood glucose has been within the desired range.

When you make rounds at 2000, you find the patient diaphoretic and unresponsive.

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin lispro (Humalog®)</td>
<td>0.25 hours</td>
<td>0.5 – 1.6 hr</td>
<td>6 – 8 hours</td>
</tr>
<tr>
<td>Extended insulin zinc suspension (Humulin ULtralente®)</td>
<td>4 – 8 hours</td>
<td>16 – 18 hrs</td>
<td>Greater than 36 hours</td>
</tr>
</tbody>
</table>

What will you do? What could have caused this situation?

You will follow the protocol for hypoglycemia rescue which will include obtaining a blood glucose, notifying the physician and administering glucagon or dextrose.

Further investigation will determine the cause of the hypoglycemic episode, but it is likely that Humalog® was administered rather than Humulin®. The similar names create a risk for error. Independent double-checks can prevent errors of this kind.

Insulin: Common But Complex

- Individuals differ in their responses to insulin.
- An individual may require more than one type of insulin.
- Many factors affect response to insulin, including activity, food intake, concurrent medications, illness, weight, type of diabetes, and other factors.
- Numerous insulin preparations are available. Know the onset, peak, duration, route, and time of administration (in relation to meals and bedtime) for the preparations in use in your organization:
  - Rapid-acting insulins, such as regular administered IV, lispro (Humalog®), aspart (Novolog®).
  - Short-acting insulins, such as regular administered subcutaneously and via subcutaneous pump.
  - Intermediate-acting insulins, such as lente, isophane insulin suspension, insulin zinc suspension.
  - Long-acting insulins, such as ultralente, insulin glargine, extended insulin zinc suspension.
  - Insulin combinations, such as isophane insulin suspension and regular insulin 70/30 and 50/50; lispro protamine suspension and lispro 75/25, and aspart protamine suspension and aspart 70/30.

Material protected by copyright
Insulin: Safety Practices

- Store insulin and heparin vials separately.
- Do NOT store insulin at the patient’s bedside.
- Give regular insulin ONLY when food or hypoglycemic rescue agents are available.
- Assure that a protocol is in place for hypoglycemic rescue and that agents such as glucagon and dextrose are available.
- Observe recommended abbreviations: units and mL.
- Know the symptoms of hypoglycemia and hyperglycemia. Know both early and late signs and symptoms.

(ASHP, 2006).

At Missouri Baptist Hospital in St. Louis, MO, clinical pharmacists receive alerts via pager or via a printer designated for hand delivery when certain indicators appear, such as:

- A patient’s blood glucose drops below 50 mg/dL
- An order is placed for a reversal agent
- A patient’s INR exceeds 5

(IHI, 2011a)

Insulin: Administration

- Double-check to assure the correct insulin, especially when the patient is receiving more than one type.
- Document time and result for blood glucose and any dose of insulin given.
- Perform independent double-checks on the vial and dose of insulin. Double-check patient identifiers, type, product, dose, and measured dose.
- Assure that insulin orders comply with policy, such as for pediatric insulin orders, include units/kg and the calculated dose for the child.
- Use ONLY insulin syringes.
- Before administering insulin, always inform the patient of the most recent blood glucose result and the type and dosage of insulin to be administered.
- Teach the patient the signs and symptoms of hypoglycemia and hyperglycemia. Instruct the patient to report symptoms.

(ASHP, 2006).

Routes of Administration for Insulin

IV – ONLY regular
Subcutaneous pump – lispro (Humalog®), aspart (Novolog®), regular Subcutaneous – all types

In the inpatient setting, a well-informed patient can serve as an additional protection against error.
**Insulin: IV Administration**

*Only regular insulin should be administered intravenously.* Other insulin preparations may be clear, but should not be administered IV. Regular insulin administered IV has an onset of 15 minutes and peaks in 15 – 30 minutes. Programming errors can have serious or lethal effects in a short period of time.

- Use the insulin line only for insulin.
- Clearly and boldly label the distal end of the line.
- Always use an infusion pump.
- Use preprinted guidelines for pump settings.
- Perform independent double-checks of the rate and pump programming. Double-check patient identifiers, type, product, and dose.
- Discontinue the infusion according to policy and protocol, such as:
  - Check blood glucose levels one hour prior to discontinuing.
  - Administer the first dose of subcutaneous insulin as ordered. Short-acting insulins, 1 – 2 hours prior, long-acting insulins, 2 – 3 hours prior.
  - Continue the infusion for 30 – 60 minutes after the subcutaneous injection to prevent rebound hyperglycemia.
  - After discontinuing the infusion, check blood glucose levels before meals and at bedtime. (ASHP, 2006).

**Insulin: Monitoring**

- Upon admission, completely assess insulin use:
  - Type
  - Time of administration
  - Sites used
  - Eating habits
  - Blood glucose pattern
  - Symptoms of hypo- or hyperglycemia that the patient has experienced
- Monitor blood glucose carefully and respond promptly to results.
- Assure that blood draws for blood glucose are NOT taken at an IV site through which glucose is running.
- Be aware that errors in capillary blood glucose per glucometer will result from dehydration, shock, increased hematocrit, hypoxia, hyperbilirubinemia, and severe hyperlipemia.
- Comply with organizational policy re: length of time between blood glucose result and administration of insulin. After that time elapses, another blood glucose result must be obtained before administering a result-based dose of insulin.
- Be alert for any circumstances that will cause insulin requirements to vary, such as NPO, infection, change in activity, steroid medications, TPN, or other circumstances that affect metabolism.
- Include nutritional status and food consumption in ongoing assessments. (ASHP, 2006)
<table>
<thead>
<tr>
<th>Symptoms of Hyperglycemia</th>
<th>Symptoms of Hypoglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restlessness</td>
<td>Headaches</td>
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<tr>
<td>Thirst</td>
<td>Hunger</td>
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<tr>
<td>Vomiting</td>
<td>Faintness</td>
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<tr>
<td>Abdominal Pain</td>
<td>Clammy skin</td>
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<tr>
<td>Hot, dry, flushed skin</td>
<td>Sweating</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>Slurred speech</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Tachy/bradycardia</td>
</tr>
<tr>
<td>Deep sighing (Kussmaul) respiration</td>
<td>Agitation and confusion</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Coma</td>
</tr>
<tr>
<td>Coma</td>
<td></td>
</tr>
</tbody>
</table>


**Narcotics and Sedatives: IHI Recommendations**

Overdoses of narcotics and sedatives cause respiratory depression which can lead to respiratory arrest. Even therapeutic doses may produce disorientation, hypotension, and unsteadiness which create risk of injury. The IHI recommends the following actions to improve safety in administering narcotics and sedatives.

- Use Pre-Printed Orders with Patient-Controlled Analgesia Pumps
- Consider Non-Pharmacological Interventions for Pain and Anxiety
- Eliminate Use of Meperidine
- Use Protocols for Prescribing Narcotics and Sedatives
- Verify Intravenous and Epidural Solution and Flow Rate at Every Shift Change
- Implement a Pain Management Team
- Use Pre-Printed Orders for Narcotics and Sedatives
- Use Only One Model of Pump for Administering Narcotics and Sedatives
- Use Pre-Made Dosing Charts with Narcotics and Sedatives
- Use Programmable Pumps and Independent Double-Checks

**Look-alike/Sound-alike Issues:**

Look-alike/Sound-alike issues are prominent with narcotics, which differ greatly have names that are very similar, for example hydrocodone [Vicodin® (hydrocodone 5 mg, acetaminophen 500 mg), Norco® (hydrocodone 10 mg, acetaminophen 325 mg), oxycodone (Oxycontin®), hydromorphone (Dilaudid®), and morphine. Equianalgesic charts indicate that is 3 – 4 times stronger than oxycodone, 4 – 10 times stronger than hydrocodone, and 10 times stronger than morphine. Tall man lettering is recommended to clarify, for example, HYDROMorphone, oxyCODONE (to distinguish from oxymorphone).

Refresh your knowledge about pain management, addiction, tolerance, and dependence. Many people have experienced pain unnecessarily because of misunderstandings.
A Narcotic-Related Sentinel Event

At Fairview Hospital in Minneapolis, MN, a 19-year-old post-surgical patient died of respiratory depression apparently caused by an overdose of morphine. The RN involved followed policy and procedure and even questioned and administered less than the ordered dose of IV push morphine 4 to 8 mg every 15 minutes – 2 hours PRN.

The RN recorded vital signs per policy; however, pain and sedation scores were not required for IV push narcotics. Pain and sedation scores were required for PCA or continuous narcotics infusions. The organization’s med-surg units had just started administering IV push narcotics. Previously, only critical care areas had administered IV push narcotics.

Over 6 hours, the RN administered a total of 32 mg of IV morphine. After the last dose, the patient was sleeping soundly and snoring lightly.

Forty-five minutes later, the nursing assistant found the patient unresponsive and cyanotic. While the patient’s parents looked on in horror the code team responded, but were not successful in resuscitating her.

The hospital supported the RN involved and her license was not affected.

Triggered by this event, Fairview Health Services instituted an interdisciplinary review and plan which has led to a dramatic reduction in narcotic-related adverse events (Meisel & Meisel, 2007).

Narcotics: Planning Safety Improvements

In response to the sentinel event at Fairview Hospital, a quality improvement team was formed. Members included nurses from the surgical unit and postanesthesia care unit (PACU), pharmacists, a house physician, anesthesiologists, respiratory therapists, a clinical nurse specialist, and a member of the clinical quality department.

The group created a flowchart to identify times during the surgical process – from OR to surgical floor – when the processes were unclear and errors could occur. The flowchart demonstrated the interdependence between the OR, PACU, and surgical unit, and how actions early in the surgical process could impact patient outcomes later in the process.

The group measured progress by reviewing all instances when a patient required naloxone to reverse respiratory sedation, and classified the severity of oversedation on a Naloxone Harm Rating Classification Scale of 0 – 4.

The organization established a pain management team and made policy and protocol changes for the OR, PACU, and surgical unit in:

- Patient assessment and monitoring,
- Individualization of therapy, and
- Communication

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Narcotics: Implementing Safety Improvements

Throughout the 7-hospital system of which Fairview was a part, leaders implemented a number of specific initiatives to improve staff and provider knowledge and critical thinking skills, documentation, sedation, and pain assessment and communication skills.

They simplified and standardized medication selection and protocols, for example pharmacists repackage hydromorphone into 0.2 mg, the usual dosage.

The postoperative documentation now includes areas to chart a patient's pain and sedation level, and respiratory rate, depth, and quality—regardless of the route of the narcotic. A thorough pain assessment should always be documented, including cause, location, and intensity of pain.

Postoperative pain orders list recommended dose ranges for IV narcotics, and prescribers are contacted when narcotics are ordered in unusually high doses. Over the six-year period following the sentinel event, the health system has consistently and dramatically reduced serious narcotic oversedation incidents.

Look-alike/Sound-alike Issues

- Dilaudid® may be confused with Demerol®, Dilantin®
- Fentanyl may be confused with alfentanil, sufentanil. Tall man lettering is recommended to clarify, fentaNYL.

Narcotics and Sedatives: Complete Assessment

- Check allergies before initiating narcotic or sedative therapy.
- Assess for factors that increase risk of respiratory depression: obesity, underweight, asthma, sleep apnea.
- Monitor carefully during the first 24 hours and at night — hypoxia occurs most frequently during these times.
- Do NOT rely on pulse oximetry as an indicator of adequate respirations. Oxygen saturation is usually maintained at a low respiratory rate.
- Assess with minimal stimulation. Stimulating the patient can cause increased respiratory rate and lead to a misleading assessment of sedation level.
- Even at appropriate doses respiratory rate, heart rate, and blood pressure may be suppressed, every four hours assess:
  - Heart rate and blood pressure
  - Sedation level
    - S – Sleeping: Normal sleep, respiratory rate more than 8 per minute
    - 0 – None: Alert, awake
    - 1 – Mild: Responds to normal voice
    - 2 – Moderate: Responds to loud voice/shaking
    - 3 – Severe: Somnolent, difficult to arouse
- Assess for evidence of allergic reaction and for nausea and vomiting.
- Assess bowel and bladder function, constipation relief may be needed. Institute a bowel regime early, particularly with elderly patients.

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Opioid allergies have resulted in harm to many patients. Verify the absence of allergy before the first dose.

**Narcotics and Sedatives: Assessing the Medication Profile**

In addition to completing an assessment of prescribed narcotics and sedatives, the nurse must also assess the entire medication profile of the patient to anticipate any possible drug interactions.

- Evaluate use of PRN medications – is a change of medication or dosage indicated?
- Pay careful attention to orders. Avoid dangerous assumptions. Sound-alike opioids, varying concentrations, and inappropriate routes of administration contribute to many opioid errors.
- Assess medication profile for concurrent opioids. **Sound-alike/Look-alike Issues**

  Morphine may be confused with hydromorphone, magnesium sulfate (when MS or MS04 abbreviations are used), MS Contin® may be confused with Oxycontin®. Avinza® may be confused with Evista®, Invanz®. RoxanolTM may be confused with OxyFast®, RoxicetTM, Roxicodone®.

**Test Yourself:**

What is the most frequent origin of anticoagulant errors? (USP, 2008)

  A. Administering - Correct
  B. Transcribing & Documenting
  C. Prescribing
  D. Dispensing
  E. Monitoring

**Opioid/Acetaminophen Combinations Assessment**

Assess total daily acetaminophen intake to prevent acetaminophen toxicity. Hepatotoxicity due to acetaminophen has proven fatal in patients who received excessive doses of combination drugs. Total daily dose for adults with normal liver function should not exceed 4,000 mg per day. Be alert for concurrent orders of more than one medication containing acetaminophen.

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Opioid Content</th>
<th>Acetaminophen Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norco®</td>
<td>Hydrocodone 10 mg</td>
<td>325 mg</td>
</tr>
<tr>
<td>Percocet-5/325®</td>
<td>Oxycodone 5 mg</td>
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<td>Codeine 30 mg</td>
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<td>Tylenol #4®</td>
<td>Codeine 60 mg</td>
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</tr>
<tr>
<td>Vicodin®</td>
<td>Hydrocodone 5 mg</td>
<td>500 mg</td>
</tr>
<tr>
<td>Vicodin Extra Strength®</td>
<td>Hydrocodone 7.5 mg</td>
<td>750 mg</td>
</tr>
</tbody>
</table>

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Narcotics: Routes of Administration
IM administration is NOT recommended due to highly variable absorption. Recommended routes include:

- oral
- transdermal
- rectal
- IV
- subcutaneous
- epidural
- intrathecal

The transdermal route is ineffective with patients who have impaired circulation, such as a severely debilitated patient or a patient who has congestive heart failure.

Equianalgesic Doses
Equianalgesic Equivalent Charts compare different opioids and different dosage forms of opioids, providing information. For example, you might use the chart to find the equivalent PO dosage for a 10 mg dose of parenteral morphine, the hydromorphone (Dilaudid) parenteral morphine dose equivalent to a 10 mg dose of parenteral morphine, or other opioid equivalents.

Access the Equianalgesic Chart used in your organization and use it as a reference in pain management to facilitate adequate pain relief and patient safety.

Click here to view examples of Equianalgesic Equivalent Charts.


Safety Improvements: Promethazine (Phenergan®) and Meperidine (Demerol®)
A multidisciplinary team at Miami Valley Hospital in Dayton, OH took actions to reduce adverse drug events (ADEs) from oversedation. They measured these ADEs and the number of naloxone (Narcan®) ampoules and the number of flumazenil (Romazicon®) ampoules used per quarter.

They found that meperidine (Demerol®) and promethazine (Phenergan®) were contributing to most of the ADEs. The forcing functions they used to change the availability of these medications were to:

- Eliminate meperidine as a choice for PCA. The choices that remained provided adequate pain relief with less risk of oversedation.
- Replace promethazine 50 mg vials with 25 mg vials to decrease the chance of an error leading to overdose.

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These changes resulted in a significant decrease in ADEs from oversedation and in naloxone use.

The team emphasized the importance of listening to frontline staff, auditing and reinforcing changes, and recognizing that events occurring within an organization such as changes in management, staffing, and patient acuity can interfere with implementing safety improvements organization-wide (IHI, 2011a).

Both IHI and the American Pain Society recommend avoiding the use of meperidine, especially in the elderly and renal-compromised patients because of the risk of neurotoxicity (Lacy, et al, 2010, p. 965).

Sound-alike/Look-alike Issues

Promethazine may be confused with chlorpromazine, prednisone, promazine. Phenergan® may be confused with Phenaphen®, phenobarbital, Phrenilin®, Theragran®. The following tall man lettering is recommended to clarify: chlorproMAZINE, predniSONE, PHENobarbital. Meperidine may be confused with meprobamate.

Demerol® may be confused with Demulen®, Desyrel®, dicumarol, Dilaudid®, Dymelor®, Pamelor®

A Fatal PCA Pump Error

- The MD ordered “fentanyl PCA per protocol:”
  - 50 mcg/mL concentration
  - 10 mcg demand dose
  - 6-minute lockout interval
  - Clinician boluses of 20 mcg every 5 minutes X 3, repeat every 4 hours as needed
- The nurse accidentally programmed 1 mcg/mL instead of the actual concentration of 50 mcg/mL. Then the nurse programmed the demand dose of 0.10 mcg instead of the ordered demand dose of 10 mcg.
- Two nurses were present when the nurse began programming the pump, but the one left to take a telephone call. When she returned, she read the settings, but missed the programming errors.
- These errors resulted in the patient receiving only half the intended dose: 0.1 mL of the 50 mcg/mL concentration with each demand dose = 5 mcg.
- The patient remained in severe pain. The nurse on the next shift administered a 20 mcg bolus. She programmed the bolus dose correctly, but because the pump was programmed for a 1 mcg/mL concentration, the patient received 20 mL of the 50 mcg/mL concentration – a dose of 1,000 mcg.
- The patient was found unresponsive 15 minutes later, was transferred to ICU and died three days later (ISMP, 2004).

Avoid trailing “zeros”
(0 after a decimal point)
The TJC National Patient Safety Goals prohibit trailing zeros in medication orders.
A Second PCA Error Discovered
Investigation of the fatal PCA error just described uncovered another PCA pump error which had not been recognized as such at the time.

A nurse had programmed the correct settings, but failed to press “Enter” within a short period of time. The pump therefore defaulted to a prior setting.

The patient received an overdose resulting in unresponsiveness and poor respiratory effort. These symptoms were thought to be caused by post-operative hemorrhage and the patient was returned to the OR.

When hemorrhage was ruled out, a seizure was suspected to have caused the symptoms. The patient recovered in ICU. It was only during investigation of the earlier fatal event that the cause of the second situation was recognized (ISMP, 2004).

PCA Safety: Policy Recommendations
- Create a privileging system for PCA prescribers.
- Use standard order sets for PCA.
  - Morphine, medication of choice; Hydromorphone for high-dose; Meperidine for allergic patient
  - Limit choices of medications per PCA. Restrict fentanyl use to anesthesia or pain management team members only
  - Dose in mg or mcg, not mL
- Standardize concentrations throughout the organization. Color code different concentrations.
- Employ independent double-checks. Define a clear independent double-check process.
- Improve label readability. Match sequence of information on PCA medication labels with the sequence of information to be programmed and the sequence required in protocols, orders and other documentation. Highlight the concentration.

Research Findings Recommend PCA Safety Improvements

Vendors should simplify the equipment used to administer the intravenous medication and provide easy-to-follow setup instructions.
Facilities should use standardized prescription order forms.
Clinicians should double-check the medication order, product, and device settings
Facilities should use bar codes and electronic medication administration records

PCA Safety: Organization-based Recommendations

- Use the same pump throughout the organization.
- Introduce new pumps slowly. When a new pump is introduced, limit use to a small, controlled setting to identify any problems and assure that safety features are operational.
  - Give training close to the time of implementing a pump.
  - In training, include simulations with errors and assessment for toxicity.
- Evaluate pumps:
  - Easy to program?
  - Intuitive?
  - Logical sequence: medications, units, strength?
  - Can be programmed for default settings for opiate in use?
  - Does the pump give feedback re: the dose?
  - Is the button clearly distinct from the call bell?
- Employ smart pumps and bar code technology where available, but do not rely solely on technology.
- Supply a quick reference sheet for nurses, including programming tips and maximum dose warnings for all medications administered per PCA.
- Study naloxone (Narcan®) use as an indicator of errors. (AHA, 2008; ISMP, 2008).

PCA Safety: Programming the Pump

- Fully employ the safety features of the pump, including:
  - Program default values for each concentration.
  - Lock out inappropriate ranges for concentrations not in use.
  - Set zero as a default to force entries if only one default setting is allowed.
  - Determine whether the pump can be set for maximum dose or maximum volume per medication.
  - Assure that biomedical checks are performed on PCA pumps. Alert staff members to situations that will trigger default settings.
- Check equipment regularly – a broken syringe or cassette can allow air to enter and cause free flow.
- Attach laminated reference to the pump.
- Verify settings each shift.
- Before refilling or when changing programming:
  - Identify the patient.
  - Check medication and concentration.
  - Check line attachments.
  - Be especially vigilant in reading medication names and concentrations on any unit stock. (ISMP, 2008)
Concentration and Volume have an inverse relationship. More concentrated drugs require less volume to deliver a specific dose. For more on this complex issue, visit: www.ismp.org/d/SpecialFollowUp.pdf.

(ISMP, 2008)

PCA Safety: Initiating PCA and Patient Teaching

- Educate the patient preoperatively. Assure that the patient understands that the lock-out interval does in no way mean that the patient MUST press the button every few minutes in order to experience pain relief.
- Emphasize the importance of ONLY the patient pressing the button (not relatives or other visitors). PCA-by-proxy has resulted in overdoses.
- Double-check patient identifiers, allergies, medication, dose, and all settings before initiating.
  - Misprogramming and calculation errors are the most frequent practice-related causes for error.
- Always use PCA with maintenance IV fluid.
- Connect to a port close to the patient to prevent dead space.
- Label the line per organizational policy and procedure.
- Clear the pump history only for medication changes.
- Change tubing when concentration or medication is changed.
- Whenever possible, the dose of a medication should be prescribed and displayed on the MAR in the same way the information will be needed to program the pump (ISMP, 2007b).

PCA Safety: Important Assessments

- Perform complete assessments as indicated for narcotics and sedatives.
- Suspect a problem. If the patient is not responding, re-verify all possible sources of error or pump malfunctions before administering a clinician bolus dose.
- Do not rely on pulse oximetry to measure adequacy of respirations. Oxygen saturation is usually maintained at a low respiratory rate. In high-risk patients or for those to whom the nurse administers the PCA dose, capnography should be employed to measure CO2 levels.
- Check order and MAR carefully to assure that the patient is not receiving concurrent doses of oral and IV opioids.

PCA: Managing Pain Effectively and Safely

A 45-year-old male patient has a 20-year history of severe rheumatoid arthritis. He is one-day post-op joint replacement surgery. At home he has been managing his pain with hydromorphone (Dilaudid®) 7.5 mg PO four times daily. His current PCA order is for Morphine 5 mg bolus every 8 minutes with no basal dose. Despite administering a bolus every 8 minutes, he rates his pain at 4 on a scale of 1 to 10.
Does the PCA order comply with requirements in your organization? What changes are most likely to manage his pain more effectively?

Most facilities have a strict guideline for PCA orders. Know your organization’s requirements and accept only orders that conform to policy.

In this situation, an 8-minute lock out interval is dangerous since IV opioids peak in 15 minutes. Fentanyl is an exception to this rule, but is not routinely used on most general units.

Dosing more frequently than every 15 minutes makes overdose likely.

Your patient has been taking 30 mg of hydromorphone (Dilaudid®) per day (7.5 mg X 4). You refer to the Equianalgesic Equivalent Chart and find that 30 mg PO Dilaudid® = 120 mg PO morphine or 40 mg parenteral morphine.

**PCA Effectiveness: Solving the Problem**

For this patient, a basal dose via PCA should provide 40 mg/day.

The dose per hour is 40 mg/24 hr or 1.7 mg/hour and for breakthrough post-operative pain, a bolus dose with a 15-minute lock out interval.

The provider might also consider hydromorphone.

Notify the patient’s physician of your assessment and recommend a change in the PCA order.


\[
\text{mg "old"opioid} = \text{mg "new" opioid} \\
\text{current mg "old" in 24 hours} \times \text{mg "new" opioid} \\
\text{7.5 mg (PO Dilaudid®)} \times 10 \text{ mg (parenteral morphine)} \\
\text{30 mg in 24 hours} \times \text{7.5 x} \\
\text{300 mg in 24 hours} \times \text{x} \\
\text{40 mg in 24 hours} \times \text{1.7 mg/hour} \\
\text{40mg/24 hours} \times \text{x}
\]

([RN.com](http://RN.com), 2007)

**PCEA Pump Safety**

Patient-controlled epidural analgesia (PCEA) requires the same precautions and assessments as PCA, including double-checks. In addition:

- The pain medication ordered per PCEA should be the only medication administered via the PCEA line.
- Question an order for PCEA for patients who are receiving low molecular weight heparin or fibrinolytic therapy. PCEA is contraindicated for these patients.
- Observe bolus dose precautions.
• Remain at the bedside during and for 5 minutes after the bolus dose.
• Administer a maximum bolus volume less than or equal to the current hourly rate of infusion.
• Maintain a closed system after discontinuing the infusion. The epidural catheter may be left in place after the infusion is discontinued. A lock is placed at the distal end of the catheter. The line does not need to be flushed since the epidural space is free space and not prone to clotting.

**Note! When a patient is receiving epidural analgesia, no other narcotics should be administered concurrently.**

**Midazolam: A High-Alert Benzodiazepine**

Midazolam (Versed, index name) belongs to the benzodiazepine classification of medications. Specific benzodiazepines vary greatly in relative potency, onset of action, and half-life.

Some benzodiazepines are used to manage anxiety, such as alprazolam (Xanax®), diazepam (Valium®), lorazepam (Ativan®), Oxazepam (Serax®), and chlordiazepoxide (Librium®).

Others are used as sedatives, such as estazolam, flurazepam (Dalmane®), quazepam (Doral®), temazepam (Restoril®), and triazolam (Halcion®).

Still others have specific uses, such as clonazepam (Clonopin®) which is used to treat seizures and panic disorders, clorazepate (Tranxene®) which is used to treat anxiety, alcohol withdrawal, and seizures, and midazolam which is used for preoperative, moderate sedation for procedures, ICU sedation, and induction and maintenance of general anesthesia.

**Midazolam: Risk for Respiratory Arrest**

Careful monitoring of respiratory and cardiovascular status is required during administration of midazolam. Personnel and equipment needed for standard respiratory resuscitation should be immediately available (Lacy et al., p. 1015).

The FDA places 2 black box warnings on midazolam:

• May cause severe respiratory depression, respiratory arrest, or apnea. Use with extreme caution, particularly in noncritical care settings.
• Initial doses in elderly or debilitated patients should be conservative: as little as 1 mg, but not to exceed 2.5 mg.

**Risks both During and After Midazolam Administration**

Safe administration of midazolam requires:

• Slow IV infusion
• Close monitoring of respiratory and cardiovascular status
• Ready availability of the benzodiazepine antidote flumazenil (Romazicon ®)
• Presence of trained personnel and equipment for respiratory resuscitation

Careful monitoring of respiratory status is extremely important during the 24 – 48 hours after the patient has received midazolam.

Risk of respiratory arrest may continue for 24 – 48 hours following administration of midazolam,
especially following extended administration by continuous IV infusion. CNS impairment may persist for this time period. Therefore performing tasks that require mental alertness and motor control is not recommended for 24–48 hours after receiving midazolam.

Alcohol and medications that have CNS effects enhance and prolong the action of midazolam. Many antiviral medications also enhance the effect of midazolam (Lacy, et al, 2010).

Midazolam: Patient-specific Risks
Elderly persons and children are particularly susceptible to adverse effects of midazolam.

Caution is required when administering midazolam to patients who have respiratory difficulties, especially chronic obstructive pulmonary disease (COPD); open-angle glaucoma; cardiac, hepatic, or renal problems; the blood disease porphyria; severe depression; a history of drug abuse or dependence; or recent use of alcohol.

Midazolam is not advised during pregnancy and breast-feeding. It is categorized as a Pregnancy Category D medication, reflecting harm to the fetus. It is excreted in breast milk (Drugs.com, 2011b).

One fatal incident included the use of conscious sedation in conjunction with an oral agent and nitrous oxide gas. A Chicago dentist received an 18-month suspension of his license and a $10,000 fine for "failure to ensure his staff was appropriately trained, his inaccurate record keeping and his willingness to exceed the scope of his sedation permit." His patient, a 5-year-old girl, did not awaken after anesthesia for a dental procedure. She died after four days on life support at a Children's Hospital (Associated Press, 2006; Waldron, 2007).

Midazolam: Adverse Effects
Severe adverse effects include:
- Allergic reactions manifested by rash; hives; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue
- Agitation
- Combative
- Chest pain
- Irregular breathing patterns, slow or difficult breathing
- Uncontrollable rapid eye movements
- Unusual or involuntary muscle movements or muscle tremor
- Seizures
- Dysphagia
- Pain, swelling, or redness at the injection site

Milder adverse effects include:
- Blurred vision
- Instability of blood pressure, respirations, and heart rate
- Coughing
- Dizziness
- Drowsiness
- Dry mouth

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- Headache
- Hiccups
- Low blood pressure (children)
- Nausea
- Pain during injection
- Pain, redness, or tenderness at the injection site
- Short-term memory loss
- Slurred speech
- Vomiting

(Drugs.com, 2011b; Mayo Clinic, 2011b; MedlinePlus, 2010b).

**A Pediatric Error with Midazolam**

Midazolam syrup (2 mg/mL) was stocked in bulk bottles on in the automated dispensing cabinet on a pediatric unit. After calculation errors caused overdoses, screens were placed on the cabinets to provide dose warnings and dose conversion charts were posted to eliminate the need for calculation. Despite these precautions, another error occurred.

The nurse was preparing midazolam syrup 6 mg as ordered. She referred to the conversion chart and identified the correct volume as 3 mL. However, she confused the dose in mg (6) with the correct volume in mL (3). She incorrectly prepared and administered 6 mL (12 mg) of midazolam to the child. Fortunately, the child was not harmed (ISMP, 2002).

**Bupivacaine: Another Anesthetic/Analgesic Agent**

Bupivacaine is used to produce local or regional anesthesia or analgesia for surgery, dental and oral surgery procedures, diagnostic and therapeutic procedures, and for obstetrical procedures.

When a patient receives bupivacaine, assess:

- Blood pressure every hour for the first four hours and every four hours thereafter.
- For orthostatic hypotension prior to ambulation.
- Strength and sensation in the lower extremities every two hours while awake for the first 24 hours.

0 – Normal strength and sensation
1 – Weak, but able to bend knees and ankles, normal sensation
2 – Unable to bend knees, normal sensation
3 – Unable to move legs, decreased sensation

**Look-alike, Sound-alike Issues:**

Bupivacaine may be confused with mepivacaine, ropivacaine, Marcaine®, Narcan®

**Safety Improvements: Interrupting Continuous Sedative Infusions**

Researchers at the University of Chicago Hospitals studied the use of continuous sedative infusions with intensive care patients who were receiving mechanical ventilation. Continuous sedation interferes with neurological assessment and requires additional diagnostic tests to evaluate changes in neurological status.
In their experimental group, they interrupted the sedative infusions daily until patients were awake. For patients in the control group, the infusions were interrupted only at the discretion of the clinicians. The patients whose infusions were interrupted daily had a significantly shorter duration of mechanical ventilation (4.9 days as compared with 7.3 days) and a shorter ICU stay (6.4 days as compared with 9.9 days). Patients in the control group required more diagnostic testing to assess mental status. There was no significant difference in the number of patients who removed their endotracheal tubes (4% in the experimental group, 7% in the control group).

**The IHI Ventilator Bundle includes daily sedation vacations based upon evidence that daily sedation vacations reduce the length of time on the ventilator and help to prevent ventilator-associated pneumonia (VAP) (IHI, 2011b).**

**Summary**
Take extra care when administering high-alert medications. These medications have narrow therapeutic indices and therefore little room for error without serious consequences. It is significant that many of the medications identified in this course are commonly used medications that have been in use for many years.

Resist the temptation to let familiarity breed complacency when administering high-alert medications.

Watchdog groups continue to identify the roles of other familiar medications in fatal errors. Keep current with safety alerts. Access resources of The Joint Commission [www.jointcommission.org](http://www.jointcommission.org) and the Institute for Safe Medication Practices [www.ismp.org](http://www.ismp.org), including ISMP Medication Safety Alert!

Comply strictly with your organization’s policies regarding the high-alert medications your organization has designated.

**Conclusion**
By studying High-Alert Medications: Safe Practices you have identified several high-alert medications that are considered to present the highest risk to patients and learned recommended ways to improve safety in administering these medications. Specifically, you have learned:

- Why certain medications and classifications of medications are designated as high-alert medications.
- Recommended practices to improve safety with high-alert medications.
- Nurses’, pharmacists’, and others’ perceptions of high-alert medications as reported in a 2007 Institute for Safe Medicine Practices study.
- Important safety precautions when administering:
  - Heparin
  - Warfarin
  - Digoxin
  - Electrolytes
  - Insulin
  - Narcotics
  - Sedatives, and specifically midazolam
  - Patient-controlled intravenous analgesia and patient-controlled epidural analgesia
References


At the time this course was constructed all URL’s in the reference list were current and accessible. rn.com is committed to providing healthcare professionals with the most up to date information available.

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References


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