Vesicant Extravasation Part I: Mechanisms, Pathogenesis, and Nursing Care to Reduce Risk

Carmel Sauerland, RN, MSN, AOCN®, Constance Engelking, MS, RN, OCN®, Rita Wickham, PhD, RN, AOCN®, CHPN, and Dominick Corbi, MS, RPh

Purpose/Objectives: To review the literature regarding the incidence, current practice, guideline recommendations, nursing management, and knowledge gaps relevant to vesicant extravasation.

Data Sources: Published research articles, books, case reports, and national guidelines.

Data Synthesis: Vesicant extravasation is a relatively rare but significant complication of chemotherapy administration. Extravasation may have a range of consequences that can cause serious physical and quality-of-life effects. Knowledge of risk factors and preventive measures can reduce patient risk. Data-based and empirical management strategies such as immediate local measures (agent withdrawal, comfort measures, and medical interventions) may minimize risk for extravasation, as well as lead to timely recognition and management and decreased morbidity should extravasation occur.

Conclusions: Vesicant extravasation and sequelae constitute a complex patient problem that clinicians should strive to prevent or to minimize injury should it occur. To this end, clinicians must demonstrate awareness of risks and use specialized knowledge while administering vesicant agents.

Implications for Nursing: Only nurses knowledgeable about extravasation and skilled in associated techniques should assume responsibility for vesicant administration.

Key Points . . .

- Pharmaceutical agents with vesicant properties can produce pain, swelling, inflammation, and progressive tissue damage, eventuating in necrosis and disability.
- Risks for vesicant extravasation include patient, clinician, therapy, and IV device factors.
- Prevention strategies include diligently monitoring infusions, selecting optimal administration devices, and using appropriate administration techniques.
- Because evidence-based data regarding management of vesicant extravasation are lacking, local comfort measures and antidotes are largely empirical.

Vesicant extravasation, although uncommon, has enormous potential to affect a patients' quality of life and survival, as well as generate substantial healthcare costs. Clinicians who administer vesicant agents must demonstrate appropriate skills and knowledge regarding the recognition and management of extravasation. The Oncology Nursing Society (ONS) book *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice* (Polovich, White, & Kelleher, 2005) condensed the minimum standards for practice and is useful in any setting where chemotherapy is administered. However, management of extravasation remains largely based on anecdotes of "efficacious" interventions in small samples or in single clinical cases (Kretzschmar et al., 2003). Consequently, oncology nurses, physicians, and pharmacists face the challenge of determining best practice with a less-than-ideal body of evidence to support clinical decision making. Practitioner awareness and patient management that include use of current guidelines, as well as systematic data collection and case reporting, can contribute to the further development of evidence-based patient care.

Spectrum of Extravasation

Extravasation is the inadvertent leakage or escape of a drug or solution from a vein or unintentional injection into surrounding healthy tissues. Occurrences of vesicant chemotherapy extravasation may be underreported but are estimated to occur in 0.1%–6% of peripheral IV infusions

Carmel Sauerland, RN, MSN, AOCN®, is an oncology clinical nurse specialist in the Nursing Cancer Center at Westchester Medical Center in Valhalla, NY; Constance Engelking, MS, RN, OCN®, is an oncology nurse consultant with the CHE Consulting Group, Inc., in Mt. Kisco, NY; Rita Wickham, PhD, RN, AOCN®, CHPN, is an oncology and palliative care consultant and an associate professor of nursing in the College of Nursing at Rush University in Chicago, IL; and Dominick Corbi, MS, RPh, is the director of clinical research in the pharmacy at Westchester Medical Center. *This research was supported by an unrestricted educational grant from sanofi-aventis to Meniscus, Ltd. Sauerland and Corbi received honoraria from Meniscus, Ltd., for the preparation of Parts I and II. Engelking served on a sanofi-aventis advisory board and as a consultant for Meniscus, Ltd. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the* Oncology Nursing Forum *or the Oncology Nursing Society. (Submitted November 2005. Accepted for publication March 12, 2006.)*

Digital Object Identifier: 10.1188/06.ONF.1134-1141

and in 0.3%–4.7% of implanted venous access port infusions (Lemmers et al., 1996; Shetty et al., 1997). The consequences of extravasation range from mild discomfort to severe tissue destruction, depending on whether the drug that leaks is a nonvesicant, irritant, or vesicant (see Figure 1). Extravasation of nonvesicant drugs generally does not cause tissue damage, whereas irritant agents induce inflammatory reactions but usually cause no persistent tissue damage. In either case, nonpharmacologic comfort measures (e.g., applying warm or cold, elevating the extremity) usually reduce swelling and discomfort.

In contrast, extravasation of vesicant agents can cause progressive tissue damage (Ener, Meglathery & Styler, 2004; Luke, 2005; Boyle & Engelking, 1995; Vargel et al., 2002). For example, a DNA-binding vesicant agent trapped in tissues can cause skin blistering and ulcer formation in days to weeks (see Figure 2). Eventually, indolent ulcers and persistent necrosis may extend to underlying tendons, ligaments, nerves, and bone and cause severe pain and functional deficit (e.g., loss in joint motility) (see Figure 3). Central venous catheter (CVC) extravasation may be complicated by local skin and soft tissue necrosis in the chest wall or neck, severe pain, effusions, dysrhythmias, or mediastinitis (Bozkurt, Uzel, Akman, Ozguroglu, & Molinas Mandel, 2003; Curran & Luce, 1990; Davies, Russell, & Thompson, 2003; Schulmeister & Camp-Sorrell, 2000). Furthermore, squamous cell skin carcinoma can occur as a late complication of chronic extravasation ulcers (Lauvin, Miglianico, & Hellegouarc'h, 1995).

One dilemma is that some drugs classified as nonvesicants, irritants, or mild vesicants (e.g., cisplatin, oxaliplatin, paclitaxel, docetaxel, mitoxantrone) have been associated with extravasation injuries (Baur, Kienzer, Rath, & Dittrich, 2000; Berghammer, Pohnl, Baur, & Dittrich, 2001; El Saghir & Otrock, 2004; Ener et al., 2004; Kennedy, Donahue, Hoang, & Boland, 2003; Kretzschmar et al., 2003; Stanford & Hardwicke, 2003). For instance, one patient who had an apparent oxaliplatin extravasation experienced immediate IV site erythema and swelling, local induration four days later, and ultimate skin sclerosis and functional limitation (Foo, Michael, Toner, & Zalcberg, 2003). Similarly, mitoxantrone extravasation into the dorsum of a patient's hand led to small area of discoloration that progressed over three months to a 2 cm by 2.5 cm necrotic lesion requiring surgical debridement and skin grafting (Luke, 2005).

Nonvesicant Agents	Irritant Agents	Vesicant Agents
Aldesleukin (interleukin-2)	Carmustine	Cisplatin[a]
Asparaginase	Cisplatin[a]	Dactinomycin
Bleomycin	Dacarbazine	Daunorubicin
Cladribine	Daunorubicin	Doxorubicin
Cyclophosphamide	Daunorubicin liposomal	Epirubicin
Cytarabine	Docetaxel	Idarubicin
Fludarabine	Doxorubicin liposomal	Mechlorethamine
Gemcitabine	Etoposide	Melphalan
Gemtuzumab ozogamicin	Floxuridine	Mitomycin
Ifosfamide	Irinotecan	Paclitaxel
Methotrexate	Mitoxantrone[b]	Vinblastine
Pentostatin	Oxaliplatin[c]	Vincristine
Rituximab	Topotecan	Vindesine
Thiotepa		Vinorelbine
Trastuzumab		

[a] Cisplatin is reported as a vesicant if greater than 20 ml of 0.5 mg/ml concentration extravasates.

[b] Mitoxantrone may act as a vesicant depending on concentration; it is classified as a vesicant in the Oncology Nursing Society chemotherapy guidelines.

[c] Oxaliplatin has been reported to have vesicant properties.

Figure 1. Vesicant Potential of Antineoplastic Agents

Note. Based on information from Ener et al., 2004; Luke, 2005; Polovich et al., 2005; Schrijvers, 2003.

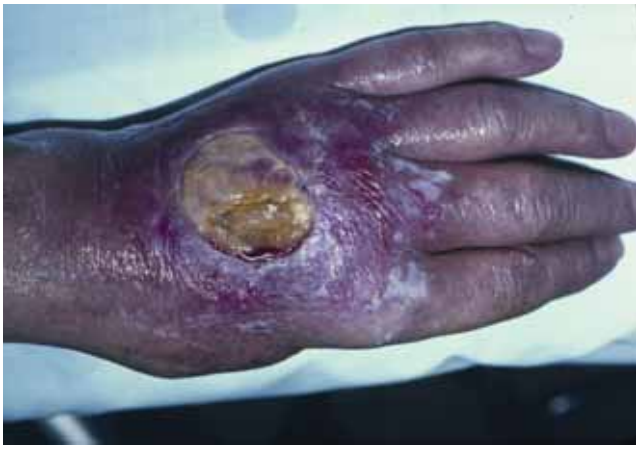

Figure 2. Extravasation-Induced Ulceration

Note. From "Vesicant Extravasation: Myths and Realities" by D.M. Boyle and C. Engelking, 1995, *Oncology Nursing Forum, 22,* p. 60. Copyright 1995 by the Oncology Nursing Society. Reprinted with permission.

Pathophysiology of Extravasation Injuries

Antineoplastic agents cause direct cellular toxicity. Severity of extravasation injuries relates to whether a drug binds to DNA (Ener et al., 2004). Furthermore, some nonantineoplastic agents have vesicant properties by virtue of different mechanisms of tissue damage.

Whether all vesicant extravasations result in the same sequence of injury is unknown. The prominent theory regarding doxorubicin extravasation is that, as affected cells die, the drug is released and taken up by surrounding normal cells, leading to progressive damage over weeks to months (Dorr, 1990). Doxorubicin extravasation into paravenous tissues also may generate superoxide radicals, hydroxyl radicals, and peroxides that damage affected cells and cell membranes and cause severe damage to small blood vessels accompanied by loss of vascular integrity, thrombosis, extravasation of red blood cells, and avascular necrosis without inflammatory cells (Rudolph & Larson, 1987; Vargel et al., 2002). Degenerative changes in cellular organization continue for weeks, altering cell proliferation and normal healing. Healing also may be impaired in patients with cancer secondary to immunosuppression and altered protein synthesis.

DNA-Binding Agents

DNA-binding agents include anthracyclines (doxorubicin, daunorubicin, idarubicin, and mitoxantrone), antitumor antibiotics (mitomycin), and some alkylating agents

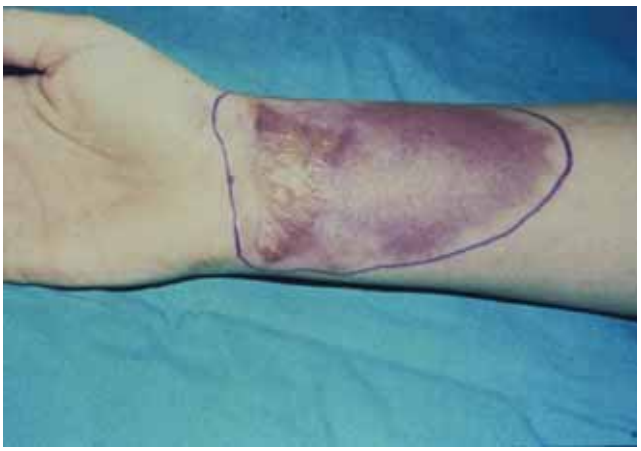

Figure 3. Progression of Extravasation Injury to Necrotic Phase

Note. From "Vesicant Extravasation: Myths and Realities" by D.M. Boyle and C. Engelking, 1995, *Oncology Nursing Forum, 22,* p. 61. Copyright 1995 by the Oncology Nursing Society. Reprinted with permission.

(mechlorethamine and platinum analogs) (Ener et al., 2004). Anthracyclines bind to nucleic acids in DNA and are toxic to topoisomerase II, leading to multiple DNA strand breaks. They generate free radicals, any of which inhibit RNA and protein synthesis, ultimately causing cell death. Free radicals are molecules that have lost electrons, making them unstable and highly reactive scavengers of missing electrons from other molecules (Dorr, 1990; Langer, Sehested, & Jensen, 2000). Other DNA-binding agents are intercalators; they bind to both DNA strands (Skeel, 1999).

The mechanisms of alkylating agent cytotoxicity are free-radical formation and lethal DNA crosslinking or strand breaks (Skeel, 1999). Platinum analogs bind to and cause DNA intra- and interstrand crosslinking and complexes (adducts), leading to apoptosis (programmed cell death) (Raymond, Faivre, Woynarowski, & Chaney, 1998; Rivory, 2002). Oxaliplatin may be more cytotoxic to cancer cells and normal tissues than cisplatin because its carrier ligand binds more persistently in tissue (Kennedy, Donahue, Hoang, & Boland, 2003).

Non–DNA-Binding Antineoplastic Agents

Intracellular microtubule toxins and topoisomerase inhibitors interfere with mitosis and do not bind to DNA (Schrijvers, 2003). Microtubule toxins include vinca alkaloids (vincristine, vinblastine, and vinorelbine), which inhibit microtubule formation, and taxanes (paclitaxel and docetaxel), which enhance microtubule stabilization. Topoisomerase inhibitors (etoposide, irinotecan, and topotecan) block enzymes that facilitate DNA unfolding and reconstruction before and after cell division. This ultimately hampers DNA transcription and replication and causes cell death. Non–DNA-binding agents are cleared more easily from extravasation sites and cause less tissue damage than DNA-binding agents (Skeel, 1999).

Nonantineoplastic Vesicant Agents

Extravasation of nonantineoplastic drugs that have vesicant properties (see Figure 4) also may result in extensive skin and soft tissue necrosis, necessitating debridement, flap reconstruction, or skin grafting (Hadaway, 2004; Schummer et al., 2005). The vesicants include hyperosmotic solutions that lead to compartment syndrome, concentrated electrolyte solutions that possibly prolong muscle depolarization and lead to ischemia, agents that alter intracellular pH (sodium bicarbonate), and those that induce severe vasoconstriction and ischemia (see Case Study 1). Such agents may be administered with chemotherapy and can confound identifying the etiology and managing extravasation injury.

Other Factors Influencing Extent of Tissue Damage

The potential for tissue damage also relates to drug concentration and amount infiltrated, duration of tissue exposure, and extravasation site (Scuderi & Onesti, 1994; Steele, 1998). Thus, a large-volume extravasation of highly concentrated DNA-binding vesicant poses a very difficult management challenge. Timeliness of postextravasation interventions is also important; delayed recognition may mean greater injury, pain, and disability. Similarly, damage is more likely with peripheral IV extravasation in areas with many nerves, tendons, and blood vessels, such as the dorsum of hand, wrist, or antecubital fossa, or where extravasation may not be evident immediately, as in the antecubital fossa, chest wall, or thoracic structures, leading to significant damage, pain and functional impairment that necessitate multiple surgeries (Heitmann, Durmus, & Ingianni, 1998; Luke, 2005).

Risk Factors for Extravasation

Risk factors for extravasation include administration device, type of treatment, and patient- and clinician-related characteristics. Multiple concurrent risk factors predict greater likelihood of extravasation and severe injury (see Figure 5).

Device-Related Risk Factors

IV device factors that affect extravasation risk include use of metal needles rather than plastic cannulas, CVC-specific issues, and infusion maintenance. Metal needles should not be used for vesicant infusions because they cause more trauma to veins during insertion than plastic cannulas and are not flexible within the vessel (Boyle & Engelking, 1995). Large-gauge plastic cannulas also are more traumatic to veins than smaller catheters and can impede blood flow, slowing dilution of infusate (Hadaway, 2004).

Concentrated Electrolyte Solutions
- Calcium chloride 5.5%
- Calcium gluconate 10%
- Potassium chloride 7.45%
- Sodium bicarbonate 4.2% or 8.4%
- Sodium chloride 10%

Hyperosmolar Agents
- Central venous nutrition
- > 10% glucose
- Mannitol 15%
- Phenytoin

Vasocompressive Agents
- Dobutamine
- Dopamine
- Epinephrine
- Norepinephrine
- Vasopressin

Other
- Penicillin
- Radiograph contrast media
- Vancomycin

Figure 4. Vesicant Potential of Nonantineoplastic Agents

Note. Based on information from Davies et al., 2003; Hadaway, 2004; Loth & Eversmann, 1991; Schummer et al., 2005; Wickham, 1989.

Case Study 1

A 70-year-old Hispanic man underwent surgery and had a triple-lumen short-term catheter placed because of limited peripheral IV access. On the day after surgery, the patient became agitated and confused. The dressing over the catheter was soaked. When it was removed, the patient's neck was swollen and the catheter was displaced from the vein. Potassium chloride (KCl) had been infusing, but the amount that had extravasated could not be confirmed. Initially, the site was treated conservatively with dry dressings. Skin ulceration was evident one week later, and local antiseptic ointment was used. Four weeks after extravasation of KCl, swelling occurred over the site and extended upward along the neck. One week later, a magnetic resonance imaging scan showed necrosis of the neck soft tissues and imminent erosion of the carotid artery. The patient did not have pain at the site. A neck dissection with local debridement was followed by two other debridements. Eight weeks after extravasation, the area of extravasation was repaired with a pectoralis flap (Schummer et al., 2005).

Extravasation from CVCs can occur with needle displacement from an implanted venous access port (IVAP), mechanical occlusion and subsequent CVC damage, catheter migration, or fibrin sleeve formation and thrombosis. Such problems, although serious, occur infrequently. The incidence of catheter thrombosis is 3%–3.5%, catheter fracture or disconnection is 0.5%, secondary dislocation is 1.5%–2%, and pinch-off is 0.1%–1.1% (Andris & Krzywda, 1997; Hackert et al., 2000).

Incorrect needle placement outside an IVAP septum or needle displacement after cannulation may lead to extravasation, which might not become clinically apparent until enough fluid has infused to cause swelling and discomfort. Incorrect placement may be more likely in patients with new IVAPs and those who have significant postoperative swelling and discomfort that impede thorough palpation. Incorrect placement and accidental displacement may be more common in obese patients and large-breasted women, who have large amounts of subcutaneous fat and need longer needles to avoid inadvertent needle dislodgement and subsequent subcutaneous extravasation (Schulmeister & Camp-Sorrell, 2000). Agitated and confused patients also are at greater risk for accidental needle displacement (Wickham, 1989).

Mechanical occlusions may be related to thrombus or drug precipitate in CVCs, retrograde catheter displacement, or pinch-off. Catheter rupture, which may not be evident immediately, can occur, particularly if a small syringe (< 10 ml) that can generate high internal pressure is used to attempt flushing a partially or totally occluded catheter (Polovich et al., 2005). Retrograde displacement of a CVC tip into the ipsilateral internal jugular or contralateral subclavian vein may lead to withdrawal occlusion, thrombosis, or damage to intima of the smaller veins, all of which increase the risk of extravasation. CVC tip migration through the superior vena cava into the mediastinum, lung, heart, or other thoracic structure has been reported. It can occur shortly after placement (related to technically difficult insertion) or as a late complication (Bozkurt et al., 2003; Hackert et al., 2000). Symptoms may include acute-onset severe pain (requiring morphine), intractable cough, dyspnea, or other life-threatening problems.

Pinch-off and subsequent catheter fracture can occur with tunneled CVCs and IVAPs inserted with the subclavian technique (see Case Study 2) (Andris & Krzywda, 1997; D'Silva, Dwivedi, Shetty, & Ashare, 2005). Pinch-off is manifested as an intermittent and positional catheter occlusion and should be suspected if infusion occlusion can be relieved by having a patient roll his or her ipsilateral shoulder, raise his or her arm, or change position from sitting upright to reclining or lying flat. Such positional changes may open the space between the clavicle and first rib and alleviate the compression and friction that can damage and ultimately fracture the catheter, leading to extravasation of infusate about the clavicle and embolization of the catheter tip to the right atrium or pulmonary artery (Debets, Wils, & Schlangen, 1995; Gorski, 2003). Pinch-off can be diagnosed by chest radiograph, which may confirm distortion, flattening, or even frank fracture of a catheter as it passes between the clavicle and first rib.

Fibrin sleeves develop along most tunneled CVCs and peripherally or centrally inserted IVAPs but do not pose a problem in most instances. A sleeve begins at the point of IV insertion and propagate along the catheter to varying lengths (unrelated to duration of catheterization) (Starkhammar, Bengtsson, & Morales, 1992). The sleeve may adhere to the vein wall of smaller veins but also may be nonadherent and float freely. Occasionally, a thrombus develops near or at the

Device Related

Peripheral IV Access
- Metal needles, large-gauge catheters
- Inadequately secured IV needle or catheter
- Undesirable IV site location (e.g., antecubital fossa, dorsum of hand or wrist rather than forearm)

Central Venous Catheter IV Access
- IV access device surgically placed in area prone to movement; poor ability to secure
- Inadequately secured needle in access device
- Inappropriate needle length for access device (i.e., too short to reach back of port body)
- Development of fibrin sheath at the tip of the catheter
- Catheter or port separation, breakage, or dislodgement
- Flushing with small-gauge syringe

Agent Related
- Vesicant potential
- Volume infiltrated
- Drug concentration vesicant
- Repeated use of same vein for vesicant administration

Patient Related
- Age (very young or old)
- Impaired communication
- Compromised circulation
- Altered sensory perception
- Poor understanding of risk related to anxiety or fear, cultural barriers, or medications

Clinician Related
- Lack of knowledge
- Lack of IV skills
- Unfamiliarity with central venous catheter use and management
- Interruptions or distractions during drug administration

Figure 5. Risk Factors for Extravasation

Note. Based on information from Camp-Sorrell, 2004; Hadaway, 2004; Luke, 2005.

Case Study 2

A 63-year-old African American woman was receiving outpatient chemotherapy through a tunneled central venous catheter (CVC). In the clinic, the nurses had problems withdrawing blood and also with infusions unless the patient reclined to 45 degrees and elevated her ipsilateral arm. When the nurse connected a 10 cc syringe of normal saline to the patient's CVC, she was unable to obtain a blood return. After the catheter was flushed with saline, the patient reported stinging near her clavicle. A nurse noted swelling in the clavicular area ipsilateral to the tunneled CVC. She did not attempt further IV withdrawal or infusion of saline or the patient's scheduled IV paclitaxel but notified the patient's oncologist of her findings. A chest x-ray confirmed that the distal CVC was between the clavicle and first rib, but no catheter was seen in the vein below the clavicle. However, the catheter tip section was confirmed to be in the right atrium. Both segments of the CVC were snared and removed, and the patient did not experience any adverse effects.

CVC tip; if a sleeve extends beyond, retrograde flow through the sleeve and along the catheter may result in extravasation (Goodman & Riley, 1997; Gorski, 2003; Mayo, 1998; Schulmeister & Camp-Sorrell, 2000).

Treatment-Related Risk Factors

Administration schedule and frequency may contribute to risk of extravasation injury, and increasing administered doses increases risks for adverse effects (Steele, 1998). Intermittent bolus chemotherapy and continuous regimens may include one or more vesicant and irritant agents that repeatedly or continuously expose the venous intima to the negative effects of harsh drugs.

Patient-Related Risk Factors

Age is a major risk factor for very young and older individuals. Infants and young children cannot easily communicate the key symptoms, pain and burning, of vesicant extravasation. Older patients may have communication problems that sometimes accompany aging or result from heightened responses to drugs for nausea, anxiety, or pain (e.g., lorazepam, diphenhydramine, opioids) that have central nervous system (CNS) effects (Luke, 2005; Polovich et al., 2005). Young and old patients have more fragile veins and skin, which also increases risk for extravasation. Other problems from cancer or other diseases that might increase risk for extravasation include compromised circulation (e.g., Raynaud syndrome, diabetes, venous obstructive process), superior vena cava syndrome, lymphadenopathy, and malnutrition (Goodman & Riley, 1997; Polovich et al.).

Patients must understand the potential severity of vesicant extravasation. But even with appropriate teaching, their anxiety, fear, and cultural beliefs can interfere with their understanding and the speed with which they report problems. Anxiety about cancer and its treatment (e.g., fear of repeated venipuncture or treatment delays) or notions about being a "good patient" might cause hesitancy in reporting discomfort. Overt expressions of discomfort or pain are not the norm in some cultural groups (Lipson, Dibble, & Minarik, 1996). A vague comment such as "Something doesn't feel right" might delay timely recognition of extravasation. Because of differences in expressions of pain, nurses should investigate even vague complaints of discomfort.

Clinician-Related Risk Factors

In addition to having chemotherapy knowledge and skills, nurses must understand the importance of avoiding distracting interruptions and not taking procedural shortcuts during chemotherapy administration. Knowledgeable clinicians are more likely to perform comprehensive assessments, identify early indicators of possible extravasation, and intervene appropriately if inadvertent extravasation occurs (Luke, 2005; Boyle & Engelking, 1995; Steele, 1998). Conversely, inadequate nursing knowledge, particularly about risks of vesicant extravasation with CVCs and the elements of adequate reassessment and documentation, is more likely to result in tissue injury (Loth & Eversmann, 1991; Polovich et al., 2005). Nurses who administer bolus or continuous chemotherapy must meet the standard of care and may be held accountable legally if extravasation injury occurs. Extravasation progressing to injury does not denote negligence per se because of inherent and unforeseeable patient factors, but it does underscore the importance of patient follow-up and timely interventions (Rudolph & Larson, 1987).

Preventing Extravasation

Vesicant extravasation is preventable in most instances (see Figure 6). All nurses in any setting (clinics, offices, oncology or nononcology hospital units, or in homes) who administer chemotherapy or monitor patients receiving continuous IV chemotherapy should complete a certified chemotherapy course and demonstrate essential knowledge and clinical skills (see Case Study 3). Education provides a basic understanding of chemotherapy, information about specific drugs to focus patient teaching, and critical-assessment skills. Nurses must have administrative support to provide safe patient care and should be leaders in developing and updating evidence-based chemotherapy administration and extravasation management policies and demonstrating continued competency. Competency includes risk identification, prevention and management of extravasation, appropriate use of venous devices (peripheral IVs, peripherally inserted central catheters, tunneled CVCs, IVAPs), and components of adequate documentation. Nurses should review the ONS *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice* (Polovich et al., 2005) regarding recommendations and controversies, but several points warrant discussion in this article.

Nurses, physicians, and pharmacists must work together to implement systems to reduce risks for vesicant (antineoplastic and nonantineoplastic) injury. Thus, pharmacies might label vesicants with bold stickers and catalogue clinical resources (e.g., policy, drug information, management of suspected extravasation). Vesicant infusions lasting less than 60 minutes may be administered through peripheral IVs, but nurses must observe the site and surrounding area during the *entire infusion,* confirming IV patency every 5–10 minutes (for continued blood return, no new swelling or erythema) and querying patients about local pain or changed sensations. Vesicant agents administered longer than one hour *never* should be infused through a peripheral IV (Polovich et al., 2005).

In optimal circumstances, nurses start IVs and then administer chemotherapy. In any case, IVs should be less than 24 hours old, and nurses should confirm blood return before beginning vesicant administration (Hadaway, 2004). Peripheral IVs should be located in areas of good circulation (arterial,

Device Related

Peripheral IV Access

- Place cannula in the muscled area of the forearm.
- Use the smallest-gauge plastic cannula feasible.
- Avoid joints (e.g., wrist, antecubital) and limbs with impaired arterial, venous, or lymphatic circulation.
- Stabilize and secure the needle in place using dressing that does not obscure visualizing site (i.e., transparent).
- Keep the peripheral IV in place less than 24 hours.
- Confirm blood return prior to and at appropriate intervals during administration.

Central IV Access

- Preferred route of administration
- Implanted venous access port: Ascertain correct needle placement in septum.
- Implanted venous access port: Stabilize and secure the needle in place using dressing that does not obscure visualizing site (i.e., transparent).
- Peripherally inserted central catheter: Confirm no catheter migration out of the vein by measuring external catheter length and comparing to the original length.
- All: If catheter tip placement is questionable, assess prior to vesicant administration (i.e., chest x-ray to visualize catheter tip location).

Patient Related

- Instruct the patient about the risks of vesicant administration.
- Instruct the patient to notify a clinician if he or she experiences any pain or burning or change in sensation at the cannula, port site, or contralateral site.
- Instruct the patient to notify a clinician if he or she feels any fluid leaking on skin.
- Instruct the patient not to disturb or dislodge the cannula.
- The patient must verbalize understanding of important teaching points.

Clinician Related

- Clinicians who administer chemotherapy should demonstrate chemotherapy knowledge and skills.
- The nurse administering bolus or continuous infusion chemotherapy must do the following.
  - Organize tasks and materials and avoid distractions or keep them to a minimum during administration.
  - Confirm IV patency prior to starting and periodically throughout infusion.
  - Flush the catheter between agents.
  - Administer IV bolus agents per organizational policy.
  - Observe the peripheral or central IV site for evidence of extravasation (e.g., swelling, erythema).
  - Query the patient about onset of pain, burning, or discomfort in or about the peripheral or central IV site.
  - Stop infusion if any suspicion arises of extravasation.
  - Implement and document suspected or actual extravasation per institutional policy.

Figure 6. Strategies to Prevent or Minimize Extravasation Risk

Note. Based on information from Hadaway, 2004; Polovich et al., 2005; Schulmeister & Camp-Sorrell, 2000; Steele, 1998.

venous, and lymphatic), without sensory impairment, and where functionality would not be impaired or surgical repair be difficult after extravasation (Ener et al., 2004). The hand, wrist, and antecubital space are not optimal IV sites because of greater risk for significant injury and functional impairment with extravasation. The risks must be considered carefully when vein choice is limited (Luke, 2005; Steele, 1998). The muscled area of the forearm is preferable, and a more proximal IV site should be selected if the initial venipuncture is unsuccessful. Nonadherence to the distal-to-proximal technique increases the risk for extravasation injury because infusate could leak from holes in the vein caused by one or more venipuncture attempts above the ultimate IV site (Polovich et al., 2005; Steele).

Establishing patency of CVCs also is necessary before vesicant administration. No blood return in a new CVC (or loss of blood return in an established CVC) means that vesicant infusions should be delayed until correct placement is confirmed by chest x-ray or fluoroscopy (Schulmeister & Camp-Sorrell, 2000; Viale, 2003). Nurses cannulating an IVAP or reassessing the site must confirm correct needle location in the IVAP port before and during vesicant drug infusions by gently grasping and pressing the needle to determine that it is located through the septum and touching the port bottom, and by flushing with a push-pull technique (Camp-Sorrell, 2004). Peripheral IVs and IVAP needles must be stabilized securely and easily observable and IV tubing anchored to allow flexibility without disturbing connections. Patients and staff members must take care to avoid dislodging IV devices during transfers, transports, and clothing changes.

Controversies include order of vesicant administration and drug dilution (Hadaway, 2004). One notion is to administer vesicants first because veins will not have been irritated by other agents and because postvesicant flushing will preserve venous integrity (Goodman & Riley, 1997). Other clinicians purport that venous integrity is better preserved if vesicants are "sandwiched" between nonvesicants. No data support either technique as better. Diluting a vesicant by sidearm administration through a free-flowing IV line might decrease the volume of extravasated drug because subcutaneous swelling or redness would be recognizable early (Hadaway, 2004), although determining the exact volume of extravasate might be difficult. Another method uses two syringes, one with chemotherapy and the other with flush solution, alternately administered directly or through a stopcock into IV tubing (Peterson & Blendowski, 2001). Recommendations are not absolute; most importantly, nurses who administer vesicant agents must be able to articulate how they determine safe IV administration.

Case Study 3

A 54-year-old Caucasian woman was hospitalized for five days every four weeks to receive doxorubicin and vincristine over 96 hours through an implanted venous access port (IVAP). She was hospitalized on a nononcology unit, but the unit staff members had the chemotherapy policy available to them and could call oncology nurses for assistance. At 44 hours, the patient tripped on her IV tubing while ambulating, and the tubing became disconnected from the Huber point needle extension tubing. The patient called the nurse, who noted that the needle seemed to be in place. The nurse resecured the needle, placed a new dressing, and restarted the infusion. At 60 hours, the patient reported some "aching" in her ipsilateral shoulder. The medical oncologist examined the site and found slight redness that he attributed to venous thrombosis. The infusion was continued and completed, and the patient subsequently had progressive ulceration about the port pocket that required IVAP removal, surgery, and analgesic management. The nursing documentation during the doxorubicin infusion was "checked port site one time per shift."

Undisturbed, diligent monitoring for changes in blood return, IV flow, and site appearance during vesicant infusions is important in preventing extravasation. Nurses also must repeatedly query patients about any discomfort, burning or stinging, or other changes in IV site sensation. Severe tissue injury has occurred because clinicians did not appropriately respond to patients' reports of discomfort, believing that the sensations were "usual" discomfort from newly inserted IVs or CVCs. Nurses who cannot differentiate between usual and extravasation pain should stop infusion (Schulmeister & Camp-Sorell, 2000). Objective and subjective manifestations should be considered collectively. Thus, extravasation might be occurring if blood return is lost suddenly, but blood return alone does not exclude the possibility of extravasation, especially if new pain, swelling, or erythema occur (Hadaway, 2004). Blood return may be present if a cannula punctures a vein wall but actually is guided back into the injured vessel during aspiration.

Frequency of site monitoring depends on whether chemotherapy is bolus or continuous IV infusion. During bolus vesicant administration through peripheral IVs, blood return is checked every 2–5 ml (Boyle & Engelking, 1995; Polovich et al., 2005; Steele, 1998). No clear directive exists that the recommendation translates directly to bolus doses of vesicant chemotherapy administered through CVCs. During continuous IV vesicant administration, hourly assessments of the CVC are recommended (Hadaway, 2002). Peripheral and CVC catheters should be flushed with 5–10 ml of normal saline (or other appropriate solution) between drugs to prevent precipitation and to assess for swelling and discomfort with flush. Nurses also must remember that IV pumps and alarms cannot be relied on in case of extravasation because infiltration usually does not cause sufficient pressure to trigger an alarm (Marders, 2005).

Patient and Family Teaching

Patient and caregiver education is crucial, particularly for patients receiving ambulatory continuous IV vesicant chemotherapy, as well as for those who return home after vesicant chemotherapy in clinics. Verbal patient teaching should be supplemented with written instructions that reinforce the nature of potential damage; which manifestations to observe for; and to whom, when, and how to report potential problems. If conservative management is used after suspected or confirmed extravasation, patient instructions should state clearly whether and how warm or cold compresses should be applied, whether limb elevation is recommended, and when follow-up visits to assess the extravasation site will be scheduled.

Teaching is particularly challenging with patients who have language or communication barriers or those who are extremely anxious. Initial teaching should be done before any medications with CNS effects are administered, and nurses should review patient information at intervals to confirm continued understanding (Polovich et al., 2005).

Follow-up is crucial after suspected or confirmed extravasation. It may involve creative strategies to examine and document site appearance, especially when patients live long distances from treatment centers. Patients must reiterate that they know they must report the onset of or increasing local pain, swelling, redness, and especially development of blisters or skin breakdown. Patients who receive bolus or continuous vesicant therapy through a CVC need to restate other manifestations of intrathoracic extravasation that must be reported, including fever, cough, chest (pleuritic) pain, and upper extremity or neck swelling (Bozkurt et al., 2003). Written instructions might review actions to take in an emergency department, including appropriate referrals.

Documentation

Thorough documentation of appropriate care is the best defense in extravasation incidents to demonstrate that care met the nursing standard of practice. Conversely, inadequate documentation may be interpreted as failing to meet standards. Chemotherapy documentation forms specific to the setting may be useful to help nurses chart by exception, including pretreatment patient education regarding the risks of vesicant extravasation and what to report to the healthcare team (Polovich et al., 2005). Documentation during and after bolus chemotherapy should include the location and type of venous access and needle gauge, number and location of venipuncture attempts, the vein in which the drug was given, and how line patency was assessed (e.g., X ml brisk blood return every X minutes, continued site monitoring for swelling or discoloration, patient comfort, and IV flow pattern). Documentation of nursing care for patients receiving continuous chemotherapy should reflect what the patients were taught, frequency of assessment of insertion site and area, and what resources patients were given.

Documentation in cases of suspected extravasation also should include objective and subjective manifestations, the estimated amount and concentration of drug extravasated, and a thorough and accurate description of the IV method used (i.e., the actual vein or device cannulated). It also should describe responses to interventions (e.g., attempts to aspirate the vesicant from the IV line or subcutaneously, notification of a physician, antidotes administered, application of warm or cold compresses, limb elevation, as applicable). If site photographs are taken, institutional policy regarding patient consent and documentation must be followed. Follow-up monitoring also should be documented with clear and detailed descriptions of the affected area (including drawings when appropriate) and the patient's response to treatment.

Conclusion

Despite health care's current shortages in human resources, knowledgeable nurses, pharmacists, and physicians must be involved with all aspect of chemotherapy preparation, administration, and post-treatment monitoring. Collaborative professionals functioning as an interdisciplinary team are more likely to provide safe care and to identify opportunities for process improvement (e.g., ongoing staff development, access to relevant information, a nonthreatening system for reporting suspected and actual events). Effective extravasation management requires exquisite communication mechanisms, knowledge of current management approaches, and a clear understanding of each team member's responsibility. Oncology nurses are in strategic positions to mobilize multidisciplinary colleagues and to lead efforts to improve care.

Author Contact: Carmel Sauerland, RN, MSN, AOCN®, can be reached at caragho2@aol.com, with copy to editor at ONFEditor@ons.org.

References

Andris, D.A., & Krzywda, E.A. (1997). Catheter pinch-off syndrome: Recognition and management. *Journal of Intravenous Nursing, 20,* 233–237.

Baur, M., Kienzer, H.R., Rath, T., & Dittrich, C. (2000). Extravasation of oxaliplatin (Eloxatin®)—Clinical course. *Onkologie, 23,* 468–471.

Berghammer, P., Pohnl, R., Baur, M., & Dittrich, C. (2001). Docetaxel extravasation. *Supportive Care in Cancer, 9,* 131–134.

Boyle, D.M., & Engelking, C. (1995). Vesicant extravasation: Myths and realities. *Oncology Nursing Forum, 22,* 57–67.

Bozkurt, A.K., Uzel, B., Akman, C., Ozguroglu, M., & Molinas Mandel, N. (2003). Intrathoracic extravasation of antineoplastic agents: Case report and systematic review. *American Journal of Clinical Oncology, 26,* 121–123.

Camp-Sorrell, D. (2004). *Access device guidelines: Recommendations for nursing practice and education*. Pittsburgh, PA: Oncology Nursing Society.

Curran, C.F., & Luce, J.K. (1990). Extravasation of doxorubicin from vascular access devices. *Selective Cancer Therapeutics, 6,* 103–107.

Davies, A.G., Russell, W.C., & Thompson, J.P. (2003). Extravasation and tissue necrosis secondary to central line infusions [Letter]. *Anaesthesia, 58,* 820–821.

Debets, J.M., Wils, J.A., & Schlangen, J.T. (1995). A rare complication of implanted central-venous access devices: Catheter fracture and embolization. *Supportive Care in Cancer, 3,* 432–434.

Dorr, R.T. (1990). Antidotes to vesicant chemotherapy extravasations. *Blood Reviews, 4,* 41–60.

D'Silva, K., Dwivedi, A.J., Shetty, A., & Ashare, R. (2005). Pinch-off syndrome: A rare complication of totally implantable venous devices [Letter]. *Breast Journal, 11,* 83–84.

El Saghir, N.S., & Otrock, Z.K. (2004). Docetaxel extravasation into the normal breast during breast cancer treatment [Case reports]. *Anti-Cancer Drugs, 15,* 401–404.

Ener, R.A., Meglathery, S.B., & Styler, M. (2004). Extravasation of systemic hemato-oncological therapies. *Annals of Oncology, 15,* 858–862.

Foo, K.F., Michael, M., Toner, G., & Zalcberg, J. (2003). A case report of oxaliplatin extravasation [Letter]. *Annals of Oncology, 14,* 961–962.

Goodman, M., & Riley, M. (1997). Chemotherapy: Principles of administration. In S. Groenwald, M.H. Frogge, M. Goodman, & C.H. Yarbro (Eds.), *Cancer nursing: Principles and practice* (4th ed., pp. 356–357). Sudbury, MA: Jones and Bartlett.

Gorski, L.A. (2003). Central venous access device occlusions. Part 2: Nonthrombotic causes and treatment. *Home Healthcare Nurse, 21,* 168–171.

Hackert, T., Tjaden, C., Kraft, A., Sido, B, Dienemann, H., & Buchler, M.W. (2000). Intrapulmonal dislocation of a totally implantable venous access device. *World Journal of Surgical Oncology, 3*(19), 1–6. Retrieved June 6, 2005, from http://www.wjso.com/content/3/1/19

Hadaway, L.C. (2002). IV infiltration: Not just a peripheral problem. *Nursing 2002, 32*(8), 36–42.

Hadaway, L.C. (2004). Preventing and managing peripheral extravasation. *Nursing 2004, 34*(5), 66–67.

Heitmann, C., Durmus, C., & Ingianni, G. (1998). Surgical management after doxorubicin and epirubicin extravasation. *Journal of Hand Surgery (British and European Volume), 23B,* 666–668.

Kennedy, J.G., Donahue, J.P., Hoang, P., & Boland, P.J. (2003). Vesicant characteristics of oxaliplatin following antecubital extravasation. *Clinical Oncology, 15,* 237–239.

Kretzschmar, A., Pink, D., Thuss-Patience, P., Dorken, B., Reichart, P., & Eckert R. (2003). Extravasations of oxaliplatin. *Journal of Clinical Oncology, 21,* 4068–4069.

Langer, S.W., Sehested, M., & Jensen, P.B. (2000). Treatment of anthracycline extravasation with dexrazoxane. *Clinical Cancer Research, 6,* 3680–2386.

Lauvin, R., Miglianico, L., & Hellegouarc'h, R. (1995). Skin cancer occurring 10 years after the extravasation of doxorubicin [Letter]. *New England Journal of Medicine, 332,* 754.

Lemmers, N.W., Gels, M.E., Sleijfer, D.T., Plukker, J.T., van der Graaf, W.T., de Langen, Z.J., et al. (1996). Complications of venous access ports in 132 patients with disseminated testicular cancer treated with polychemotherapy. *Journal of Clinical Oncology, 14,* 2916–2922.

Lipson, J., Dibble, S., & Minarik, P. (Eds.). (1996). *Culture and nursing care: A pocket guide.* San Franciso: University of California, San Francisco, Nursing Press.

Loth, T.S., & Eversmann, W.W., Jr. (1991). Extravasation injuries in the upper extremity. *Clinical Orthopaedics and Related Research, 272,* 248–254.

Luke, E. (2005). Mitoxantrone-induced extravasation. *Oncology Nursing Forum, 32,* 27–29.

Marders, J. (2005). Sounding the alarm for IV infiltration. *Nursing 2005, 35*(4), 18, 20.

Mayo, D.J. (1998). Fibrin sheath formation and chemotherapy extravasation: A case report. *Supportive Care in Cancer, 6,* 51–56.

Peterson, J., & Blendowski, C. (2001). Tips for administering chemotherapy. In R. Gates & R. Fink (Eds.), *Oncology nursing secrets* (2nd ed., pp. 67–77). Philadelphia: Hanley and Belfus.

Polovich, M., White, J., & Kelleher, L. (Eds.). (2005). *Chemotherapy and biotherapy guidelines and recommendations for practice* (2nd ed.). Pittsburgh, PA: Oncology Nursing Society.

Raymond, E., Faivre, S., Woynarowski, J.M., & Chaney, S.G. (1998). Oxaliplatin: Mechanism of action and antineoplastic activity. *Seminars in Oncology, 25*(2, Suppl. 5), 4–12.

Rivory, L.P. (2002). New drugs for colorectal cancer—Mechanisms of action. *Australian Prescriber.* Retrieved October 9, 2006, from http://www.australianprescriber.com/magazine/25/5/108/10/

Rudolph, R., & Larson, D.L. (1987). Etiology and treatment of chemotherapeutic agent extravasation injuries: A review. *Journal of Clinical Oncology, 5,* 1116–1126.

Schrijvers, D.L. (2003). Extravasation: A dreaded complication of chemotherapy. *Annals of Oncology, 14*(Suppl. 3), 26–30.

Schulmeister, L., & Camp-Sorrell, D. (2000). Chemotherapy extravasation from implanted ports. *Oncology Nursing Forum, 27,* 531–538.

Schummer, W., Schummer, C., Bayer, O., Muller, A., Bredle, D., & Karzai, W. (2005). Extravasation injury in the perioperative setting. *Anesthesia and Analgesia, 100,* 722–727.

Scuderi, N., & Onesti, M.G. (1994). Antitumor agents: Extravasation, management, and surgical treatment. *Annals of Plastic Surgery, 32,* 39–44.

Shetty, P.C., Mody, M.K., Kastan, D.J., Sharma, R.P., Burke, M.W., Venugopal, C., et al. (1997). Outcome of 350 implanted chest ports placed by interventional radiologists. *Journal of Vascular and Interventional Radiology, 8,* 991–995.

Skeel, R.T. (1999). *Handbook of cancer chemotherapy* (5th ed.). New York: Lippincott Williams and Wilkins.

Stanford, B.L., & Hardwicke, F. (2003). A review of clinical experience with paclitaxel extravasations. *Supportive Care in Cancer, 11,* 270–277.

Starkhammar, H., Bengtsson, M., & Morales, O. (1992). Fibrin sleeve formation after long term brachial catheterisation with an implantable port device. A prospective venographic study. *European Journal of Surgery, 158,* 481–484.

Steele, C. (1998). Extravasation. In J. Yasko (Ed.), *Nursing management of symptoms associated with chemotherapy* (4th ed., pp. 191–224). Bala Cynwyd, PA: Meniscus Health Care Communications.

Vargel, I., Erdem, A., Ertoy, D., Pinar, A., Erk, Y., Altundag, M.K., et al. (2002). Effects of growth factors on doxorubicin-induced skin necrosis: Documentation of histomorphological alterations and early treatment by GM-CSF and G-CSF. *Annals of Plastic Surgery, 49,* 646–653.

Viale, P.H. (2003). Complications associated with implantable vascular access devices in the patient with cancer. *Journal of Infusion Nursing, 26,* 97–102.

Wickham, R. (1989). Extravasation from venous access devices. *Outpatient Chemotherapy, 3*(4), 3–4, 8, 10–11.