Vesicant Extravasation Part II: Evidence-Based Management and Continuing Controversies

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Purpose/Objectives: To review the literature, synthesize current recommendations, and discuss remaining controversies regarding vesicant extravasation management.

Data Sources: Published evidence-based reports, clinical articles, and anecdotal case reports about antineoplastic and nonantineoplastic vesicant agent management.

Data Synthesis: Prevention of vesicant extravasation sequelae requires knowledge about vesicant extravasation manifestations and differentiation of vesicant extravasation from other local IV site reactions. When evidence is weak or missing, logical application of data-based or empirical management strategies is critical. Actions may include timely administration of subcutaneous or topical antidotes, comfort measures, and surgical interventions to minimize the extent of tissue damage and morbidity should extravasation occur.

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

Implications for Nursing: Nurses who administer vesicant agents should understand the nursing and collaborative actions that should be taken to minimize patient morbidity, pain, and disability.

Key Points . . .

- Certain chemotherapy drugs and some nononcology agents have vesicant properties and, thus, are capable of causing progressive and persistent painful ulceration if incorrectly administered.
- Initial manifestations of extravasation may be subtle, and extravasation must be differentiated from other local paravenous reactions.
- Little evidence exists to guide management of vesicant extravasation; therefore, most suggestions to use local comfort measures, local antidotes, debridement, or other surgical interventions remain empirical and controversial.

Unrecognized, inadvertent extravasation by vesicant agents may lead to severe and progressive tissue damage if timely and appropriate local therapies are not implemented. Thus oncology and other nurses must be knowledgeable about which antineoplastic agents and other noncancer-related drugs and solutions (see Figure 1) can cause tissue damage if administered via IV. Nurses who administer vesicant agents must demonstrate adequate clinical knowledge and skills (see Part I, page 1134). In addition, nurses must be able to differentiate extravasation from other local reactions.

The reported incidence of vesicant extravasation is relatively low, and the likelihood that an individual nurse may be involved in extravasation is very small. Therefore, nurses and physicians may find differentiating between suspected and actual extravasation difficult. Furthermore, management recommendations, particularly for surgical interventions, have not been incorporated into current clinical practice. This article will discuss differentiating extravasation from other reactions and examine and organize the evidence for management of vesicant agents with locally or systemically administered antidotes, conservative measures, and surgical procedures.

Distinguishing Extravasation From Other Local Reactions

Confirming extravasation during drug administration can be challenging because manifestations vary. Furthermore, extravasation must be distinguished from other local reactions, particularly flare and recall. Patients with irritant reactions typically report aching, pain, or tightness; the vein may be erythematous, dark, and accompanied by swelling and loss of blood return (Goodman & Peterson, 1997; Polovich, White, & Kelleher, 2005). Flare reactions are rare (3%), localized,

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Antineoplastic Agents	Nonantineoplastic Agents
Cisplatin[a]	Calcium chloride (5.5%)
Dactinomycin	Calcium gluconate (10%)
Daunorubicin	Central venous nutrition
Doxorubicin	Dobutamine
Epirubicin	Dopamine
Idarubicin	Epinephrine
Mechlorethamine	Glucose (> 10%)
Melphalan	Mannitol (15%)
Mitomycin	Penicillin
Mitoxantrone[b]	Phenytoin
Oxaliplatin[c]	Potassium chloride (7.45%)
Paclitaxel	Radiograph contrast media
Vinblastine	Sodium bicarbonate (4.2%–8.4%)
Vincristine	Sodium chloride (10%)
Vindesine	Vancomycin
Vinorelbine	Vasopressin

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

[b] Mitoxantrone may act as a vesicant dependent on concentration.

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

Figure 1. Antineoplastic and Nonantineoplastic Agents Reported to Be Vesicants

Note. Based on information from Davies et al., 2003; Dorr, 1990; Ener et al., 2004; Loth & Eversmann, 1991; Luke, 2005; Polovich et al., 2005; Schrijvers, 2003; Schummer et al., 2005; Wickham, 1989.

self-limiting hypersensitivity responses along peripheral veins to an anthracycline or mechlorethamine (Mustargen®, Ovation Pharmaceuticals, Deerfield, IL). They are accompanied by itching and streaking erythema or hives along the affected vein, without edema or loss of blood return (Curran, Luce, & Page, 1990; Steele, 2001). Flare reactions typically resolve within one to two hours, rarely longer, but less than 24 hours (Rudolph & Larson, 1987). Flare (and irritant) reactions cannot occur during central venous catheter (CVC) infusions because infusates are diluted rapidly within large-diameter central veins. When a nurse cannot differentiate extravasation from another local reaction, the nurse should err on the side of caution and stop the infusion, proceeding as if extravasation has occurred.

Mitomycin and paclitaxel rarely cause recall, a delayed, local response at a prior administration site (Dorr, 1990; Meehan & Sporn, 1994; Shapiro & Richardson, 1994) (see Case Report 1). Patients who experience recall may have no evidence of extravasation during or directly following drug administration, but erythema, burning, and pain can progress to ulcers over days to weeks (Patel & Krusa, 1999).

Managing Suspected or Actual Extravasation

Indicators of peripheral IV extravasation range from immediate (pain or burning, obvious swelling, erythema, and loss of blood return) to none (manifestations appear hours to days later). Manifestations of CVC extravasation may be less obvious because of the variable and potentially large areas of extravasation (see Table 1). Pain is common, and its site varies according to the location of the extravasation such as the ipsilateral or contralateral neck or shoulder with punctured or eroded superior vena cava (Curran & Luce, 1990; Schulmeister & Camp-Sorrell, 2000). Similar discomfort can occur with retrograde migration or displacement of a catheter tip into the jugular vein or smaller central veins (e.g., internal mammary), which are more sensitive to irritating or vesicant agents (Wickham, 1989). Chest or mediastinal extravasation can cause substernal or other chest pain, burning or stinging, chest palpitations, fever, and respiratory symptoms (cough, dyspnea) secondary to pleural effusion or infiltrates (Anderson, Walters, & Hortobagyi, 1996; Bozkurt, Uzel, Akman, Ozguroglu, & Molinas Mandel, 2003; Curran & Luce, 1990; Viale, 2003).

Optimal management of vesicant extravasation requires ongoing communication and collaboration among team members. An extravasation kit that includes alcohol swabs, 3 cc syringes, 25-gauge needles, gauze squares, cold and warm compresses, and paper tape may be useful. Other useful kit items might include the institution's extravasation policy, management algorithm (or standing orders), and an extravasation documentation form for suspected or confirmed extravasation (Polovich et al., 2005). Some institutions include antidotes that should be supplied with syringes and needles, diluent, and reconstitution instructions. The kit should provide information about how to quickly obtain antidotes that are stored in the pharmacy (because of drug cost or shelf life).

A continuing dilemma in vesicant extravasation is the absence of evidence-based management strategies. Currently, the choices of therapeutic action are administration of antidotes through the existing needle or by subcutaneous injection, infiltration with an agent to dilute the extravasated agent, manual extraction of extravasate (i.e., through the IV or a subcutaneously placed needle), or simple supportive care (i.e., applying warm or cold), including anticipatory management with surgery as needed or immediate aggressive surgical intervention at the site (Langstein, Duman, Seelig, Butler, & Evans, 2002). Even though some of the interventions are considered standard, treatment decisions largely are based on what Langstein et al. termed "theoretical optimism" (p. 370).

Because of the paucity of data, many puzzles regarding measures for vesicant extravasation management remain

Case Report 1

A 48-year-old African American man was being treated with peripheral IV bolus mitomycin every four weeks in the clinic and had received it several times without incident. His last treatment was given through an IV started just above the wrist. The nurse used a 23-gauge winged-set needle secured with tape. The patient did not move the limb during treatment, and the nurse observed no resistance to IV flow, no swelling about the IV site, and brisk blood return by aspiration every 2–3 ml.

The patient returned to the clinic two weeks later for a white blood count. He had a 1.5 x 2 cm eschar-covered ulcer at the previous IV site. The ulcer was painful, and the hand and fingers distal to the ulcer were very swollen. Mitomycin recall was thought to be most likely, although actual extravasation could not be ruled out. The ulcer was debrided several times and ultimately healed by secondary intention. The patient's pain resolved, but he was left with limited range of motion in the wrist and hand.

Table 1. Extravasation From Central Venous Catheters

Event	Can Occur With	Etiology	Potential Objective Manifestations	Potential Subjective Manifestations
Needle dislodgement	IVAP	Improper cannulation (e.g., needle not in port) Needle not stable and secure Incorrect needle length (e.g. obese, large breasted)	Sudden swelling about port pocket or dependent chest No or loss of blood return Erythema around port or dependent chest or site Palpable subcutaneous fluid (crepitus) Fluid leaking around needle	Pain, stinging, or burning at port pocket or dependent chest
CVC damage	IVAP Tunneled CVC	Separation of port from catheter Nicked catheter at insertion	Swelling in port pocket or catheter tunnel with infusion No or loss of blood return Erythema around port or tunnel with infusion	Pain or burning around port or CVC tunnel with infusion
CVC pinch off	IVAP Tunneled CVC	Subclavian insertion medial to midclavicular line	Loss of blood return Swelling and erythema in clavicular area with infusion	Supra- or infraclavicular pain or burning with infusion
CVC tip displacement through SVC	IVAP Tunneled CVC PICC	Early: difficult insertion Late: unknown; thrombosis of SVC or great veins may increase risk.	Intractable cough with infusion Pleural effusions Abnormal chest radiography, computed tomography scan	Substernal chest pain Dyspnea Fatigue
CVC tip displacement from SVC	IVAP Tunneled CVC PICC	Unknown Possible increased risk with severe coughing	Loss of blood return Erythema in neck (if CVC in internal jugular vein)	Discomfort in ipsilateral chest about CVC or tip with infusion of irritants or vesicants
Fibrin sleeve and backtracking	IVAP Tunneled CVC PICC	Fibrin sleeves are nearly universal; thrombosis is uncommon.	Erythema at venous insertion site during infusion Backtracking can be confirmed by radiograph.	Discomfort at CVC insertion site

CVC—central venous catheter; IVAP—implanted venous access port; PICC—peripherally inserted central catheter; SVC—superior vena cava

unresolved. Controversial issues include the benefit of cold or heat, elevation of the affected limb, administration of local antidotes, and surgical interventions. Common recommendations are to leave the needle in place, aspirate residual drug from the IV (peripheral or CVC), avoid pressure on the site, and elevate the affected limb for 24 hours (Polovich et al., 2005; Schrijvers, 2003). Attempts to subcutaneously aspirate the port pocket if aspiration of extravasated agent through the IV needle is unsuccessful (after IV access port extravasation) also have been suggested (Wickham, Purl, & Welker, 1992).

Evidence for Vesicant "Antidotes"

With the exceptions of sodium thiosulfate and hyaluronidase (Vitrase®, ISTA Pharmaceuticals, Irvine, CA), data regarding other local antidotes is limited (see Table 2). Information about potentially useful local antidotes has been gleaned largely from case reports of peripheral extravasation, and there is little data about CVC extravasation (Anderson et al., 1996; Bozkurt et al., 2003).

Evidence-Based Antidotes

Sodium thiosulfate 1/6 molar (0.16 M) solution is the only antidote currently recommended by the Oncology Nursing Society for extravasation of mechlorethamine or concentrated cisplatin (> 20 cc of 0.5 mg/ml) (Polovich et al., 2005). Two ml of sodium thiosulfate for each 1 mg of mechlorethamine hydrochloride (or for every 100 mg of cisplatin) extravasated should be injected subcutaneously as soon as possible. Sodium thiosulfate also has been reported as effective in one instance of oxaliplatin (Eloxatin®, sanofi-aventis, Bridgewater, NJ) extravasation, but this has not been substantiated (Fenchel & Karthaus, 2000; Wilkes, 2005).

Evidence from animal and human studies supports the efficacy of hyaluronidase for vinca alkaloid or taxane extravasations (Bertelli et al., 1994; Fenchel & Karthus, 2000). Hyaluronidase modifies connective tissue permeability and enhances drug resorption from subcutaneous tissues. Hyaluronidase was not commercially available for three years because its manufacture was discontinued, but lyophilized ovine hyaluronidase now is marketed for the treatment of extravasation.

Potentially Useful Antidotes

Other potentially useful antidotes include dimethyl sulfoxide (DMSO), dexrazoxane, and growth factors. DMSO (70%–90% solution) is used in many countries to relieve pain, inflammation, interstial cystitis, arthritis, scleroderma, and

Table 2. Reported Interventions for Extravasation of Irritant or Vesicant Antineoplastic Agents

Drug	Classification	Temperature Application	Suggested Subcutaneous Antidote(s)
Cisplatin	Irritant (< 20 ml, 0.5 mg/ml) Vesicant (> 20 ml, 0.5 mg/ml)	Cold	Sodium thiosulfate 0.16 M[a]
Dactinomycin	Vesicant	Cold	None known
Daunorubicin	Vesicant	Cold	Topical DMSO 99% Dexrazoxane
Docetaxel	Irritant	Cold	Normal saline (dilutional effect) Hyaluronidase Topical DMSO 99%
Doxorubicin	Vesicant	Cold	Topical DMSO 99% Dexrazoxane G-CSF or GM-CSF
Epirubicin	Vesicant	Cold	Topical DMSO 99%
Idarubicin	Vesicant	Cold	Topical DMSO 99%
Mechlorethamine	Vesicant	None recommended	Sodium thiosulfate 0.16 M[a]
Mitomycin	Vesicant	Cold	Topical DMSO 99%
Mitoxantrone	Irritant Vesicant	Cold	Topical DMSO 99%
Oxaliplatin	Irritant Vesicant	Warm	Sodium thiosulfate 0.16 M[a]
Paclitaxel	Irritant Vesicant	Cold	Normal saline (exerts dilutional effect) Topical DMSO 99%
Streptozocin	Vesicant	Cold	None known
Vinblastine	Vesicant	Warm	Hyaluronidase
Vincristine	Vesicant	Warm	Hyaluronidase
Vinorelbine	Vesicant	Warm	Hyaluronidase

[a] Only agent currently recommended by Polovich et al. (2005)

DMSO—dimethyl sulfoxide; G-CSF—granulocyte–colony-stimulating factor; GM-CSF—granulocyte macrophage–colony-stimulating factor

Note. Based on information from Dorr, 1990; Ener et al., 2004; Schrijvers, 2003.

elevated intracranial pressure (Muir, 1996). However, the solution is approved for human use in the United States only as a preservative for transplant organs and for treatment of interstitial cystitis. Animal data have confirmed that topical DMSO has some efficacy in anthracycline and mitomycin extravasation, but human data are limited (Dorr, 1990; Steele, 2001). DMSO is believed to scavenge free radicals, causing potent vasodilation or pain reduction, anti-inflammatory mechanisms, or stabilization of cell membranes (Muir; Rospond & Engel, 1993). In one prospective study of 127 patients who had experienced extravasation of doxorubicin, epirubicin, mitomycin, mitoxantrone, cisplatin, carboplatin, ifosfamide, or fluorouracil, Bertelli et al. (1995) concluded that DMSO applied for seven days may prevent ulcer formation. In another study, 20 patients who had DMSO applied every six hours for 14 days after anthracycline extravasations did not develop ulceration (Olver et al., 1988). However, local DMSO application with intraperitoneal or IV dexrazoxane after anthracycline extravasation did not protect against injury and seemed to lessen the effectiveness of dexrazoxane (Langer, Thougaard, Sehested, & Jensen, 2006). DMSO may cause transient local burning, erythema, and urticaria during application (Ener, Meglathery, & Styler, 2004).

Dexrazoxane is used to prevent anthracycline-induced cardiotoxicity. The actual mechanism of cardioprotection is not known, but dexrazoxane may become an intracellular chelater and decrease free-radical formation. In mice, one to three intraperitoneal or IV doses of dexrazoxane administered within three hours of subcutaneous doxorubicin, daunorubicin, or idarubicin reduced the duration of extravasation lesions by 70% compared to mice treated with subcutaneous saline (Langer et al., 2006; Langer, Sehested, & Jensen, 2000). Dexrazoxane use for extravasation in humans is limited to case reports (Bos, van der Graaf, & Willemse, 2001; El Saghir & Otrock, 2004; Jensen, Lock-Andersen, Langer, & Mejer, 2003). For example, a patient who suffered extravasation of a large amount of docetaxel (180 mg diluted in 250 cc of normal saline) administered through an implanted port over one hour was given three doses (1,000 mg/m^2 within three hours of anthracycline extravasation, 1,000 mg/m^2 24 hours later, then 500 mg/m^2 48 hours later) and experienced no tissue necrosis (El Saghir & Otrock).

Growth factors regulate and coordinate wound healing, and they may play a role in altering damage from vesicant extravasation (Schrijvers, 2003). Animal data have shown that granulocyte macrophage–colony-stimulating factors ([GM-CSFs] sargramostim; Leukine®, Berlex, Montville, NJ) and granulocyte colony-stimulating factors ([G-CSFs] filgrastim; Neupogen®, Amgen, Thousand Oaks, CA) are significantly better than saline or no treatment to decrease the severity and extent of ischemic necrosis from doxorubicin (Vargel et al., 2002). In one study, control animals (no treatment) were most likely to develop extravasation injury and 92% experienced the largest ulcers, 50% of the saline-treated mice had smaller ulcers, and 17% of GM-CSF– and 3 (25%) of G-CSF–treated animals had the smallest ulcers ($p < 0.05$). GM-CSF and G-CSF also may be useful in treating doxorubicin extravasations in humans. For example, in a patient who did not respond to locally injected dexrazoxane, GM-CSF injected into an ulcerated area led to tissue granulation and complete healing over eight weeks (El Saghir & Otrock, 2004).

Discredited Antidotes

In the past, topical corticosteroids were advocated for doxorubicin extravasation because of their purported anti-inflammatory benefit. However, few inflammatory cells are found in tissues damaged by extravasation. Therefore, topical steroids probably have no value and may lead to greater skin ulceration after vinca alkaloid or anthracycline extravasation (Dorr, 1990; Langer et al., 2000). Conversely, oral dexamethasone for 10–14 days may be beneficial to reduce inflammation after oxaliplatin extravasation (Kretzchmar et al., 2003; Sorich, Taubes, Wagner, & Hochester, 2004).

Conservative Measures

Conservative measures, including application of cold or heat and elevating the affected extremity, have been used empirically for years (Rudolph & Larson, 1987). However, no data exist to confirm their benefit, from attempting to

Case Report 2

A 43-year-old Caucasian female patient came to the clinic to receive cycle three of doxorubicin and cyclophosphamide, which was to be given through her implanted venous access port (IVAP). She was wearing a v-neck pullover, and the nurse who cannulated the IVAP visualized the area about the port by pulling the shirt toward the patient's shoulder. The nurse stabilized the needle in the port with tape and easily obtained a brisk 3 ml blood return. The nurse flushed the IVAP with 10 cc normal saline and began the chemotherapy by slow IV bolus. She obtained a brisk blood return every five minutes, but toward the end of the infusion, the patient reported "itchy" discomfort in the lower ipsilateral breast. She reported no swelling, erythema, or discomfort around the port itself.

The nurse took the patient into the bathroom where she could disrobe in private after the infusion. The lower half (dependent) portion of the breast was noticeably reddened, and the patient reported increasing pain. The patient was sent home with instructions to apply ice to the site for 15 minutes four times a day and was followed in the clinic a week later. At this time, the lower breast skin was somewhat blistered, but conservative measures were continued because the patient's discomfort was characterized as "mild to moderate." By the next follow-up, the patient had an ulcerated area and severe pain. She was not moving her arm because activity increased the pain. Surgical debridement was done several times, but the patient ultimately required a simple mastectomy and a 12 x 12 cm skin graft.

withdraw extravasated vesicant, or from instilling antidotes to successfully treat extravasation (Schummer et al., 2005). Cold compresses are proposed for doxorubicin extravasations because cold causes vasoconstriction, which may decrease local dispersion, slow cellular uptake of drug, and perhaps decrease extent of injury (Dorr, 1990; Polovich et al., 2005). Cold has no benefit after taxane extravasation, however, and cold is controversial after oxaliplatin extravasation because it may or may not induce acute neuropathy (Foo, Michael, Toner, & Zalcberg, 2003; Kretzchmar et al., 2003; Schrijvers, 2003; Steele, 2001; Wilkes, 2005). On the other hand, warm compresses are recommended after extravasations of vinca alkaloids, which are non-DNA binders, to induce vasodilatation and enhanced drug dispersion and tissue uptake (Goodman & Riley, 1997). Intermittent applications (i.e., every four hours for 15 minutes for 24–48 hours) of warm or cold compresses typically are recommended (Polovich et al., 2005; Steele, 2001).

Surgical Interventions

The appropriate timing of surgery for extravasation still is not clearly defined, and some clinicians advocate a conservative approach (Anderson et al., 1996; Bozkurt et al., 2003). However, diligent and frequent patient follow-up is critical to identifying early blistering or ulcers that necessitate debridement or more aggressive plastic surgery interventions (Rudolph & Larson, 1987). A plastic surgical consultation is recommended after large volume vesicant extravasations, when a patient has severe pain, or if healing has not occurred one to three weeks after extravasation (Ener et al., 2004; Polovich et al., 2005). However, the volume that constitutes a large extravasation is undefined, the time point and pain intensity that warrant consultation are not clear, and one to three weeks is a relatively large time interval.

A wait-and-see approach is not appropriate if a patient has persistent pain, swelling, and erythema; blistering; or early necrosis that may result in an enlarging eschar-covered ulcer surrounded by a 2–3 cm rim of erythematous, painful skin that cannot heal (Rudolph & Larson, 1987). Such a patient should be seen by a plastic or hand surgeon who is knowledgeable about extravasation (see Case Report 2). Furthermore, as pointed out in Part I, permanent functional impairment may result after protracted tissue exposure, and delaying surgery may necessitate repeated debridement, wide excision, and split thickness skin grafting or flap reconstruction (Boyle & Engelking, 1995). For instance, two patients with peripheral doxorubicin or epirubicin extravasation referred for surgery one month after extravasation did not regain full function in the involved arm, whereas a third patient who had local debridement on days 2 and 14 regained full movement (Heitmann, Durmus, & Ingianni, 1998). Similarly, progressive CVC extravasation injury may require mastectomy or other aggressive surgery (Schulmeister & Camp-Sorrell, 2000). Early surgical consultation and conservative local intervention (within 24 hours) of anthracycline extravasation thus may be more prudent (see Case Report 3). One algorithm for addressing vesicant extravasation (as shown in Figure 2) focuses on timing of surgical intervention (Schummer et al., 2005).

Another approach is based on evidence that the local toxicity of vesicant agents is directly proportional to the concentration and amount injected. Scuderi and Onesti (1994) advocated injecting large amounts of sterile normal saline (NS) into an extravasation site to dilute the extravasated drug and induce local edema that activates reabsorption and facilitates drug uptake into bloodstream. When patients with confirmed peripheral extravasation of doxorubicin or vinca alkaloid had NS (20–90 ml) injected locally within 24–48 hours after extravasation and repeated three to six times over the next few days, 93% experienced resolution of pain and erythema by day 4, induration by day 7, and superficial ulceration in 10–14 days. This technique was unsuccessful in patients with deep ulcerations who required surgery, sometimes with local or free-flap reconstruction.

Case Report 3

An 18-year-old Caucasian man's treatment was continuous infusion doxorubicin over 120 hours that was concentrated and administered through his implanted venous access port (IVAP) by ambulatory infusion pump at home. On day four (a Saturday), his IVAP site felt "sore," so the patient and his parents went to the emergency department (ED) of a local hospital. The ED staff discontinued the doxorubicin and decannulated his IVAP. The patient was discharged home with instructions to see his oncologist in two to three days.

When he came to the clinic the following Monday, his chest around the IVAP was mildly edematous and moderately erythematous with an area of blanching about the port. He denied pain. The nurse instructed him to apply ice packs (a bag of frozen peas wrapped in a towel) to the area for 15 minutes every two hours and return to the clinic the following morning. On Tuesday, the erythema, blanching, and swelling had decreased. The patient was seen by the plastic surgeon, and the decision was made to remove the IVAP. Fluorescein dye was instilled into the port pocket at removal that confirmed the presence of doxorubicin. The site was flushed copiously with sterile normal saline, and the incision was closed. Healing was uneventful with no evidence of extravasation injury.

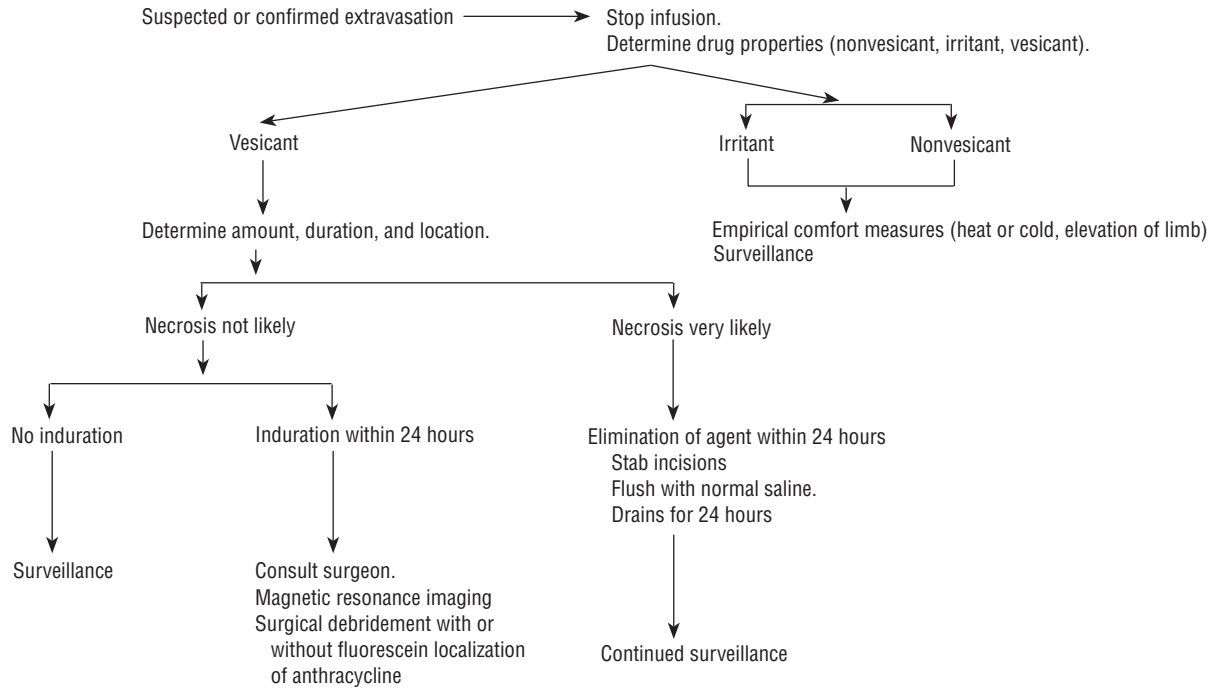

Figure 2. Proposed Strategy for Management of Extravasation

Note. From "Extravasation Injury in the Perioperative Setting," by W. Schummer, C. Schummer, O. Bayer, A. Muller, D. Bredle, & W. Karzai, 2005, *Anesthesia and Analgesia, 100,* p. 725. Copyright 2005 by *Anesthesia and Analgesia.* Adapted with permission.

A similar early "washout" technique has been used to successfully prevent progressive injury in hands after vinca alkaloid or anthracycline extravasation (Giunta, 2004). Washout is recommended within six hours of extravasation, if possible. Two or three incisions were made in the extravasation site and the area was infiltrated with 300–500 ml NS administered through a large catheter. The saline flushed out of the other incisions and also could be withdrawn using a smaller catheter. All patients treated in this manner experienced normal healing and no impairment of range of motion or loss of function.

Other clinicians advocate a similar technique to washout vesicant agents by placing stab incisions as soon as possible after extravasation and inserting surgical drains. Before a washout procedure, magnetic resonance imaging may be used to demarcate the area of injury and subsequent surgical approach. After confirmed norepinephrine extravasation, one group of patients had extravasation sites flushed with 500 ml of NS (Schummer et al., 2005). Drains were kept in place for at least 24 hours to eliminate the vesicant from the site, and no patients experienced local necrosis.

Other techniques that may demonstrate the presence of doxorubicin in local tissues are ultraviolet (UV) light and fluorescein (Fluoresite®, Alcon, Ft. Worth, TX). UV light causes the tissue or ulcer to glow a dull red, and IV fluorescein aids in defining necrotic tissue (Rudolph & Larson, 1987). If early and thorough debridement is not done after confirmed doxorubicin extravasation, the injury progressively enlarges and becomes encased by thick, leathery eschar surrounded by a large (2–3 cm) rim of erythematous and painful skin. Healing cannot occur in an area covered by eschar, and large ulcers require excision of the entire reddened and painful area around the ulcer to remove damaged and doxorubicin-containing tissue.

Managing Pain Accompanying Extravasation Injury

Progressing extravasation injuries with blistering, ulceration, or necrosis are painful. Nondrug conservative measures (i.e., warm or cold compresses) are unlikely to alleviate discomfort. Although nonopioids may be somewhat beneficial, patients reporting moderate to severe pain usually

1. Current incidence of vesicant chemotherapy extravasation in peripheral and central venous access devices
2. Nurses' awareness of the vesicant potential of nonchemotherapy agents
3. Effect of nurse education on extravasation occurrence
4. Methods to increase patient knowledge about extravasation
5. Relationship between patient education and early recognition and amelioration of extravasation effects
6. Potential efficacy of combination vesicant antidote regimens
7. Effect of antidote doses and schedules on injury outcomes after vesicant extravasation
8. Effects of surgical intervention in relationship to procedures, timing, and concomitant local therapies

Figure 3. Areas of Potential Research Regarding Vesicant Extravasation

require an opioid for adequate pain control, especially if the pain interferes with movement of the extremity or chest, daily activities, and rehabilitative efforts. Doses should be titrated aggressively to relief, and adverse effects should be anticipated and managed, particularly prophylaxis for constipation.

Conclusion

Interventions to decrease morbidity resulting from vesicant extravasation, including conservative measures, antidotes, surgical interventions, and symptom management, still are not defined clearly and applied uniformly. However, nurses involved with or caring for patients receiving vesicant agents must be knowledgeable about current evidence and empirical measures and should be involved in developing institution-specific interdisciplinary management strategies. Furthermore, several questions and controversies about vesicant extravasation management still require further study (see Figure 3), and nurses can be involved in addressing these issues. They may help to identify predictors of extravasation injury severity and strengthen the evidence for effective prevention and intervention measures that minimize morbidity and maintain patient quality of life.

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