LETTERS TO THE EDITOR

Article on Mitoxantrone-Induced Extravasation Raised Useful Questions

The case study on mitoxantrone-induced extravasation presented in the "Clinical Challenges" column (Vol. 32, pp. 27–29) is a valuable addition to the scant published documentation of these types of injuries. I applaud the case study author for sharing her observations and photographic documentation of mitoxantrone-induced tissue necrosis and taking action to review the literature and change nursing practice at her institution.

The authors of the column raised intriguing questions about mitoxantrone classification and administration. At the case study author's institution, mitoxantrone was added to the institution's vesicant list. The reclassification appears to be based on the author's experience of personally observing a mitoxantrone extravasation injury and the classification of mitoxantrone as a vesicant by the Oncology Nursing Society and authors of two journal articles.

Mitoxantrone-induced tissue necrosis has been documented in case reports (Levin, Caravone, & Geiser, 1996; Peters, Beijnen, & ten Bokkel Huinink, 1987) and research studies (Bertelli et al., 1995 [13 cases]; Tsavaris et al., 1990 [7 cases]), so additional evidence indicates that mitoxantrone has vesicant properties. As noted in the column, the manufacturer of mitoxantrone does not explicitly state that mitoxantrone is a vesicant; however, it advises that "care should be taken to avoid extravasation" and that "signs or symptoms of extravasation" include "burning, pain, pruritus, erythema, swelling, blue discoloration, or ulceration" (Serono, Inc., 2003, p. 33).

Mitoxantrone is classified as an antracenedione and has a mechanism of action that is similar to the action of the anthracylines, such as doxorubicin and daunorubicin, which are known vesicants. Mitoxantrone intercalates into DNA through hydrogen bonding, which causes crosslinks and DNA strand breaks. It also interferes with RNA synthesis and is an inhibitor of topoisomerase II (an enzyme responsible for uncoiling and repairing damaged DNA). The mean alpha half-life of mitoxantrone is 6–12 minutes; therefore, it is rapidly tissue bound if it inadvertently extravasates from a vein (Fox & Smith, 1990; Serono, Inc., 2003).

The collective documented evidence of 23 mitoxantrone extravasation injuries, manufacturer's recommendations, and pharmacology of the drug suggest that mitoxantrone is indeed a vesicant and should be classified as such. The author notified her institution's pharmacy and the U.S. Food and Drug Administration of the mitoxantrone extravasation injury. In addition, nurses who observe tissue injury secondary to extravasation of drugs classified by their manufacturers as nonvesicants, irritants, or exfoliants (a term commonly used in the United Kingdom) also should notify the drug's manufacturer and perhaps advocate for revision of package insert information. (I sent a copy of the article to Serono, Inc., along with a copy of this letter, and have asked for a response.)

Whenever it is suggested that oncology drugs are reclassified, an important question needs to be asked, and that is how will a change in drug classification affect clinical practice? In the case of mitoxantrone, reclassification as a vesicant would warrant implementation of vesicant precautions when administering the drug. Quite simply, nurses would use greater care when administering mitoxantrone.

Nurses would inform patients about the risk for extravasation-induced tissue injury, instruct patients to report pain or any unusual sensations at the infusion site, and advise patients to refrain from movement during vesicant administration. Nurses would insert a new IV catheter using a "clean stick" (nonprobing) technique and administer the mitoxantrone in accordance with vesicant administration guidelines, which include verifying a blood return prior to and every 2–3 ml during an IV bolus (push) or monitoring an infusion approximately every five minutes (Brown et al., 2001). Also, as noted in the column, veins in the forearm as opposed to hand are preferred for vesicant administration because the dorsum of the hand has little subcutaneous tissue and vesicant extravasation injuries in this area often are severe.

Mitoxantrone is used as a treatment for multiple sclerosis and, depending on the setting, is administered by oncology or nononcology nurses. Changing the classification of mitoxantrone to vesicant may have practice implications in settings where policies dictate that vesicants must be administered by chemotherapy-certified nurses.

Although it may be tempting to conclude that the patient's extravasation injury would not have occurred if mitoxantrone had been classified as a vesicant, vesicant extravasation injuries still can occur even when vesicant administration precautions are utilized. Several factors that increase the risk for vesicant extravasation were described in the column. An additional factor, patient movement, merits mention. Movement of arms and hands may increase the risk for peripheral vesicant extravsation, and arm and shoulder movement may increase the risk of vesicant extravasation from an implanted port. Advising patients to refrain from movement during vesicant administration may help decrease the risk for extravasation.

Suspected vesicant extravasations must be assessed and managed promptly. If a mitoxantrone extravasation is known or suspected, elevation and ice packs are recommended by the manufacturer. The manufacturer further states that "because of the progressive nature of extravasation reactions, the area of injection should be frequently examined and surgery consultation obtained early if there is any sign of a local reaction" (Serono, Inc., 2003, p. 33).

Tsavaris et al. (1990) conservatively treated seven mitoxantrone extravasation injuries with hydrocortisone and antibiotic ointment. Time to recovery ranged from 6–48 days, and none of the patients required surgery. Bertelli et al. (1995) treated 13 mitoxantrone extravasations with topical dimethylsulfoxide (DMSO) (99% solution, with four drops applied per 10 cm^2 of skin surface every eight hours for one week) and observed that 11 of the 12 evaluable patients had complete recovery within one week and one experienced residual hyperpigmentation. Mitoxantrone extravasation details, including drug concentration, estimated amount extravasated, location of extravasation, and photographs, were not included in the study report. Further evaluation of DMSO treatment of vesicant extravasations is needed before it can be advocated as a mitoxantrone extravasation treatment. Also, medical grade 99% DMSO solutions are not available in the United States but are available in other countries.

In addition to changing the classification of mitoxantrone at the author's institution, another change was to begin administering it as an IV push through a free-flowing IV line rather than as an infusion. The manufacturer states that doses of mitoxantrone should be diluted to at least 50 ml with either normal saline (NS) or dextrose 5% (D5W). It may be further diluted with NS, D5W, or D5W with NS. The diluted solution is administered into

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the tubing of a freely running infusion of NS or D5W over a period of not less than three minutes (Serono, Inc., 2003). Perhaps the author's rationale for IV push administration of mitoxantrone is to ensure that the nurse would remain with the patient and continuously monitor mitoxantrone administration. However, short-duration vesicant infusions can be administered safely when vesicant precautions are used. The key safety factor is nurse monitoring and not method of administration. Also, drugs should be administered in accordance with manufacturers' instructions, and if clinical practice deviates from these instructions, some evidence should support the deviation. Institutional protocols also need to be revised to support the practice change. Lastly, the drug manufacturer should be contacted to explore changing the drug's administration instructions.

Vesicant extravasation injuries are rare events. Their rare occurrence is why so little is known about them and their management. Most are managed according to institutional guidelines, which vary widely, and very few are reported in the literature. In the United Kingdom, the National Extravasation Information Service (www.extravasation.org.uk) is collecting data in an effort to learn more about the incidence and treatment of vesicant extravasation injuries. No similar organization exists in the United States, so nurses need to continue sharing accounts of vesicant extravasations and their management. I know I join other readers in thanking the authors and case study patient for sharing important, clinically relevant information about mitoxantrone extravasation.

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Article on Risk Modeling Addressed Little-Studied Topic

It is with great interest that we read Ropka, Padilla, and Gillespie's article, "Risk Modeling: Applying Evidence-Based Risk Assessment in Oncology Nursing Practice" (Vol. 32, pp. 49–56). The authors should be applauded for addressing concepts of risk assessment and management of risk in the context of evidence-based research. To date, little evidence-based research has covered the topic of risk assessment. The authors wrote about identifying patients at high risk for cancer, which is especially important.

Oncology nurses, as patient educators, can use risk modeling and assessment to educate individuals and families not only about risk of developing a disease or complication but also how to manage associated risks. This article encourages all oncology nurses to think of risk assessment not only in the context of prevention and early detection of malignancy, but also as a strategy to manage the myriad of side effects associated with cancer and its treatment.

The authors presented a nice overview of the widely used Gail, Claus, and BRCAPRO risk assessment models and suggested "the BRCAPRO model can estimate individual breast cancer risk based on the probability that a family carries a mutation in one of the BRCAPRO genes" (p. 51). We would like to note that BRCAPRO calculates the an individual's probability of carrying a *BRCA1* or *BRCA2* gene mutation based on family history of breast and/or ovarian cancer using Bayes' theorem (Euhus et al., 2002). Although, as the authors stated, BRCAPRO can calculate individual breast cancer probabilities based on the probability of carrying a *BRCA* mutation (Euhus, 2001), clinically the model is primarily used for assessing whether it is appropriate to offer genetic testing based on the probability that an individual carries a *BRCA1* or *BRCA2* gene mutation (BayesMendel Lab, 2004).

This point illustrates the complexities of using risk assessment information in an evidence-based practice. Nurses need to be sure that they choose the correct model to make the risk assessment and explain to the individual the rationale for the selection of that model as well as any inherent strengths or weaknesses (Mahon, 2003). Evidence-based risk assessment was summarized nicely by the authors, and the tables explaining terms are especially useful. The authors should be commended for addressing an important aspect of clinical practice in the context of evidence-based practice.

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The Author Responds

Thank you for the clarification of our statement regarding the BRCAPRO model and its use in cancer risk assessment. Quantitative prediction models used in breast cancer risk assessment can be divided into two major categories: (a) epidemiologic and (b) genetic (Rubenstein, O'Neill, Peters, Rittmeyer, & Stadler, 2002). The Gail and Claus models are epidemiologic tools, used to estimate an unaffected woman's absolute risk of developing breast cancer over a specified period of time. In contrast, genetic prior probability models, such as Couch (University of Pennsylvania) (Couch et al., 1997), Shattuck-Eidens (Domchek et al., 2003), Myriad (Frank) (Frank et al., 1998), and Berry-Parmigiani-Aguilar (BRCAPRO) (Berry et al., 2002), estimate the likelihood of detecting a *BRACA1* or *BRCA2* mutation in an individual (which also can indirectly reflect breast cancer risk). They give complementary information. Other related models focus on specific populations, such as Ashkenazi Jewish heritage (King, Marks, Mandell, & New York Breast Cancer Study Group, 2003), or on identifying individuals who should be referred for genetic counsel-

ing (Hampel, Sweet, Westman, Offit, & Eng, 2004).

My coauthors and I would like to take this opportunity to emphasize a few related points.

- Cancer risk models should be considered in light of the assumptions on which they are based, including the populations in which they were developed, their limitations, their best use, and whether they are useful for clinical purposes as opposed to research (Claus, 2001; Marroni et al., 2004).
- The breast cancer risk assessment models are merely tools to be used in the context of clinical expertise and clinical judgment and not as a substitute for them.
- Cancer risk assessment, regardless of which healthcare provider is involved, is but one piece of a comprehensive process that also should include cancer risk education and counseling—consisting of assessment, education, information exchange, and psychosocial counseling.
- For those at higher risk and those at general population risk, the goal in the end is to have individuals and families who understand what their cancer risk means to their health and what they can do about it (National Comprehensive Cancer Network, 2003; Pichert, Bolliger, Buser, Pagani, & Swiss Institute for Applied Cancer Research Network for Cancer Predisposition Testing and Counseling, 2003; Sauven & Association of Breast Surgery Family History Guidelines, 2004; Washburn et al., 2005).

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Share Your Stories of Nursing at War

I would like to let Oncology Nursing Society (ONS) members know about an exciting project being carried out at the Brigham Young University College of Nursing. I am engaged in a project called Nurses at War. Nurses rarely tell their stories. They assume that they are just doing what they have to do or what they are expected to do and that it is nothing special. However, I know that nurses have great stories to tell. Those of us who served in military organizations during periods of armed conflict are a special group who made a special contribution to the profession. We have exciting experiences to share. Many of these stories already have been lost as nurses from former wars have become unable to tell them. What a loss to our profession.

The goal of the project is to record the experiences of nurses who have served during armed conflict. These stories will be archived in the L. Tom Perry Special Collections department of the Harold B. Lee Library here at Brigham Young University. Archiving in a permanent location ensures that the accounts will not be lost and will be available for study by students in nursing, history, and women's studies, as well as other interested persons. The project already has collected about 125 accounts of nurses from both World Wars, Korea, Vietnam, Operation Desert Storm, and Operation Iraqi Freedom, as well as Red Cross volunteers who assisted in the 9-11 disaster, nurses who were benefited by the Cadet Nurse Corps program during World War II, and nurses who served in the Japanese internment camps in the United States during World War II. Though archiving the accounts is the most important goal for the project, the materials also have been shared in presentations and publications, thus assisting the public to better understand the role of nurses in wartime and enriching the nursing profession. A book that includes accounts received early in the project is currently in process of publication.

I would like to invite members of ONS who may have served in any capacity in any branch of the U.S. military or any other nation's military organization during a time of war to share their stories with the Nurses at War project. If an ONS member did not personally serve but knows someone who did serve or has letters, diaries, accounts, or memorabilia from nurses who served and are longer no able to share their own accounts, please let the project know. I especially invite nurses whose oncology experiences began in the military, as mine did, or whose oncology experiences were impacted by their military experience to be sure to contribute that part of their experience to the project. The sharing of such experiences will help to enrich us as an organization and make others aware of the history and contribution of oncology nursing to the profession. Nurses with stories to share can e-mail me at Patricia_Rushton@byu.edu, call my office phone (801-422-5375), or visit the project's Web site at http://nursing.byu.edu/nursesatwar. Accounts can be submitted via the project's Web site as well.

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