A group of EONS members has worked hard to consolidate much of the existing knowledge on extravasation of cancer therapies in order to develop a new guideline for the web-based toolkit. This module is a practical guide to extravasation management which provides advice on how to deal with extravasations and how to implement the new guidelines in day-to-day clinical practice. The Extravasation Guideline is in the same interactive format as the previous modules in the EONS Guidelines Implementation Toolkit.

The goal of the guideline is to help nurses understand and recognise extravasation and improve the prevention and overall management of extravasations in cancer patients. The more specific targets and aims are to:

- increase nurses’ knowledge of specific elements of extravasation including early recognition;
- implement appropriate interventions;
- update and inform nurses of the current management standards from guidelines and protocols;
- encourage adoption of procedures for extravasation that fit with the current guidelines

The toolkit has six sections. Below is a brief description of the content of each of these sections.

**What is extravasation?**
Extravasation refers to the process by which one substance (e.g., fluid, drug) leaks into the surrounding tissue (1). In terms of cancer therapy, extravasation is defined as the accidental leakage of chemotherapy from its intended compartment (the vein) into the surrounding tissue (2). A broader definition of extravasation includes the injury which occurs following extravasation. The degree of injury can range from a very mild skin reaction to severe necrosis depending on the type of substance which has extravasated (1–4). The types of extravasation are explained in the guidelines.

**When does extravasation occur?**
Extravasation is not as rare as some people may think. In cancer therapy experts estimate that it accounts for 0.5% to 6.0% of all adverse events associated with treatment (4). But, when you consider that adverse events with cancer therapy are quite common, the absolute number of extravasations which take place is significant (5).

Some extravasations are caused by an error in the intravenous (i.v.) procedure (4, 6). Cancer patients receiving chemotherapy may have multiple risk factors that make i.v. infusion difficult. For example, patients with a tendency for thin, fragile and mobile veins are at risk of extravasation (4). In addition to factors relating to the procedure and to the patient, factors associated with the equipment and material used, concomitant medications and the treatments themselves can also increase the likelihood of extravasation. The most common factors known to increase the risk of extravasation are listed in the guidelines.

**What are the implications of extravasation?**
Extravasation is to be avoided. Although not all extravasation incidences result in ulcerative and necrotic tissue damage, patients may still experience pain and discomfort as well as indirect consequences such as disruption of treatment and prolonged hospitalisation for the management of extravasation (3, 4). The specific symptoms of extravasation, as well as their wider consequences, are discussed in this section of the guidelines and these include the initial symptoms, tissue damage, surgery, impact on cancer therapy, and other consequences.

**How is extravasation recognized?**
It is critical that an extravasation is recognised and diagnosed early. The most effective way to assess extravasation in its early stages is to be aware of and act on all relevant signs and symptoms. Signs and symptoms can be gathered from simple visual assessment of the injection site and careful observation of the i.v. device. Once an extravasation is suspected to have occurred, it is important to rule out other possible conditions, such as flare reaction or phlebitis (4, 6). The quality of the nursing assessment during administration of cytotoxic drugs plays a key role in minimising frequency and severity of extravasations, since delays in the recognition and treatment of vesicant extravasation increase the likelihood of developing tissue damage and necrosis (4, 7). If there is any doubt as to whether or not an extravasation has occurred, stop the infusion and ask for advice. Early detection of an extravasation is often based on the following factors: patient reporting, visual assessment, checking the infusion line, and distinguishing extravasation vs. other conditions.

**How is extravasation prevented?**
The most important approach to minimising the consequences of extravasation is prevention (8). Healthcare professionals involved in the handling and administration of i.v. cancer therapies should become familiar with their local procedures and protocols. Healthcare professionals should develop an understanding of the important precautionary steps that should be taken to avoid extravasations and their resulting injuries. This section in the guidelines provides advice for good practice in order to help prevent extravasation and minimise injury.

**How is extravasation managed?**
The management of extravasation includes detection, analysis and action. The first course of action is to stop the infusion, aspirate as much of the infusate as possible, mark the affected area and then remove the cannula (while continuing to aspirate from the extravasation site). Elevate the affected limb if required. If possible take a photo of the extravasated area. Then, depending on the drug being infused, the correct protocol should be followed to determine the next steps.

If the drug is a non-vesicant, application of a simple cold compress and elevation of the limb may be sufficient to limit the adverse effects (9). In contrast, the extravasation of a vesicant requires several steps and differs for the various classes of drug. There are two main approaches to limiting the damage caused by extravasation: localisation and neutralisation or dispersion and dilution (9).

The localise and neutralise strategy involves the use of cold compresses to limit the spread of the extravasation. Antidotes such
as Savene™ for anthracycline extravasations may be used to counteract vesicant actions. The disperse and dilute strategy involves the initiation of appropriate measures for the extravasation of vinca alkaloids, the use of warm compresses to prompt vasodilation and encourage blood flow in the tissues which helps to spread the extravasation and the use of hyaluronidase to dilute the infusate.

Antidotes are agents applied or injected to the extravasated area to counteract the effects of the infiltrated agent. They form an important part of the “localise and neutralise” and the “disperse and dilute” strategies.

The table below (adapted from the Extravasation Guidelines) provides a quick reference for antidote use after extravasation:

<table>
<thead>
<tr>
<th>Extravasated drug</th>
<th>Suggested antidote</th>
<th>Level of evidence</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracyclines</td>
<td>Savene™ (dexrazoxane)</td>
<td>Efficacy in biopsy-verified anthracycline extravasation has been confirmed in clinical trials</td>
<td>3 day course of Savene™ treatment: 1000 mg/m² IV as soon as possible (no later than 6 hours) after extravasation on day 1; 1000 mg/m² on day 2; and 500 mg/m² on day 3 See Appendix 4 for full details</td>
</tr>
<tr>
<td>Anthracyclines</td>
<td>Topical DMSO (99%)</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>Apply locally as soon as possible. Repeat every 8 hours for 7 days See Appendix 5 for full details</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>Topical DMSO (99%)</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>Apply locally as soon as possible. Repeat every 8 hours for 7 days See Appendix 5 for full details</td>
</tr>
<tr>
<td>Mechloretamine (Nitrogen mustard)</td>
<td>Sodium thiosulfate</td>
<td>Due to lack of evidence, this antidote is not recommended</td>
<td>2 mL of a solution made from 4 mL sodium thiosulfate + 6 mL sterile water for subcutaneous injection</td>
</tr>
<tr>
<td>Vinca alkaloids</td>
<td>Hyaluronidase</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>150-1500 IU subcutaneously around the area of extravasation See Appendix 6 for full details</td>
</tr>
<tr>
<td>Taxanes</td>
<td>Hyaluronidase</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>150-1500 IU subcutaneously around the area of extravasation See Appendix 6 for full details</td>
</tr>
</tbody>
</table>

Even if extravasation is identified early, progressive extravasation can give rise to ulcerated and necrotic tissue over time. Early steps to prevent and manage extravasation such as using antidotes may help to limit the need for surgery (10). About one-third of extravasations due to anthracyclines result in ulcerations. In these cases, surgery should not be considered as the initial primary treatment of choice (4). Surgery to excise damaged tissue is indicated when there is ulceration or continued pain.

Summary

Managing extravasation in accordance with the latest scientific understanding and medical consensus allows for optimal treatment of the patient. By following the example set out in these guidelines, which include the latest information on extravasation and a selection of current protocols and policies from prominent centres (9), nurses can contribute to improving the standard of care in cancer therapy.

By learning how to effectively recognise extravasation and by becoming familiar with local protocols for dealing with it, including the use of antidotes, nurses can help to minimise the incidence of this complication of cancer treatment and, subsequently, play a crucial role in expanding the use of best practice. By implementing the Extravasation Guidelines in their practice setting, nurses can provide best practice based on clinical evidence.

References