EXTRAVASATION
Prevention and Therapy

Karin Jordan
University Hospital Heidelberg
DISCLOSURE OF INTEREST

Prof. Dr. Karin Jordan

- **Personal financial interests, honoraria for speaker, consultancy or advisory role, royalties, direct research funding:** MSD, Merck, Amgen, Hexal, Riemser, Helsinn, Tesaro, Kreussler, Voluntis, Pfizer, Pome-med, Pharma Mar, Prime Oncology, OnkoUpdate, Annals of Oncology, UpToDate

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EXTRAVASATION

Courtesy S W Langer
EXTRAVASATION

clinical practice guidelines

Management of chemotherapy extravasation: ESMO-EONS Clinical Practice Guidelines

J. A. Pérez Fidalgo, MD, L. García Fabregat, RN, A. Cervantes, MD, A. Margulies, RN, C. Vidall, RN & F. Roila, MD on behalf of the ESMO Guidelines Working Group

1Department of Hematology and Medical Oncology, Institute of Health Research INCLIVA, University of Valencia, Valencia, Spain; 2European Oncology Nursing Society, Zurich, Switzerland; 3Healthcare at Home Ltd, Staffordshire, UK; 4Department of Medical Oncology, S. Maria Hospital, Terni, Italy

- Current ESMO/EONS guideline from 2012
- Will be updated soon
POSTOPERATIVE RESULTS

Severe aesthetic defects
Limb damage
FREQUENCY OF EXTRAVASATION

Between 0.7 % and 6.0 %
TYPES OF DAMAGES

- Vesicant Substances (Necrosis)
- Irritant Substances (Irritation)
- Non-Vesicant Substances
# NECROSIS POTENTIAL

<table>
<thead>
<tr>
<th>Vesicants; High risk for ulceration</th>
<th>Irritants; Low risk for necrosis</th>
<th>No or low risk for inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsacrine</td>
<td>Mitomycin C</td>
<td>Alemtuzumab</td>
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<tr>
<td>Carmustine¹</td>
<td>Oxaliplatin¹</td>
<td>Azacytidin</td>
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<tr>
<td>Dactinomycin</td>
<td>Paclitaxel¹</td>
<td>Asparaginase</td>
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<tr>
<td>Daunorubicin</td>
<td>Cisplatin-Conc. &gt;0,4 mg/ml</td>
<td>Bevacizumab*</td>
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<tr>
<td>Docetaxel¹</td>
<td>Vinblastine</td>
<td>Bleomycin</td>
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<tr>
<td>Doxorubicin</td>
<td>Vincristine</td>
<td>Bortezomib*</td>
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<tr>
<td>Epirubicin</td>
<td>Vindesine</td>
<td>Cladribin</td>
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<tr>
<td>Idarubicin</td>
<td>Vinorelbine</td>
<td>Clofarabin</td>
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<tr>
<td>Mitoxantrone</td>
<td>Vinflunine*</td>
<td>Decitabin</td>
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<td></td>
<td></td>
<td>Cyclophosphamid</td>
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<td></td>
<td></td>
<td>Etoposidphosphat</td>
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<td></td>
<td></td>
<td>Fludarabin</td>
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<td>5-FU</td>
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<td>Ifosfamid</td>
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<td></td>
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<td>Irinotecan</td>
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<td></td>
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<td>Methotrexat</td>
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<tr>
<td></td>
<td></td>
<td>Nimustine</td>
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<tr>
<td></td>
<td></td>
<td>Pegasparaginase</td>
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<tr>
<td></td>
<td></td>
<td>Pemetrexed</td>
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<tr>
<td></td>
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<td>Pentostatine</td>
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<tr>
<td></td>
<td></td>
<td>Raltitrexed</td>
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<td></td>
<td></td>
<td>Rituximab</td>
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<td></td>
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<td>Thiotepa</td>
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<td></td>
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<td>Topotecan</td>
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<td></td>
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<td>Trastuzumab</td>
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<tr>
<td></td>
<td></td>
<td>Zytokine (Interferon, Interleukin)</td>
</tr>
</tbody>
</table>

* According to manufacturer

¹ lesser toxicity in some literatures and according to a few experts
“THE MEANEST”

- Anthracyclines
- Vinca-alkaloids
RISK FACTORS

- Selection of cannulation site
  
  Forearm > back of hand > elbow (unfavourable)

- Time pressure, exhausted staff

- Fragile veins (e.g. elderly, cancer patients)

- Multiple venipuncture of blood vessels proximal to cannulation area

- Reduced venous drainage
THE USAGE OF PORT SYSTEMS DOES NOT PREVENT EXTRAVASATION
All measurements are **not** tested through larger studies, but based on case reports or small case series.
MANAGEMENT OF EXTRAVASATION

1. Stop infusion immediately; leave the cannula
2. Disconnect the infusion
3. Aspirate through the cannula
4. Remove cannula while aspirating
5. Large extravasation should be aspirated from all directions
6. Immobilisation or elevation of limb
7. If required application of warmth or cold
8. If required antidote
9. Documentation of extravasation, also document progression
10. If vesicants, contact surgeon within 72 hours
LOCAL MEASURES

- Dry cooling
- Dry warmths
LOCAL MEASURES

- **Dry cooling**
  - In: Anthracyclines, Cisplatin, Amsacrine, Mitomycin C
  - Initially Cold-Hot-Pack for one hour
  - Subsequently several times a day for 15 minutes
  - Usage together with DMSO except for extravasation due to liposomal Dauno- and Doxorubicin
LOCAL MEASURES

- Dry warmth
  - In Vinca-Alcaloids
  - Four times a day for 20 minutes with Cold-Hot-Pack
  - No usage together with DMSO
ANTIDOTES FOR EXTRAVASATION

The “only” evidence

- Dexrazoxane and
- Hyaluronidase and
- DMSO
PORT EXTRAVASATION BEFORE AND AFTER DEXRAZOXANE

08/08

12/08
<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Evidence-based recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B</strong></td>
<td>For extravasation due to anthracyclines (excluding liposomal anthracyclines) Dexrazoxan should be applied</td>
</tr>
<tr>
<td>Procedure:</td>
<td>• Infusion of Dexrazoxan through a vein at the unaffected extremity</td>
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<tr>
<td></td>
<td>• Dosage: Day 1 and 2: 1000mg/m², Day 3: 500mg/m² (dosis reduction for renal insufficiency, see specialized information)</td>
</tr>
<tr>
<td></td>
<td>• Application preferably early within 6 hours of extravasation</td>
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<tr>
<td></td>
<td>• Infusion time: 1-2h</td>
</tr>
<tr>
<td><strong>0</strong></td>
<td>Can be dispensed for small extravasations and absence of clinical symptoms (e.g. pain, swelling)</td>
</tr>
<tr>
<td>Level of evidence</td>
<td>Literature: (Mouridsen, Langer et al. 2007, Fontaine, Noens et al. 2012)</td>
</tr>
<tr>
<td>2a</td>
<td>Plenary Vote: Strong consensus</td>
</tr>
</tbody>
</table>

Leitlinienprogramm Onkologie (Deutsche Krebgesellschaft, Deutsche Krebshilfe, AWMF): supportive Therapie bei onkologischen PatientInnen – Langversion1.0, 2016, AWMF Registernummer: 032/054OL
SPECIFIC MEASURES – VINCA-ALKALOIDS / TAXANES

„should“ for Vinca, „can“ for Taxanes

- Dosage: 1-10 ampoule à 150 IU (indications vary in the literature between 100 up to 1500 IU)
- Dissolve Hyaluronidase in 1ml solvent (e.g. NaCl 0,9 %)
- During injection an appropriate analgesia should be applied (e.g. Lidocaine 1 %)

Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): supportive Therapie bei onkologischen PatientInnen – Langversion1.0, 2016, AWMF Registernummer: 032/054OL
Abbildung 7: Applikation von Hyaluronidase durch periläsionale Injektionen (aus Schmoll 2006, Kompendium für internistische Onkologie, mit freundlicher Genehmigung durch den Springer Verlag)
### DMSO

<table>
<thead>
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<tbody>
<tr>
<td><strong>A</strong></td>
<td>For extravasation due to Amsacrine, Cisplatine, Dactinomycin-and Mitomycin C the extravasation site should be dabbed with Dimethylsulfoxid (DMSO) 99%</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>For extravasation due to anthracyclines, for which Dexrazoxan was not applied, the application of DMSO should be performed</td>
</tr>
</tbody>
</table>

**Procedure:**
- Application every 8 hours for at least 7-14 days
- Dabbing, no rubbing and no use of pressure
- Do not cover extravasation site after DMSO application, because DMSO is supposed to air dry

For simultaneous application of local therapy with cold, there should be an interval of 15 minutes in between

**Level of evidence**
- Literature.
- DMSO application: (Olver, Aisner et al. 1988, Bertelli, Gozza et al. 1995)

**3a**
- Plenary Vote: Strong consensus
**EMERGENCY KIT**

- Disposable syringes 1 ml, 2 ml, 5 ml, 10 ml
- Disposable cannulas 18G, 26G
- Sterile gloves
- Sterile compresses and ball swabs
- NaCl 0.9 %, Glucose 5 % (for Oxaliplatin extravasation), Aqua dest.
- Cold-Hot-Pack
- Dimethylsulfoxid (DMSO) 99 %
- Hyaluronidase 1500 IE (store refrigerated at 2-8° C)
- Dexrazoxane
- Lidocaine 1%
- Instructions “Management of extravasation”
Schnitzel
Pfifferlinge
mit
Bratkartoffeln
12,5