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# Extravasation Update

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# Disclosure

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- Robert McLauchlan has no real or apparent conflicts of interest to report

# Learning Objectives

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- Identify agents that commonly cause extravasations
- Discuss methods of prevention and methods to minimize such adverse events
- Discuss pharmacologic, as well as nonpharmacologic, treatment options for extravasations

# Introduction

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- Extravasation – a serious consequence
- Warrants special attention
- Will examine:
  - Nature of extravasations
  - Prevalence, risk factors, tissue damage, diagnosis, prevention, management

# Extravasation

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- “The accidental leakage of chemotherapy from its intended compartment (the vein) into the surrounding tissue. Usually this occurs when intravenous medication passes from the blood vessel into the tissue around the blood vessels and beyond”

# Types of Extravasation

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Nonvesicant

Irritant

Vesicant

DNA Binding

Non-DNA  
Binding

Anthracyclines  
Alkylators

Vinca Alkaloids  
Taxanes

# Nonvesicants

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- Asparaginase
- Bleomycin
- Carboplatin
- Cladribine
- Cyclophosphamide
- Cytarabine
- Fludarabine
- Gemcitabine
- Interferons
- Interleukin-2
- Methotrexate
- Monoclonal antibodies
- Pemetrexed
- Pentostatin
- Raltitrexed
- Thiotepa

# Irritants

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- Bortezomib
- Carmustine
- Dacarbazine
- Docetaxel
- Etoposide
- Fluorouracil
- Fotemustine
- Ifosfamide
- Melphalan

- Mitozantrone
- Streptozocin
- Teniposide

## ***Possible Irritants***

- *Cisplatin*
- *Irinotecan*
- *Oxaliplatin*
- *Paclitaxel*
- *Topotecan*

# Vesicants

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## **DNA Binding Drugs**

- Dactinomycin
- Daunorubicin
- Doxorubicin
- Epirubicin
- Idarubicin
- Mitomycin C
- Mustine

## **Non-DNA Binding Drugs**

- Vinblastine
- Vincristine
- Vindesine
- Vinorelbine
  
- Docetaxel
- Paclitaxel

# Prevalence

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- Continues to occur despite precautionary measures
- Occurs with both peripheral and central lines
- Accounts for 0.5% to 6.0% of all adverse events associated with treatment
- Absolute number may be significant

# Risk Factors

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- Patient-related factors
  - Small blood vessels (pediatric population)
  - Fragile veins (elderly population)
  - Hard, sclerosed veins
  - Mobile veins
  - Impaired circulation
  - Obstructed vena cava
  - Pre-existing conditions
  - Obesity

# Risk Factors

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- Trouble reporting early symptoms
  - Inability to report stinging/discomfort
  - Decreased sensation
- Cannulation and infusion procedure
  - Inexperienced staff
  - Multiple cannulation attempts
  - Unfavorable cannulation site
  - Bolus injection
  - High flow pressure

# Risk Factors

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## ■ Equipment

- Steel butterfly needle
- Catheter size and type

## ■ Treatment

- Nature of drug being given
- Ability to cause tissue or vascular dilatation
- pH, osmolality
- Characteristics of diluent

# Tissue Damage

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- Extent of damage may vary greatly
- Progressive in nature

Inflammation  
Blisters

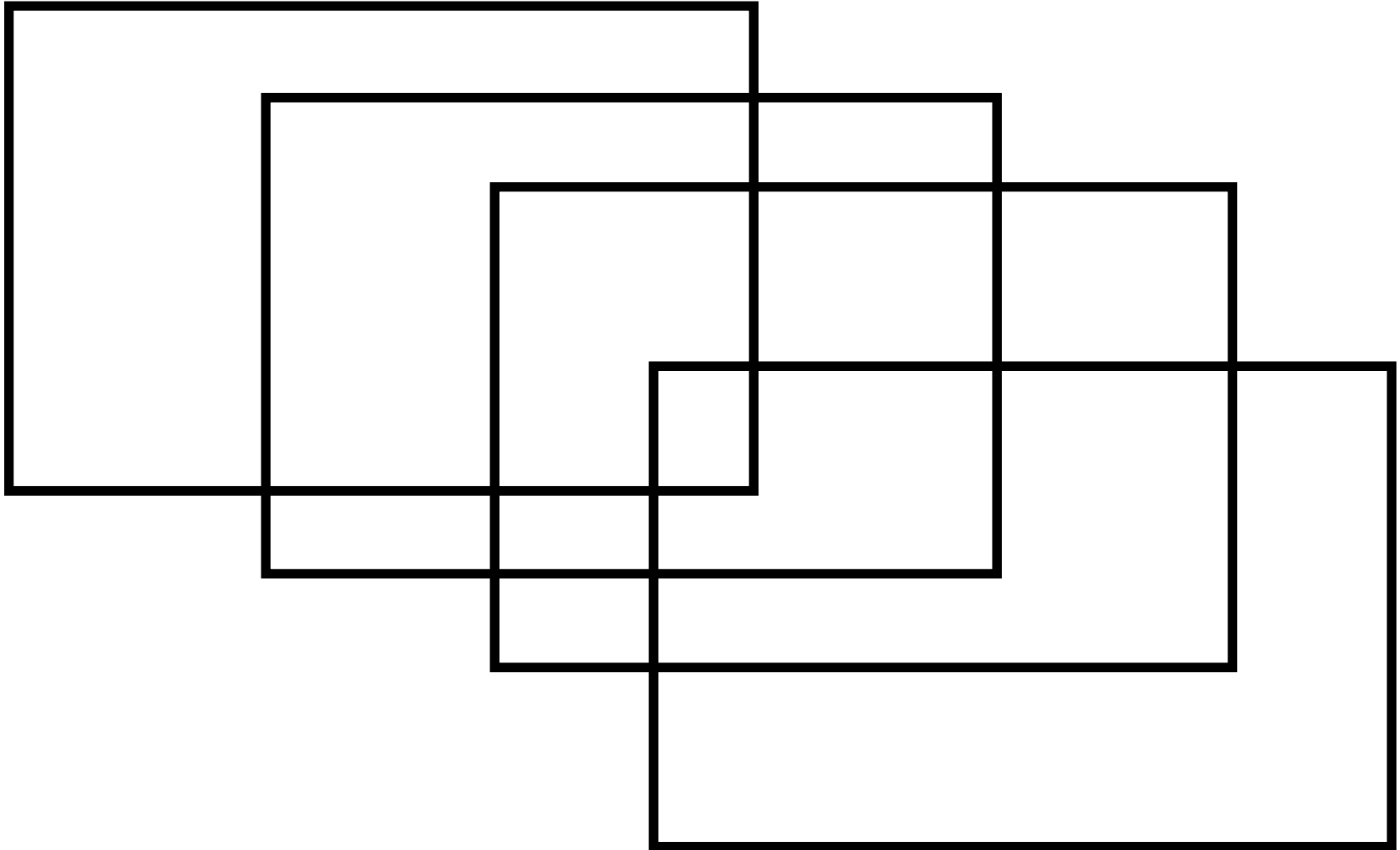
Ulceration

Local Tissue  
Necrosis

- Skin and subcutaneous tissue damage
- If nerves, ligaments, tendons involved, may lead to impact on sensation and function

# Tissue Damage

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# Mechanism of Tissue Damage

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## ■ DNA binding drugs

- Complex with DNA and cause cell death
- After lysis of cell drug released to interact with additional cells
- Repetitive process results in chronic injury

## ■ Non-DNA binding drugs

- Cleared more readily
- More easily neutralized

# Prevention of Extravasation

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- Develop standard protocols
- Train and educate staff
- Educate patients on signs and symptoms
- Select appropriate vein for administration
- Do not use a site distal to a previous puncture
- Select appropriate equipment for administration

# Prevention of Extravasation

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- Consider administration technique carefully
  - Consider use of a central line
  - Avoid using a pump
  - Check vein patency regularly
  - Do not allow patients out of clinic area
  - Consider order of administration
    - Vesicant drug first
    - Vesicant drug last

# Initial Symptoms

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- Occur immediately after blood vessel breached
  - Pain or discomfort
  - Mild to intense, often described as burning
- Over the next few hours
  - Erythema and edema, discoloration or redness
  - Symptoms similar for different agents
  - Progression differs for irritants and vesicants

# Recognition of Extravasation

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- Patient reporting
  - Pain, swelling, redness, discomfort, burning, stinging
- Visual assessment
  - Early symptoms
    - Edema, erythema
  - Later symptoms
    - Inflammation, induration, blistering

# Recognition of Extravasation

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- Check of infusion line
  - Increased resistance, slow infusion, change in flow, lack of blood return
- Differential diagnosis
  - Flare reaction, vessel irritation, venous shock, phlebitis, hypersensitivity

# Differential Diagnosis

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Characteristic	Flare Reaction	Vessel Irritation	Venous Shock	Extravasation
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# Cases for Discussion

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- 1.** Doxorubicin
- 2.** Vincristine
- 3.** Oxaliplatin

# Management of Extravasation

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- Initial response
  - STOP infusion immediately
  - DO NOT remove cannula at this time
  - Aspirate as much drug as possible
  - Mark affected area and photograph
  - Remove cannula/needle
  - Notify other members of team
  - Collect extravasation kit

# Management of Extravasation

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**Armsacrine**  
**Carmustine**  
**Dacarbazine**  
**Docetaxel**  
**Anthracyclines**  
**Mitomycin C**  
**Mustine**  
**Paclitaxel**  
**Streptozocin**

**Localize and  
Neutralize**

**Vincristine**  
**Vinblastine**  
**Vindesine**  
**Vinorelbine**  
**Oxaliplatin**

**Disperse and  
Dilute**

# Localize and Neutralize

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# Disperse and Dilute

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# Nonvesicants

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# Antidotes

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- Agents applied or injected to counteract effects of infiltrated drug – usually vesicant
- May help to prevent progression to ulcerating, blistering, and necrosis
- Evidence supporting use inconclusive
- Pros and cons of use should be carefully considered

# Antidotes

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Extravasated Drug	Antidote	Evidence	Advice
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# Antidotes

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Extravasated Drug	Antidote	Evidence	Advice
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# Other Antidotes

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- Corticosteroids
  - Largely ineffective in clinical trials
  - Acute inflammation not major mechanism
  - Multiple injections may be deleterious
  - Possible benefit for oxaliplatin extravasation
- Sodium bicarbonate
- Butylated hydroxytoluene (BHT)
- DHIM3

# Dexrazoxane Evidence

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- 2 Multicenter, open-label, single-arm studies
  - TT01 n = 17, TT02 n = 36
  - Fluorescence positive tissue biopsy
  - Localized cooling allowed but no DMSO
  - Dexrazoxane given within 6 hours of incident
  - All patients received standard dose regimen
  - 1<sup>o</sup> endpoint prevention of necrosis requiring surgery

# Dexrazoxane Evidence

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# Dexrazoxane Evidence

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## ■ Results

- Prevention of surgery TT01 100%, TT02 97.4%
- 71% continued chemotherapy on schedule
- Sequelae
  - Sensory disturbances 16.7%, skin atrophy 9.3%, pain 18.5%, disfigurement 2.8%, limitation of movement 5.6%
- Toxicities
  - Injection site reactions 14.0%, nausea 18.8%, wound infections 10.0%, vomiting 7.5%

# Dexrazoxane Evidence

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# Administration of Dexrazoxane

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- Follow initial steps to localize and neutralize
- Give NO LATER than 6 hours after incident
- Remove cooling from area at least 15 minutes before administration of drug
- Give as intravenous infusion daily for 3 days
  - Day 1                    1000 mg/m<sup>2</sup>
  - Day 2                    1000 mg/m<sup>2</sup>
  - Day 3                    500 mg/m<sup>2</sup>

# Administration of DMSO

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- Follow initial steps to localize and neutralize
- Apply within 10 to 25 minutes of incident
- Wearing gloves, apply a thin layer of DMSO to marked, affected area
- Allow to air dry
- Apply a nonocclusive dressing
- Application repeated 8 hourly for 7 days

# Administration of Hyaluronidase

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- Follow initial steps to disperse and dilute
- Administration within 1 hour of incident
- Dilute 150 to 1500 IU in 1 mL WFI
- If no blood return, consider giving through affected IV line
- Give remaining dose SC around site
- Up to 5 injections of 0.2 mL may be given around extravasation site

# Extravasation Kit

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- Instant hot/cold pack
- Antidotes according to local policy
- Needles, syringes, and alcohol swabs
- Marker to define affected area
- Copy of extravasation management procedure
- Forms required to document incident
- Patient information

# Documentation and Reporting

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- To provide an accurate account of the incident
- To allow for proper clinical follow-up
- To protect health care professionals involved
- To gather data on extravasation events
- To highlight any deficits in practice that may require review

# Documentation and Reporting

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- Patient details
- Clinic area
- Date and time
- Drug involved
- Signs and symptoms
- Nature of IV access
- Extravasation area
- Step-by-step management
- Patient's comments
  - Patient information supplied
  - Follow-up information supplied
- Staff involved

# Documentation and Reporting

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# Standards and Guidelines

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- [www.isopp.org](http://www.isopp.org)
- [www.cancercare.on.ca](http://www.cancercare.on.ca)
- [www.bccancer.bc.ca](http://www.bccancer.bc.ca)
- [www.treatment.cancerinstitute.org.au](http://www.treatment.cancerinstitute.org.au)
- [www.extravasation.org.uk](http://www.extravasation.org.uk)