A Call-to-Action Workshop: Oncology Nurse Management of Hypersensitivity Reactions

Continuing Education Regional Symposium for Oncology Nurses

Sponsored by:

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TARGET AUDIENCE
This activity has been designed to meet the educational needs of patient care oncology nurses.

PURPOSE
To educate nurses on effective treatment strategies for the management of hypersensitivity reactions (HSRs).

PROGRAM OVERVIEW
Numerous cancer therapies are associated with HSRs. These infusion-related reactions can range in severity from mild flushing and itching, to anaphylaxis, and in rare cases, death. The accurate identification of the signs and symptoms of HSRs can directly affect treatment decisions. If patients at high risk for experiencing a second reaction can be safely rechallenged, discontinuation of an effective agent may be avoided. It is imperative that oncology nurses are aware of the potential for HSRs when administering therapeutic agents and have protocols in place to prevent and manage these reactions in order to minimize their effects on future treatment.

LEARNING OBJECTIVES
Upon completion of this program, participants should be better able to:

• Identify which systemic cancer therapies often cause HSRs
• Describe the pathophysiology of HSRs caused by systemic cancer therapies
• Describe the clinical signs and symptoms of mild, moderate, and severe HSRs
• Identify the variations in timing of HSRs across systemic cancer treatments
• Describe the appropriate prophylaxis and management of HSRs
• Identify the optimal circumstances and methods for rechallenging patients who have experienced HSRs to systemic cancer therapy

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University of California, San Francisco

ACCREDITATION STATEMENTS
This educational activity for 1.0 contact hour will be provided by IMER. IMER is an approved provider of continuing education by the Georgia Nurses Association, an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation.

IMER is approved by the California Board of Registered Nursing, Provider Number 14763 for 1.2 contact hours.

Application pending approval with the American Academy of Nurse Practitioners (including pharmacology hours).

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Hypersensitivity reactions (HSRs) may occur in response to treatment with any chemotherapeutic or biologic agent. They tend to be disturbing for patients and staff alike. The incidence of HSRs is approximately 5%, however, in some cases, agents are known to present a much higher risk (e.g., specific monoclonal antibodies [MoAbs]). Consequently, it is essential that oncology nurses caring for patients are equipped with the tools to effectively diagnose and manage these adverse reactions. The pathophysiology of HSRs is complex. They are classified as type I, II, III, or IV, depending on the severity. Type I reactions (most chemotherapy-induced HSRs) are believed to be the result of IgE-mediated release of histamines, leukotrienes, and prostaglandins from mast cells in the blood. A common type I HSR is anaphylaxis which is a generalized reaction manifested by a variety of symptoms ranging from a feeling of impending doom, urticaria and rash, to full respiratory or cardiovascular collapse. Oncology nurses must be vigilant in their monitoring of patients undergoing chemotherapy and MoAb treatments in order to guard against the possibility of developing HSRs, including anaphylaxis. Some patients may experience biphasic reactions (with symptoms returning hours after the original reactions). Therefore, postobservation of patients is key in the identification of delayed HSRs. In addition, patient education regarding the early signs and symptoms is important, especially because some reactions may be managed with early premedication intervention, such as steroids and H1/2 antagonists. The goal of this workshop is to increase awareness of HSRs, their causes, manifestations, and strategies for preventing and treating them.
A Call to Action Workshop: Oncology Nurse Management of Hypersensitivity Reactions

Educational objectives

- Identify which systemic cancer therapies often cause hypersensitivity reactions (HSRs)
- Describe the pathophysiology of HSRs caused by systemic cancer therapies
- Identify the variations in timing of HSRs across systemic treatments
- Describe the appropriate assessment of HSRs
- Discuss the appropriate prophylaxis and management of HSRs caused by various systemic cancer treatments
Hypersensitivity: Definition of Terms

- Drug reaction
  - All adverse drug events related to administration
- Drug allergy
  - Reaction specifically mediated by the immune system and IgE
- Drug hypersensitivity
  - Four different responses
    - Type I (immediate IgE)
    - Type II (antibody-mediated by IgG or IgM)
    - Type III (immune complex-mediated reaction)
    - Type IV (cell mediated or delayed; usually T cell)
- Cytokine release syndrome
  - Drug reaction more specific to agents directed against immune system targets (e.g., antibodies)

Cancer Therapies and Hypersensitivity Reactions

- Almost all chemotherapy drugs and treatments have the ability to cause HSRs
- In general, overall incidence of HSRs to most chemotherapy treatments is 5%; however, specific individual agents may present a much higher risk
  - L-asparaginase and taxanes may have HSRs as a major treatment-limiting toxicity
  - Some monoclonal antibodies result in fatal infusion-related reactions in small numbers of patients

Chemotherapy Agents: Potential for HSRs

<table>
<thead>
<tr>
<th>Occasional potential for HSR</th>
<th>Anthracyclines</th>
<th>Mercaptopurine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare potential for HSR</td>
<td>• Bleomycin</td>
<td>• Cyclophosphamide</td>
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<tr>
<td></td>
<td>• Chlorambucil and melphalan</td>
<td>• ifosfamide</td>
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<tr>
<td></td>
<td>• Decarbazine</td>
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<td></td>
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<td>• Fluorouracil</td>
<td></td>
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<tr>
<td></td>
<td>• Hydroxyurea</td>
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<tr>
<td></td>
<td>• Methotrexate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Polyethylene glycol-modified E. coli</td>
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</tr>
<tr>
<td></td>
<td>• Asparaginase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Vincristine and vinblastine</td>
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</tbody>
</table>

Gobel, 2005.

Commonly Administered Chemotherapy Agents: Incidence of Severe HSRs

<table>
<thead>
<tr>
<th></th>
<th>Incidence of Severe HSRs</th>
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<tbody>
<tr>
<td>Carboplatin</td>
<td>2%</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>2 - 3%</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>2 - 4%</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>1 - 3%</td>
</tr>
<tr>
<td>Etoposide</td>
<td>1 - 2%</td>
</tr>
<tr>
<td>Ixabepilone</td>
<td>1%</td>
</tr>
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</table>

Pathophysiology

- Human immune system is complex
  - Protects human host against infectious disease and pathogens
  - Recognizes self versus nonself
- Hypersensitivity: An inappropriately triggered or excessive immune response
  - Produces undesirable effects
  - Triggered by antigen-antibody or antigen-lymphocyte interaction

Pathophysiology (cont.)

- Chemotherapy-induced HSRs are primarily type I
  - IgE mediated
    - Produced by specialized B cells
    - Normally circulate at low levels in the blood
    - Upon exposure to antigen (e.g., drug or its metabolite) B cells produce IgE antibodies which bind to mast cells and sensitize them to the antigen
    - Subsequent exposure of the mast cell to the antigen results in degranulation of the mast cell
Pathophysiology (cont.)

- Mast cell degranulation → Anaphylaxis
  - Release of potent chemicals (e.g., histamine) that produce inflammatory reaction
  - Histamine is responsible for
    - Vascular permeability
    - Vasodilatation
    - Urticaria
    - Smooth muscle constriction
    - Increase mucus secretion
    - Pruritus
    - Increased gastrointestinal permeability

Pathophysiology (cont.)

- Infusion reactions to monoclonal antibodies
  - Related to destruction of antigen-expressing tumor cells
  - Mediated by cytokine release
    - TNF-alpha
    - Interleukin-6 (IL-6)
    - Interferons
    - Histamines
  - Presentation is identical to type I reactions

Copestead & Banasik, 2005.

HSRs: Platinum Salt

- Carboplatin and oxaliplatin have been used extensively during the last decade
  - Increased incidence of HSRs in response to treatment with these agents
- Exact mechanism is unknown; may be related to
  - IgE-mediated HSR
  - Direct histamine release
  - Idiosyncratic reactions attributed to massive release of TNF-alfa and IL-6 (based on elevated serum levels of affected patients)
- HSR frequency estimations
  - Carboplatin (12%–30%)
  - Cisplatin (5%–20%)
  - Oxaliplatin (mild reactions 10%–12%)
- Reactions typically occur after the fifth through eighth cycle of carboplatin

Platinum Salts

- Carboplatin
  - Carries a boxed warning stating that anaphylactic-like reactions may occur within minutes of administration
  - Reactions can be delayed; one report showed a 1% risk of HSR with patients receiving less than six courses of therapy increasing to 27% after seven courses of drug

- Oxaliplatin
  - Carries a boxed warning stating anaphylactic-like reactions have been reported and may occur within minutes of administration
  - Reactions can be delayed; incidence increases with multiple courses of drug, generally occurring after seven courses

TNF = tumor necrosis factor; IL = interleukin.
Leguy-Seguin et al., 2007; Polyzos et al., 2001.
Zanotti et al., 2001; Gammon et al., 2004.
Platinum Salts (cont.)

- **Cisplatin**
  - Carries a boxed warning stating anaphylactic-like reactions may occur within minutes of administration in patients previously exposed to cisplatin
  - Studies indicate that cisplatin may be used in patients with platinum-sensitive ovarian cancer who experience hypersensitivity to carboplatin

Platinol®-AQ prescribing information, 2006; Kandel et al., 2005.

Platinum-Free Interval and Hypersensitivity

- Many GYN patients require re-treatment with carboplatin (when risk for HSR is highest)
- No definitive way to predict those who are at risk
  - Schwartz et al. (2006) identified 126 patients who had multiple carboplatin regimens
    - 50% had HSRs; 29% were severe
    - Researchers examined the platinum-free interval and determined that a duration of greater than 12 months between carboplatin regimens is associated with increased risk of any grade HSR as well as severe HSR

GYN = gynecology.
Schwartz et al., 2006
Taxanes

- **Paclitaxel**
  - Carries a boxed warning reporting severe HSR incidence of 2%–4%, with fatal reactions occurring despite premedication
  - All patients should be pretreated with corticosteroids, diphenhydramine, and H2 antagonists

- **Docetaxel**
  - Carries a boxed warning reporting severe HSRs in patients with very rare anaphylaxis, despite the recommended 3-day premedication protocol with dexamethasone
  - Patients should be observed closely for HSRs, especially during the first and second infusion

Biologic Agents

- **Interferons**
  - Interferon alfa
    - Chills, fever, rigors, which improve with subsequent treatments
  - Interferon beta (1A and 1B)
    - Chills, fever, rigors, diaphoresis
  - Interferon gamma
    - Chills, fever, rigors, diaphoresis, night sweats

- **Interleukin**
  - Aldesleukin
    - Flu-like symptoms of chills, fever, rigors common
    - Usually occur 2–4 hours after drug administration
  - Denileukin diftitox
    - Acute HSR reported in 69% of patients in the clinical trials
    - 1% anaphylaxis reported in clinical trials
    - Flu-like symptoms common

Taxol® prescribing information, 2007; Taxotere® prescribing information, 2007.
### Types of Monoclonal Antibodies

<table>
<thead>
<tr>
<th>Types</th>
<th>Agents</th>
<th>Incidence</th>
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</thead>
<tbody>
<tr>
<td>Murine</td>
<td>Tositumomab</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td>Ibritumomab</td>
<td>1%</td>
</tr>
<tr>
<td>Chimeric</td>
<td>Rituximab</td>
<td>&lt; 10%</td>
</tr>
<tr>
<td></td>
<td>Cetuximab</td>
<td>3%</td>
</tr>
<tr>
<td>Humanized</td>
<td>Trastuzumab</td>
<td>&lt; 1% (although can be delayed up to 24 hours post dose)</td>
</tr>
<tr>
<td></td>
<td>Bevacizumab</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td></td>
<td>Alemtuzumab</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>Gemtuzumab</td>
<td>Not reported</td>
</tr>
<tr>
<td>Human</td>
<td>Panitumumab</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

Incidence of Severe HSRs in Response to Monoclonal Antibody Agents

Lenz, 2007; Bexxar® prescribing information, 2005; Zevalin® prescribing information, 2007.
Hypersensitivity: Effect on Nursing Staff

- HSRs may be disturbing for oncology nurses
- A recent study of oncology nurses at ONS Congress was presented in the *Journal of Infusion Nursing* in 2007
  - Study found that nurses perceived grade 3 or 4 reactions as disruptive for patients and nurses
  - 36% said reactions affected them emotionally, making them feel apprehensive and stressed
  - 50% felt that infusion reactions are very draining and frightening
  - 88% of outpatient nurses and 62% of inpatient nurses said that reactions were frightening to the other patients
  - 42% felt that doctors don’t adequately inform patients about the risks of infusion reactions

Severe Infusion Reactions: Assessment of Clinical Consequences

- A retrospective chart review of severe infusion reactions to rituximab, cetuximab, and bevacizumab was conducted in community oncology practices
  - 19 practice sites
  - Patient average age = 62 yrs
  - 76 patients suffered severe infusion reaction (rituximab n = 47; cetuximab n = 24; bevacizumab n = 5)
  - Most occurred during first cycle of therapy

Conclusion: Severe infusion reactions are intensive events presenting a serious challenge to patients and practices.

MoAb = monoclonal antibody.
Schwartzberg et al., 2007.
Hypersensitivity: Prevention

- Comprehensive allergy history
- Premedication
- Skin testing
- Desensitization
- Alteration of infusion rates
- Knowledge of potential geographic differences in allergic response rate for specific medications

Factors Determining the Development and Severity of Anaphylaxis

- Antigen’s route of entry
- Amount of antigen introduced
- Rate of antigen absorption
- Individual's degree of hypersensitivity to a drug

Hypersensitivity Prophylaxis

- Identification of high-risk individuals is important, but can be challenging
- Proposed risk factors include
  - Repeated use of the agent (such as with the platinum drugs)
  - Personal history of allergy
  - Patients treated with rituximab may also benefit from examination of other risk factors such as age, gender, and primary tumor type


Hypersensitivity Prophylaxis (cont.)

- Prevention of severe HSRs is the key
- Many agents require or are recommended with premedication
  - Although no evidence-based standard premedication regimen has been published, many agents are recommended with premedication (specific MoAbs, taxanes)
  - Premedications usually include H1 blockers, such as diphenhydramine, acetaminophen, and less frequently, corticosteroids, depending on the agent

Lenz et al., 2007; Gobel, 2007.
Hypersensitivity Prophylaxis: Skin Testing

- **Skin prick test**
  - Performed by placing a drop of a solution containing a possible allergen on the skin with a series of scratches of needle pricks to provide entry point for the solution
  - Positive if wheal is produced

- **Intradermal skin test**
  - Performed by injecting a small amount of the solution containing potential allergen into the skin
  - Often performed after a negative skin prick test and is more sensitive than the skin prick test, but may produce a false positive


Hypersensitivity Prophylaxis: Skin Testing (cont.)

- Skin testing has been employed with several chemotherapy agents (e.g., bleomycin, L-asparaginase, and carboplatin)
- Investigated skin test to predict which patients may receive carboplatin safely
- Concluded this could reduce the incidence of HSRs in patients needing repeated doses of carboplatin
- ONS guidelines recommend skin test after the seventh dose of carboplatin
- Zanotti’s skin test protocol for carboplatin
  - Intradermal injection of 0.02 mL of undiluted aliquot of carboplatin dose onto volar surface of the arm
  - 30 minutes after skin test, chemotherapy premedication agents given (e.g., steroid, diphenhydramine, famotidine, granisetron)
  - Carboplatin given over 30 minutes
  - Skin tests read at 5, 15, 30 minutes after test prior to delivery of chemotherapy
  - Positive skin test defined as a wheal of at least 5 mm in diameter with flare

Zanotti, 2001; Markman et al., 1999; Markman et al., 2003; ONS, 2005.
Hypersensitivity Prophylaxis: Oxaliplatin

- As oxaliplatin is used more frequently in clinical practice, HSRs are increasingly prevalent.
- In one review, 15% of the patients receiving the agent (27/180) were identified as allergic, with numbers higher for those receiving the drug in second-line settings (vs. adjuvant; 19.6%).
- The majority of the reactions occurred after a median of 8.5 doses, with 2.2% of the patients suffering grade 3–4 severity reactions.
- Rechallenge was attempted in some patients suffering milder reactions after premedication protocol; HSR rate was notably higher.
- Consideration of premedication and longer infusion times have been suggested to reduce the likelihood of HSRs.

Siu et al., 2006; Eloxatin® prescribing information, 2002.

Hypersensitivity: When to Rechallenge

- With specific agents, a mild or moderate reaction can be managed with a slower infusion (such as taxanes or moAbs).
- If patients have a severe initial HSR, it is usually not recommended to rechallenge the agent for that patient.
- Prior to rechallenge, premedicate with anithistamine and corticosteroids.
- Patients who are rechallenged after experiencing a HSR often receive their next administration in an inpatient setting:
  - Ensures that higher level of emergency equipment is available.
  - Advanced life support and other respiratory resuscitative equipment is also recommended.

Lenz et al., 2007; Gobel, 2005.
Desensitization Protocols

- Desensitization protocols have been employed to manage HSRs to platinum compounds
  - Many reports in the literature on carboplatin desensitization
  - One example calls for
    - Premedication with dexamethasone 8–12 mg single dose immediately before infusion of drug
    - Ondansetron single dose immediately before drug
    - Carboplatin each solution diluted in 150 mL of D5W
      - 1/1,000 of the total dose over 1.5 hrs if tolerated
      - 1/100 of the total dose over 1.5 hrs if tolerated
      - 1/10 of the total dose over 1.5 hrs if tolerated
      - The remainder of the dose over 1.5 hrs

HSRs: Desensitization With Oxaliplatin

- Gammon et al. (2004) describe a successful desensitization protocol of oxaliplatin for a single patient
  - Four serial dilutions of 1:10,000; 1:1,000; 1:100, and 1:10 of the total oxaliplatin dose are prepared in 100 cc D5W
  - Each dilution is infused over 60 minutes with careful monitoring of vital signs
  - Final dilution is infused over 2 hours (containing 90% of the total dose in 500 mL D5W)
Hypersensitivity: Recommendations for Administration

- **Rituximab**
  - Good example of attempts to reduce reaction by titrated drug administration rate
    - First infusion: Initiate infusion rate at 50 mg/hr; if no reaction, increase by 50 mg/hr increments until maximum of 400 mg/hr
    - Subsequent infusions: Initiate infusion rate at 100 mg/hr; if no reactions, increase by 100 mg/hr increments until maximum of 400 mg/hr
    - Interrupt infusion or slow rate for infusion reactions

Researchers hypothesize the reaction may be due to a plant, pollen, or mouse antigen that is regionally based.

Regional Differences in Hypersensitivity Reactions

- Incidence rate of HSRs for cetuximab was ≤ 3% in clinical trials
  - Anecdotal evidence suggested a much higher incidence in certain geographic areas (e.g., Tennessee and N. Carolina)
  - Data from patients on clinical trials (n = 88) at three research sites were analyzed for grade 3/4 HSRs
- Patients included in the analysis had a variety of tumor types
  - The overall rate of grade 3/4 HSRs was 22%
  - All HSRs occurred during first dose
  - Strong relationship noted between prior allergy history and chance of HSRs
  - Area may extend to Arkansas and N. Georgia

O’Neil et al., 2007.
Cetuximab-Induced Anaphylaxis

- Although the 3% rate for severe HSRs was noted in the clinical trials, certain geographic areas in the southeast have rates as high as 22%.
- Researchers analyzed serum samples from four groups of subjects (predominantly from Tennessee, Arkansas, and N. Carolina) for IgE antibodies against cetuximab.
- Among 76 treated patients, 25 experienced HSRs to the drug.
  - IgE antibodies against cetuximab were found in pretreatment samples from 17 of the subjects; only 1/51 who did not have an HSR had such antibodies ($p < .001$).
  - IgE antibodies against cetuximab were found in 15 out of 72 samples from control subjects in Tennessee, in 3 out of 49 samples from N. California, and in 2 out of 341 samples from Boston.
  - The IgE antibodies were shown to be specific for an oligosaccharide, galactose-$\alpha$-$1,3$-galactose, which is present on the Fab portion of the cetuximab heavy chain.
- Conclusion: In most of the subjects who had a hypersensitivity reaction to cetuximab, IgE antibodies were present before treatment with the drug.

Chung et al., 2008.

Delayed Hypersensitivity Reactions

- Serious delayed HSRs have been reported.
  - Trastuzumab approved in 1998 for MBC.
  - Postmarketing reports of serious infusion reactions were reported several years later:
    - In most cases, symptoms occurred during or within 24 hours of administration of drug.
    - Fatal infusion reactions occurred; label changed in 2000.
  - Case report of serious delayed reactions was noted in a patient receiving oxaliplatin:
    - 81-year-old woman with MCRC experienced a delayed reaction to oxaliplatin (Cycle 1), with respiratory symptoms appearing 20 hrs after infusion requiring support with steroid and bronchodilator drug.
    - Rechallenged 3 weeks later with premedication and a longer infusion time of 6 hours, however same respiratory symptoms appeared exactly 20 hours after infusion.

MBC = metastatic breast cancer; MCRC = metastatic colorectal cancer.
Herceptin® prescribing information, 2006; De Vries et al., 2006.
Possible signs and symptoms of acute infusion reactions:

- Allergic reaction/hypersensitivity (drug fever)
- Pruritus/itching
- Urticaria (e.g., hives, welts, wheals)
- Rigors/chills
- Headache
- Arthralgia/myalgia
- Tumor pain

- Fatigue
- Dizziness
- Sweating
- Nausea/vomiting
- Cough
- Dyspnea
- Bronchospasm
- Hypotension/hypertension
- Tachycardia

Hypersensitivity: Assessment

Anaphylaxis: Signs and Symptoms

- Serious upper airway (laryngeal) edema or lower airway edema (asthma) may develop
  - Stridor, wheezing
  - Rhinitis
- Cardiovascular collapse
  - Vasodilation produces hypovolemia
  - Increased capillary permeability produces intravascular volume loss
  - Patient may be agitated or anxious, flushed, or pale
  - Cardiac dysfunction may occur from disease or ischemia from epinephrine
- Gastrointestinal signs and symptoms
  - Abdominal pain, vomiting, and diarrhea

American Heart Association, 2005.
Positive Allergic Reactions

Hypersensitivity to Oxaliplatin

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Clinical management

- Observation and evaluation of symptoms such as urticaria
- Administration of diphenhydramine, cimetidine, and/or corticosteroids per MD’s order or according to standing protocol
- Monitor vital signs at least every 15 minutes for 1 hour or as needed
- Document episode, including treatments and patient’s response, according to institutional policies

Stop chemotherapy infusion immediately

Maintain an IV line with NS or another appropriate solution

Stay with the patient; have another staff member notify the MD and emergency tech or if outside the hospital setting, the local emergency medical service

Place the patient in a supine position if possible

Monitor vital signs every 2 minutes until the patient is stable, then every 5 minutes for 30 minutes, then every 15 minutes

Maintain airway, assessing the patient for increasing edema of respiratory tract

Oxygen if needed; anticipate need for CPR

Administer emergency medications

Provide emotional support for family and patient

Document

NS = normal saline.
Hypersensitivity: Implications for Nursing

- Anticipate
  - Know allergy history
  - Get baseline vital signs
  - Know the high-risk chemotherapy/biotherapy drugs
  - Educate patients regarding potential for HSRs and possible symptoms to report
- Be prepared for anaphylaxis and/or need for cardiopulmonary resuscitation
  - Oxygen should be readily available
  - Fever and chills may be managed with acetaminophen, diphenhydramine, and intravenous saline infusion in mild-to-moderate HSRs
  - Rigors may be treated with meperidine or opioid

Hypersensitivity: Implications for Nursing (cont.)

- Know drugs at risk for delayed HSRs
- If no standing protocol exists in your institution, advocate for one; clinical pathways or directives help to guide for appropriate responses to HSRs
  - Laminated cards with resuscitation protocols/algorithms and emergency medications should be close at hand
    - Examples: Above medicine carts, at patient’s bedside
    - Inservice nursing personnel with mock HSRs to ensure knowledge base and comfort over appropriate responses

Gobel 2007; ONS, 2005; Lenz et al. 2007.

Myers, 2002; Schwartzberg et al., 2007.
Hypersensitivity: Implications for Nursing (cont.)

- Have emergency kit available with appropriate medications
  - Know how to use them
- Crash carts, resuscitation teams
- Different protocols may be in place for inpatient vs. outpatient settings: KNOW your protocol
  - Is code team available?
  - Do you call 911 or local emergency group response team?

Key Takeaways

- As noted, HSRs can occur with many different agents and in varying severities
- Oncology nurses should be aware of specific high-risk agents and those at risk for delayed HSRs
  - Key is anticipation of these events
  - Recognition of prophylaxis to help reduce the severity of some reactions
- HSRs have been shown in some studies to be very distressing and anxiety-producing for both staff and patients
- Oncology nurses have a critical role in the recognition of symptoms and management of acute HSRs
REFERENCES


### APPENDIX A. Pharmaceutical Glossary

<table>
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<tr>
<th>Generic Name</th>
<th>Brand Name</th>
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<tr>
<td>acetaminophen</td>
<td>Tylenol®</td>
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<td>Blenoxane®</td>
<td>interferon beta 1b</td>
<td>Betaseron®</td>
</tr>
<tr>
<td>carboplatin</td>
<td>Paraplatin®</td>
<td>interferon gamma</td>
<td>Actimmune®</td>
</tr>
<tr>
<td>cetuximab</td>
<td>Erbitux®</td>
<td>ipratropium</td>
<td>Atrovent®</td>
</tr>
<tr>
<td>chlorambucil</td>
<td>Leukeran®</td>
<td>ixabepilone</td>
<td>Ixempra®</td>
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<tr>
<td>cimetidine</td>
<td>Tagamet®</td>
<td>melphalan</td>
<td>Alkeran®</td>
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<tr>
<td>cisplatin</td>
<td>Platinol®</td>
<td>mercaptopurine</td>
<td>Purinethol®</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>Cytoxan®, Neosar®</td>
<td>methotrexate</td>
<td>Rheumatrex®</td>
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<tr>
<td>dacarbazine</td>
<td>DTIC®, DTIC-Dome*</td>
<td>methyprednisolone/</td>
<td>Medrol®</td>
</tr>
<tr>
<td>dactinomycin</td>
<td>Cosmegen Lyovac®</td>
<td>prednisolone methylprednisolone sodium</td>
<td></td>
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<tr>
<td>denileukin diftitox</td>
<td>Ontak®</td>
<td>succinate</td>
<td>Solu-Medrol®</td>
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<td>dexamethasone</td>
<td>Decadron®</td>
<td>oxaliplatin</td>
<td>Eloxatin®</td>
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<td>dexameth</td>
<td>Dexe®, Hexadrol®</td>
<td>paclitaxel</td>
<td>Taxol®</td>
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<tr>
<td>diphenhydramine</td>
<td>Benadryl®</td>
<td>panitumumab</td>
<td>Vectibix®</td>
</tr>
<tr>
<td>docetaxel</td>
<td>Taxotere®</td>
<td>ranitidine</td>
<td>Zantac®</td>
</tr>
<tr>
<td>epinephrine</td>
<td>Adrenalin®, Chloride Solution EpiPen® Auto-Injector</td>
<td>rituximab</td>
<td>Rituxan®</td>
</tr>
<tr>
<td>etoposide</td>
<td>Toposar®, Vepesid®</td>
<td>tositumomab</td>
<td>Bexxar®</td>
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<tr>
<td>famotidine</td>
<td>Pepcid®</td>
<td>trastuzumab</td>
<td>Herceptin®</td>
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<td>fluorouracil</td>
<td>Carc®</td>
<td>vinblastine</td>
<td>Velban®</td>
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<td>gemtuzumab ozogamicin</td>
<td>Mylotarg®</td>
<td>vincristine</td>
<td>Oncovin®</td>
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<td>granisetron</td>
<td>Kytril®</td>
<td></td>
<td>Vincasar PFS®</td>
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<td>hydrocortisone topical</td>
<td>Corticaine®, Cortizone 10®, Lanacort® 10</td>
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<td>Vincrex</td>
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<td></td>
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<td>Velsar</td>
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**APPENDIX B. NCI CTC v. 3.0 Adverse Event Criteria Grading**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allergic reaction</strong></td>
<td>Transient flushing or rash; drug fever &lt; 38º C (&lt; 100.4º F)</td>
<td>Rash; flushing; urticaria; dyspnea; drug fever ≥ 38º C (≥ 100.4ºF)</td>
<td>Symptomatci bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema, hypotension</td>
<td>Anaphylaxis</td>
<td>Death</td>
</tr>
<tr>
<td><strong>Cytokine release syndrome/acute infusion reaction</strong></td>
<td>Mild reaction; infusion interruption not indicated; intervention not indicated</td>
<td>Requires therapy or infusion interruption but responds promptly to symptomatic treatment (eg, antihistamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for ≤ 24 hrs</td>
<td>Prolonged (ie, not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for other clinical sequelae (eg, renal impairment, pulmonary infiltrates)</td>
<td>Life threatening; pressor or ventilatory support indicated</td>
<td>Death</td>
</tr>
</tbody>
</table>

National Cancer Institute, 2006.

---

**Appendix C. Recommended HSR Premedication for Selected MoAbs**

<table>
<thead>
<tr>
<th>MoAb</th>
<th>Boxed Warning</th>
<th>Premedication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibritumomab tiuxetan</td>
<td>Yes</td>
<td>Targeted against CD 20 positive-cells; premedication with acetaminophen and diphenhydramine recommended</td>
</tr>
<tr>
<td>Tositumomab</td>
<td>Yes</td>
<td>Targeted against CD 20 positive-cells; premedication with acetaminophen and diphenhydramine recommended</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Yes</td>
<td>Targeted against CD 20 positive-cells; premedication with acetaminophen and diphenhydramine recommended</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Yes</td>
<td>EGFR-inhibitor agent; premedication with H1 antagonist recommended</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>Yes</td>
<td>Anti-VEGF agent; no premedication required</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Yes</td>
<td>Targeted against HER2/neu-positive cells; no pre-medication required</td>
</tr>
<tr>
<td>Gemtuzumab</td>
<td>Yes</td>
<td>Targeted against CD33-positive cells; premedication with diphenhydramine and acetaminophen initially; two additional doses of acetaminophen recommended</td>
</tr>
<tr>
<td>Panitumumab</td>
<td>Yes</td>
<td>EGFR-inhibitor agent; no premedication required</td>
</tr>
</tbody>
</table>

Zevalin® prescribing information, 2007; Bexxar® prescribing information, 2005; Rituxan® prescribing information, 2007; Erbitux® prescribing information, 2007; Avastin® prescribing information, 2007; Heceptin® prescribing information, 2006; Mylotarg® prescribing information, 2007; Vectibix™ prescribing information, 2007.
### APPENDIX D. Potential Reactions and Management by Specific Agent

<table>
<thead>
<tr>
<th>Agent</th>
<th>Symptoms</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>Rash, urticaria, erythema, pruritus; rare bronchospasm and hypotension</td>
<td>Epinephrine, corticosteroids, and antihistamines</td>
</tr>
<tr>
<td>Oxalplatin</td>
<td>Rash, urticaria, erythema, pruritus; rare bronchospasm and hypotension</td>
<td>Epinephrine, corticosteroids, and antihistamines</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Dypsnea, flushing, chest pain, tachycardia, hypotension, angioedema, and generalized urticaria</td>
<td>Severe reactions require immediate cessation of therapy (hypotension, dyspnea requiring bronchodilators, angioedema; minor symptoms such as flushing, skin reactions, dyspnea, hypotension or tachycardia do not require treatment interruption)</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Rash/erythema, hypotension, and/or bronchospasm</td>
<td>Severe reactions require immediate cessation of therapy; do not rechallenge. Minor reactions do not require treatment infusion interruptions.</td>
</tr>
</tbody>
</table>

### APPENDIX E. Monoclonal Antibodies: Symptoms and Management

<table>
<thead>
<tr>
<th>Agent</th>
<th>Symptoms</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>Urticaria, hypotension, angioedema, hypoxia, pulmonary infiltrates, ARDS, myocardial infarction, ventricular fibrillation, or cardiogenic shock</td>
<td>Interruption of infusion with supportive care, oxygen, bronchodilators, diphenhydramine, acetaminophen until symptoms resolve. Consider rechallenge with 50% reduction in infusion rate.</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Rapid onset of airway obstruction, urticaria, hypotension, and/or cardiac arrest</td>
<td>If the patient experiences a grade 1/2 infusion reaction, the rate should be permanently reduced by 50%; the drug should be immediately and permanently discontinued in patients who experience sever (grades 3/4) reactions</td>
</tr>
<tr>
<td>Trastuzmab</td>
<td>Anaphylaxis, urticaria, bronchospasms, angioedema, and/or hypotension</td>
<td>Treatment interruption, supportive therapy (epinephrine, corticosteroids, diphenhydramine, oxygen, IV fluids); monitoring until symptoms resolve. Cessation should be strongly considered for those who develop anaphylaxis, angioedema, or ARDS. Rechallenge with premedication has been successful in select pts.</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>Hypertension, hypertensive crises associated with neurologic signs and symptoms, wheezing, oxygen desaturation, grade 3 HSR, chest pain, H/A, rigors, diaphoresis</td>
<td>Treatment interruptions and supportive therapy; info on rechallenge not available</td>
</tr>
<tr>
<td>Panitumumab</td>
<td>Anaphylactic reaction, bronchospasm, fever, chills, hypertension</td>
<td>Mild-to-moderate events require reductions in infusion rate by 50%. Severe events require immediate and permanent cessation of therapy.</td>
</tr>
</tbody>
</table>

**APPENDIX F. Algorithm for Anaphylaxis Management and the Prevention of Cardiopulmonary Arrest**

**General Management**

- **Moderate:**
  - Epinephrine IM (1:1,000) 0.3–0.5 mg q 15–20 min (as needed)
  - Subcutaneous administration absorption may be delayed with shock: IM favored

- **Severe:**
  - Epinephrine IV (1:10,000) 0.1 mg over 5 minutes or 1–4 µg/min (prevents need for repeated injections); may be diluted to a 1:10,000 solution for infusion
  - Patients taking β-blockers have higher incidence/severity of anaphylaxis and a paradoxical response to epinephrine. Consider glucagon and ipratropium for those patients.

- Monitor closely and avoid fatal overdose

- Start aggressive fluid resuscitation (ie, normal saline) if hypotension is present without rapid response to epi. 1–4 liters may be needed

- Patients with bronchosapm need inhaled albuterol (β-adrenergics) or inhaled ipratropium for patients on β-blockers

- Other treatment considerations:
  - Vasopressin: For severely hypotensive patients
  - Atropine: For cases with relative or severe bradycardia
  - Glucagon: For patients not responsive to epinephrine

- O2 at high flow rate

- Corticosteroids: High-dose IV early in course of treatment; effects delayed 4–6 hrs

- H1 blockers: Antihistamines such as diphenhydramine 25–50 mg IM or IV slowly

- H2 blockers: Such as cimetidine 300 mg orally, IM or IV

*p = intramuscularly; IV = intravenously.
Adapted from the American Heart Association, 2005.*
## APPENDIX G. Hypersensitivity Management: Emergency Drugs and Actions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Epinephrine**     | • Administered by inhalation, SQ, IM, or IV in anaphylaxis or allergic reaction  
                      | • Potent adrenoreceptor agonist                                               
                      | • Significant vasoconstrictor                                               
                      | • Causes increased heart rate and force of contraction, increasing cardiac output, and BP |
| **Antihistamine:**  | • Given to block the effects of histamine                                    |
| • H1 blocker        | • Diphendydramine                                                           |
| **H2 Blocker**      | • Cimetidine                                                                
                      | • Ranitidine                                                                 |
                      | • Famotidine                                                                 |
| **Aminophylline**   | • Enhances bronchodilation                                                  |
| **Dopamine**        | • Increases cardiac output and blood pressure                               |
| **Steroids:**       | • Steroids are used to prevent a prolonged event or recurrence of symptoms  
                      | • 20% reactions are biphasic, causing symptoms up to 38 hours after original episode  
                      | • Help to ease bronchoconstriction and cardiac function                      |

IM = intramuscularly; IV = intravenously.
## APPENDIX H. Adult Hypersensitivity Reaction Orders

**PATIENT** ____________________________________________ **MR #** ________________________________

**REGIMEN:** Hypersensitivity Protocol  **DIAGNOSIS:** Acute infusion reaction / Hypersensitivity reaction

**ALLERGIES:** □ NONE

At the first sign of reaction:
- **Stop infusion of drug immediately**
- **Initiate infusion of normal saline at 250 mL/Hr**
- Stay with patient, have second staff person call physician [and/or 911 based on clinic policy]
- Monitor and document vital signs (pulse, respirations, blood pressure, pulse ox.) every 2 minutes until stable, then every 5 minutes for 30 minutes, then every 15 minutes
- **Initiate treatment based on symptoms below**

For signs of bronchial constriction (dyspnea, wheezing, stridor):
- Epinephrine 0.3 mg IM into anterior lateral thigh slowly [EpiPen = 0.3 mg automatic device or 0.3 mL of 1:1000 solution]

For signs of shortness of breath, tachypnea (rate >20) or decreased oxygen saturation by pulse oximeter:
- Initiate oxygen at 6-10 liters/min by face mask
- Administer inhaled Albuterol 2.5 mg (3 mL of 0.083% inhalation solution) by nebulizer (HOLD if HR > 110)

For hypotension: (> 30% decrease in systolic B/P from baseline)
- Place patient in supine position (unless short of breath or vomiting)
- Elevate legs for shock (systolic BP < 60)
- Epinephrine 0.3 mg IM into anterior lateral thigh slowly [EpiPen = 0.3 mg automatic device or 0.3 mL of 1:1000 solution]
- Normal Saline IV fluid bolus (500 mL over 10 minutes x 1), then as ordered

For hives, itching, flushing, swollen lips-tongue-vuva:
- Diphenhydramine 50 mg IVP over 3 minutes
- Famotidine 20 mg IV or Ranitidine 50 mg IV over 3-5 minutes
- Acetaminophen 650 mg PO x 1
- □ Dexamethasone 10–20mg IV over 1-2 minutes
- □ Methylprednisolone 30–60mg IV over 10-20 min

- Anticipate the need for cardiopulmonary resuscitation
- Monitor vital signs every 15 minutes for at least one hour after resolution of symptoms.
- Resume infusion after mild infusion reactions ONLY upon the order of the provider.
- Anticipate inpatient admission for severe or persistent reactions.

NP/PA ____________________________ **DATE** ___________ **MD** ____________________________ **DATE** ____________

Signature

RN SIGNATURES ____________________________ **RN** ____________________________ **RN** ____________________________

---

APPENDIX I. New Mexico Cancer Center Standing Orders for Common Drug Reactions

In the event that a patient has a drug reaction and a physician is not available, the nurse will stop the infusion immediately and may administer the following medications to alleviate the symptoms of that reaction:

| Urticaria (rash) | • No treatment is necessary for the majority of cases  
| | • Benadryl® 25–50 mg po IV  
| | • Decadron® 10 mg IV  
| | • Tagamet® 300 mg IV  
| Bronchospasm | • Obtain oxygen Sat: Administer oxygen as necessary to achieve Sat > 90  
| | (can administer oxygen per nasal cannula up to 6 liters then switch to mask)  
| | • Administer hydrocortisone 100 mg IV  
| | • Administer nebulization: Albuterol or DuoNeb® (ipratropium bromide and albuterol)  
| Hypotension with tachycardia | • Elevate legs or Trendelenburg position  
| | • Monitor vital signs including pulse oximet  
| | • Administer oxygen as necessary to achieve a Sat > 90  
| | (can administer oxygen per nasal cannula up to 6 liters then switch to mask)  
| | • Rapid infusion of normal saline (500–1,000 cc)  
| Hypotension with bradycardia | • Elevate legs or Trendelenburg position  
| | • Monitor vital signs including pulse oximet  
| | • Administer oxygen as necessary to achieve a Sat > 90  
| | (can administer oxygen per nasal cannula up to 6 liters then switch to mask)  
| | • Rapid infusion of normal saline (500–1,000 cc)  
| Facial flushing with drug reaction | • Benadryl® 25–50 mg IV  
| Anxiety | • Ativan® 0.5–1 mg prechemotherapy  

IV = intravenous.  
New Mexico Cancer Center, 2008.
APPENDIX J. Systemic Drug Reactions Example Protocol

Systemic Drug Reactions

CRITERIA FOR INTERVENTION:
Any patient receiving drug therapy who experiences adverse symptoms judged by the nurse or pharmacist to be attributable to treatment. These adverse symptoms may include but not be limited to dyspnea, flushing, hypo- or hypertension, tachy- or bradycardia, broncospasm, pain, rash, or change in mental status.

INTERVENTION:
When a patient has symptoms suspected by a nurse or pharmacist to be due to drug treatment, the following steps shall be implemented (some interventions are implemented simultaneously):

1. Stop administration of the drug immediately and contact the attending physician, on-call physician or nurse practitioner.
2. Maintain existing IV access and keep line open with normal saline or D5W.
3. Call code or 911 if warranted or indicated by cardiopulmonary arrest or inability to maintain patent air way.
5. Start O2 at liters by nasal cannula, if indicated, to maintain O2 above 90 percent.
6. Monitor and record vital signs.
7. Notify Pharmacy and/or respiratory therapy if indicated.
8. Check patient’s allergies.
9. Give the following (one or more, order decided by treating RN), if indicated:
   □ Diphenhydramine 25 to 50 mg IV
   □ Hydrocortisone 50 to 100 mg IV
   □ Dexamethasone 10 to 20 mg IV
   □ Albuterol MDI Inhaler 2 puffs PRN
   □ Lorazepam 0.25-1mg IV
   □ Morphine Sulfate 2-4 mg IV
   □ Acetaminophen 650 mg- 1000mg Po
## APPENDIX K. Drug Reaction Protocol Form

<table>
<thead>
<tr>
<th>DRUG REACTION PROTOCOL</th>
<th>DATE/TIME</th>
<th>PROGRESS NOTES</th>
<th>DATE/TIME</th>
<th>DOCTOR'S ORDERS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>For SYSTEMIC DRUG REACTIONS:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ immediately stop administration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ contact attending physician, physician on call, or nurse practitioner</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ maintain existing IV access and keep line open</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>with Normal Saline or D5W</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ call code or activate 911 if warranted or indicated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>by cardiopulmonary arrest or inability to maintain patent airway</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ monitor and record O₂ sats</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ start O₂ by nasal cannula, if indicated, to maintain O₂ sats above 90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ monitor and record vital signs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ notify pharmacy and/or respiratory therapy if indicated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ check patient allergies</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ give the following (one or more, order decided by treating R.N.) if indicated:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ diphenhydramine 25 - 50 mg IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ hydrocortisone 50 - 100 mg IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ dexamethasone 10 - 20 mg IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ albuterol MDI 2 puffs pm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ lorazepam 0.25 - 1 mg IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ morphine sulfate 2 - 4 mg IV</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ acetaminophen 650 - 1000 mg po</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>➤ meperidine 12.5 mg IV for rigors. May repeat x 1.</td>
</tr>
</tbody>
</table>

**SIGNATURE:**

**DATE:**

**APPENDIX L.** Treatment Algorithm for Carboplatin Hypersensitivity Reactions

Patient develops carboplatin hypersensitivity reaction during the infusion at any treatment cycle (symptoms include minor rash to diffuse erythroderma, pruritis, severe anxiety, dyspnea, tachycardia, hypotension)

Stop infusion and appropriate supportive care and resuscitation measures

Symptoms subside after 30 minutes?

- **No**
  - Continue supportive care and no more treatment on the same day

- **Yes**
  - May reininitiate infusion at lower rate

  Symptoms recur during infusion?

- **Yes**
  - Stop infusion and appropriate supportive care and resuscitation measures, no more treatment on the same day

- **No**
  - Continue infusion

A patient who has previously received more than six cumulative cycles of platinum-based chemotherapy

An *intradermal skin test* 0.02 mL (0.002 mg) of carboplatin may be considered to predict hypersensitivity reaction

Positive skin test

- **Is alternative chemotherapy agent to carboplatin available?**

- **Yes**
  - Proceed with different chemotherapy regimen

- **No**
  - Discuss with patient and consider carboplatin desensitization protocol in the next treatment cycle

Negative skin test

- Proceed chemotherapy

References


*A positive test is defined as an observation of at least a 5 mm wheal with a surrounding flare after 15 minutes.*

**NOTE:** Premedication schedule: Dexamethasone 20 mg orally 12 hours, 6 hours, and 30 minutes before the infusion; 30 minutes prior to the desensitization administer diphenhydramine 50 mg IV and H2 blockers (cimetidine 300 mg or ranitidine 50 mg IV).
**APPENDIX L. Treatment Algorithm for Carboplatin Hypersensitivity Reactions (cont.)**

Treatment of Hypersensitivity Reactions:

1. Discontinue infusion
2. Administer 50 mg diphenhydramine IV and 100 mg hydrocortisone IV immediately
3. If hypotension is present, administer epinephrine 0.35–0.5 mL IV every 15–20 minutes until the reaction subsides or a total of six doses are given
4. If hypotension is present that does not respond to epinephrine, administer IV fluids
5. If wheezing is present that is not responsive to epinephrine, administer 0.35 mL of nebulized albuterol solution
6. Depending on severity of the reaction, the infusion may be reinitiated in 30 minutes after the symptoms have subsided
APPENDIX M. Prophylaxis and Treatment of Paclitaxel Hypersensitivity Reactions – Prophylactic and Treatment Algorithm

Prior to paclitaxel infusion, premedicate the patient with standard prophylactic doses of steroids and antihistamines.

Prior to paclitaxel infusion, premedicate the patient with standard prophylactic doses of steroids and antihistamines. Paclitaxel hypersensitivity reaction (chest tightness, back pain, diffuse erythroderma, dyspnea, tachycardia, hypertension, hypotension, and sensation of extreme anxiety)

Stop infusion and appropriate supportive care and resuscitation measures

Symptoms subside after 30 minutes?

Yes

May reinitiate infusion at lower rate

No

Continue supportive care and no more treatment on the same day

Symptoms recur during infusion?

Yes

Stop infusion and appropriate supportive care and resuscitation measures, no more treatment on the same day

No

Continue infusion

Is alternative chemotherapy agent to paclitaxel available?

Yes

Proceed with different chemotherapy regimen

No

Discuss with patient and consider paclitaxel desensitization protocol in the next treatment cycle

References
APPENDIX M. Prophylaxis and Treatment of Paclitaxel Hypersensitivity Reactions – Prophylactic and Treatment Algorithm (cont.)

Prophylaxis

1. For every 3-week (135–225 mg/m²) paclitaxel infusions, 30 minutes prior to infusion the patient should receive:
   a) 20 mg dexamethasone orally 12 hours and 6 hours before taxane (for paclitaxel only) and 20 mg IV before treatment
   b) 50 mg diphenhydramine IV before treatment
   c) H₂ blocker (cimetidine 300 mg IV or rantidine 50 mg IV) before treatment
   d) Slowly withdraw the patient (if possible) from any beta-blocker medication that could potentiate a reaction or make it harder to treat

2. For weekly 50–90 mg/m²/week) paclitaxel infusion, 30 minutes prior to the first weekly dose:
   a) 10 mg dexamethasone before treatment
   b) 25 mg diphenhydramine IV before treatment
   c) H₂ blocker (cimetidine 300 mg IV or rantidine 50 mg IV) before treatment

   NOTE: If no hypersensitivity reactions occur, all premedications can be deleted for subsequent weekly paclitaxel doses. If hypersensitivity reactions occur, every 3-week premedication protocol should be followed.

3. Treatment of reactions

   If hypersensitivity reaction occurs:
   a) Discontinue infusion
   b) Administer 50 mg diphenhydramine IV and 100 mg hydrocortisone IV immediately
   c) If hypotension is present, administer epinephrine 0.35–0.5 mL IV every 15–20 minutes until the reaction subsides or a total of six doses are given
   d) If hypotension is present that does not respond to epinephrine, administer IV fluids
   e) If wheezing is present that is not responsive to epinephrine, administer 0.35 mL of nebulized albuterol solution
   f) Depending on severity of the reaction, the infusion may be reinitiated in 30 minutes, after the symptoms have subsided
A Call-to-Action Workshop: 
Oncology Nurse Management of 
Hypersensitivity Reactions

Did your oncology nursing colleagues miss this event?

An archive of the live presentation for A Call-to-Action Workshop: Oncology Nurse Management of Hypersensitivity Reactions will be posted on www.imeronline.com

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