Advanced Oncology Certified Nurse Practitioner

REVIEW COURSE 2024

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

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Nursing Professional Development Specialist

Objectives

- Discuss the goal and role of chemotherapy treatment
- Describe the classifications of chemotherapy agents
- Identify the side effects and immediate complications of chemotherapy
- Discuss the safe handling of chemotherapy agents
- State the key points in the safe and effective administration of chemotherapy
- State factors to remember when prescribing chemotherapy as a Nurse Practitioner

ROAD MAP

- Chemotherapy Agent
- Mechanism of Action
- Chemotherapy Toxicities
- Safe handling of Hazardous Drugs
- Immediate Complications
- Extravasation

Systemic Cancer Treatment Modalities

	Chemotherapy	Hormone Therapy	Molecular Targeted	Immunotherapy
Target	Fast-growing cells (both cancer cells & certain populations of normal cells)	Tumor cells that express hormone receptors and thrive in a hormonal environment	Gene/protein molecules and pathways that cancer cells use to proliferate, metastasize and avoid apoptosis	Cells and pathways of the Immune system
Based on	Principles of cell kinetics & cell cycle	Hormonally driven tumors via cell signaling e.g. prostate and breast cancers	Gene mutations specific to the patient's cancer that cause dysregulated cell signaling	Theory of immunosurveillance and immune system manipulation

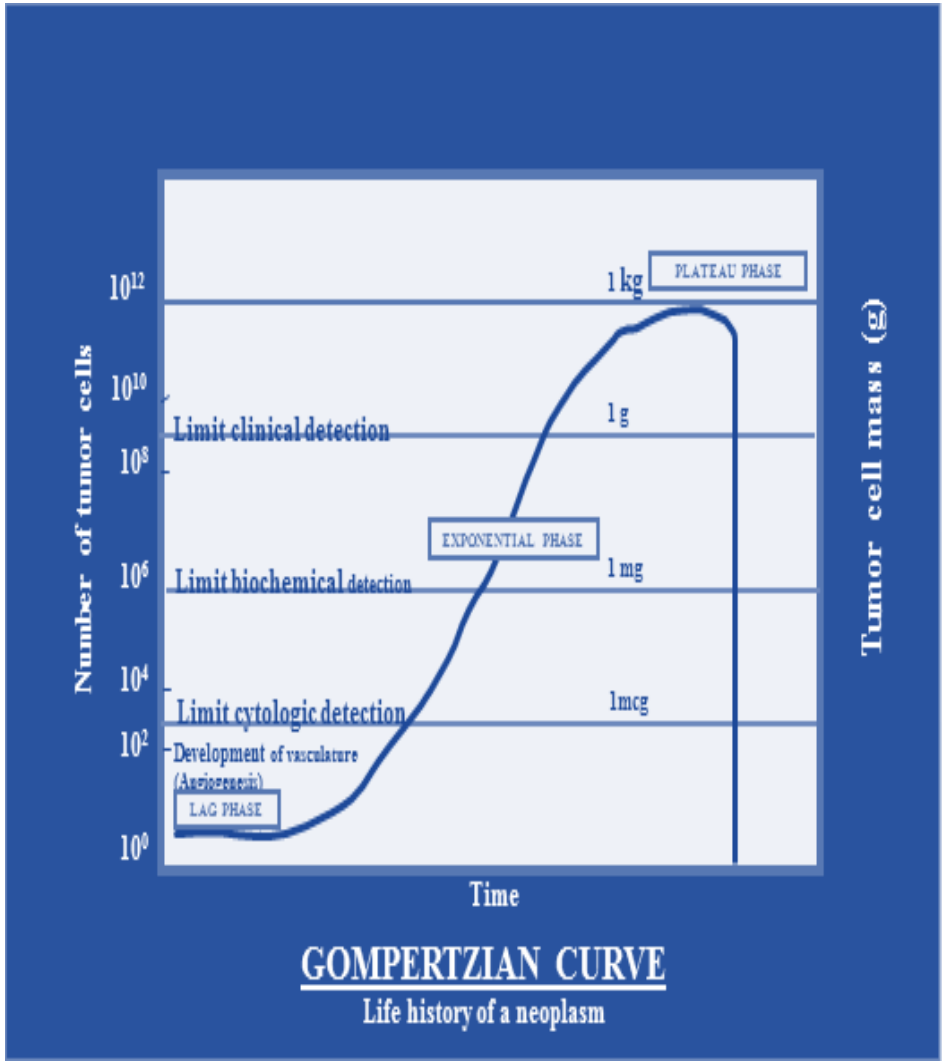
Chemotherapy

- **Chemotherapy is the practice of using chemicals to treat cancer.**

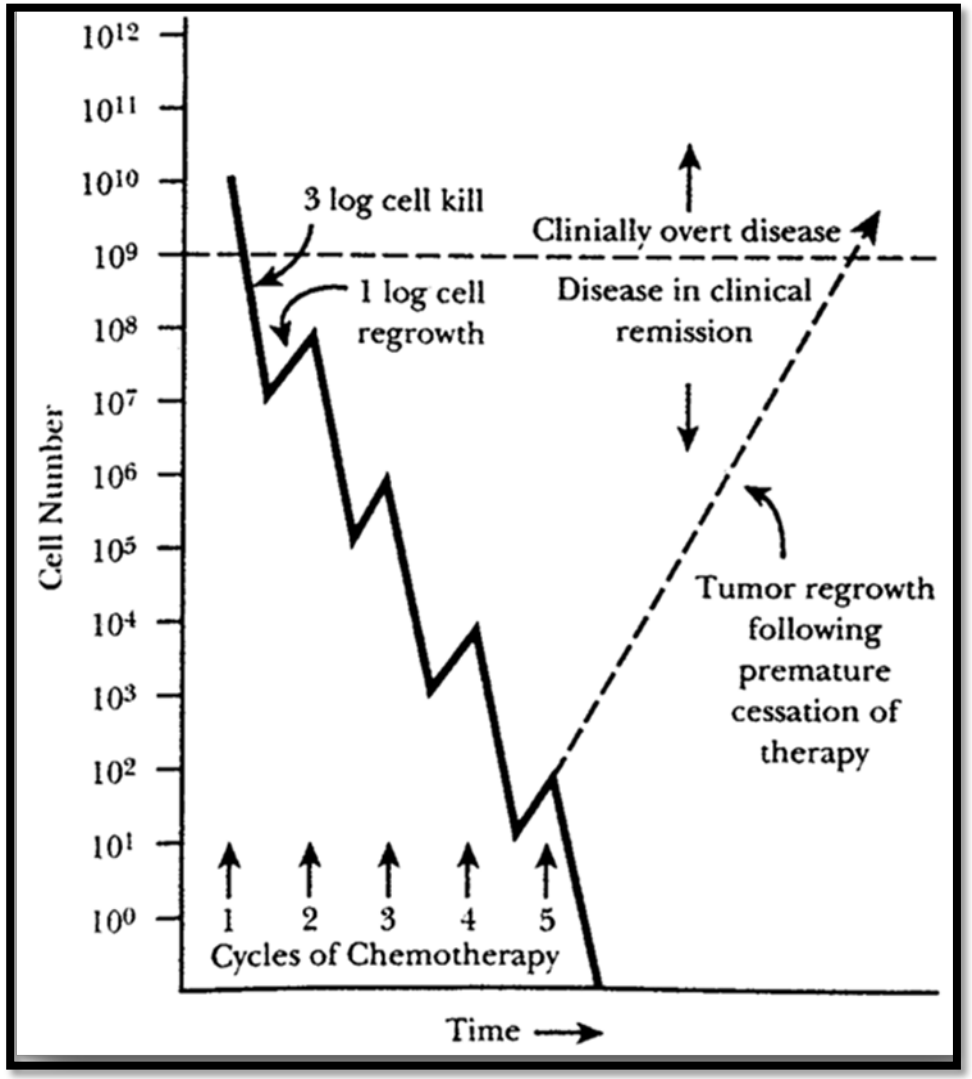
- Kills cells without any specific target
  - ❖i.e. affects rapidly dividing cells, both cancer and normal body cells.

- Side effects occur from damage to rapidly dividing normal body cells;
  - ❖Example: bone marrow stem cells, resulting in myelosuppression

Gompertzian Curve Growth Kinetics



Cell Kill Hypothesis: Skippers Law



Goals of Chemotherapy

- **Prevention-** use of agents to prevent cancer in high-risk individuals
  Antiestrogen (tamoxifen) to prevent breast cancer in high-risk individuals

- **Cure-** the objective is total tumor eradication;
  prolonged absence of detectable disease

- **Control-** the objective is to "arrest" or slow
  tumor growth; extend length and quality
  of life when a cure is not realistic

- **Palliation-** the objective is to alleviate symptoms
  when neither cure nor control is possible;
  relieve pressure on nerves, lymphatics, and vasculature;
  reduction of organ obstructions.

Curative Intent

Non-Curative Intent

Role of Chemotherapy

Primary approach- induction tx for hematological tumors & advanced solid tumors

Adjuvant - chemo used **after** the primary tx

Neoadjuvant - use of chemo before primary tx (i.e. surgery) to shrink the tumor before removal and/or decrease likelihood of micro-metastasis

Chemoprevention- use of agents to prevent cancer in high-risk individuals; e.g. tamoxifen to prevent breast Ca

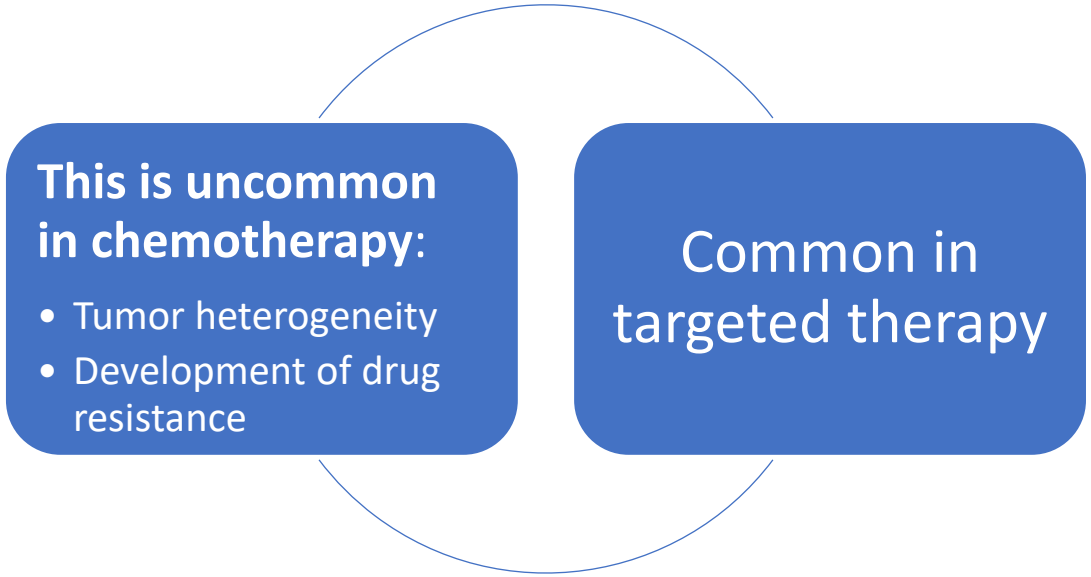
Myeloablation/immunosuppression(non- myeloablation)-obliterate bone marrow in preparation for Hematopoietic stem cell transplant (HSCT)

Radiation Sensitizer

Treatment Plans

Vary based on Diagnosis, Stage, and grade of Disease, & Tumor Genomics

Single Agent



Combination Agents

- **Selected based on:**
  - Synergistic action between agents
  - Different mechanisms of action on cell proliferation, which…
    - Improves cell kill in heterogeneous tumors
    - Decreases potential for resistance
- Need to minimize overlapping toxicities
- Improves outcomes but increases toxicity requiring more supportive care for symptom management

Response to Treatment: Influencing Factors

- Tumor Burdon
- Rate of tumor growth
- Combination vs. single-agent therapy
    - Strategy to provide maximum cell kill (tumor heterogeneity)
    - Provides synergy with minimal overlapping toxicities e.g. CHOP
    - Nadir occurs on days 7 – 10 with cyclophosphamide, whereas with doxorubicin it occurs on days 10 – 14
    - Oncovin (neurotoxin) and Prednisone (hyperglycemia) are non-myelosuppressive
- Dose or dose intensity
- Drug Resistance

Dose Limiting Toxicities (DLT)

- Generally, have serious sequelae, which may be potentially lethal
- If toxicity is serious enough, it may be identified as a BOXED WARNING
- Toxicities may require
    - **Dose Dela**y/interruption in therapy
    - **Dose Reduction** or
    - **Dose Discontinuation**
- Toxicities may be reversible or irreversible, based upon severity and/or early collaborative interventions
- CTCAE Grade 3 and 4 toxicities are often DLTs and require:
    - Assessment using CTCAE grading and timely communication
    - Documentation of onset, severity, and duration

CTCAE v5.0 (Common Terminology Criteria for Adverse Events)

Classification of Chemotherapy

Classifications of Chemotherapy Agents

Classified according to the following:

- Biochemical structure (mechanism of action)
- Cell Cycle Activity
  - **Cell cycle-specific drug** – Schedule Dependent
  - **Cell cycle non-specific** – Dose-Dependent

CHEMICAL CLASSIFICATION (Key * = Radiosensitizer ** = Cross BBB)

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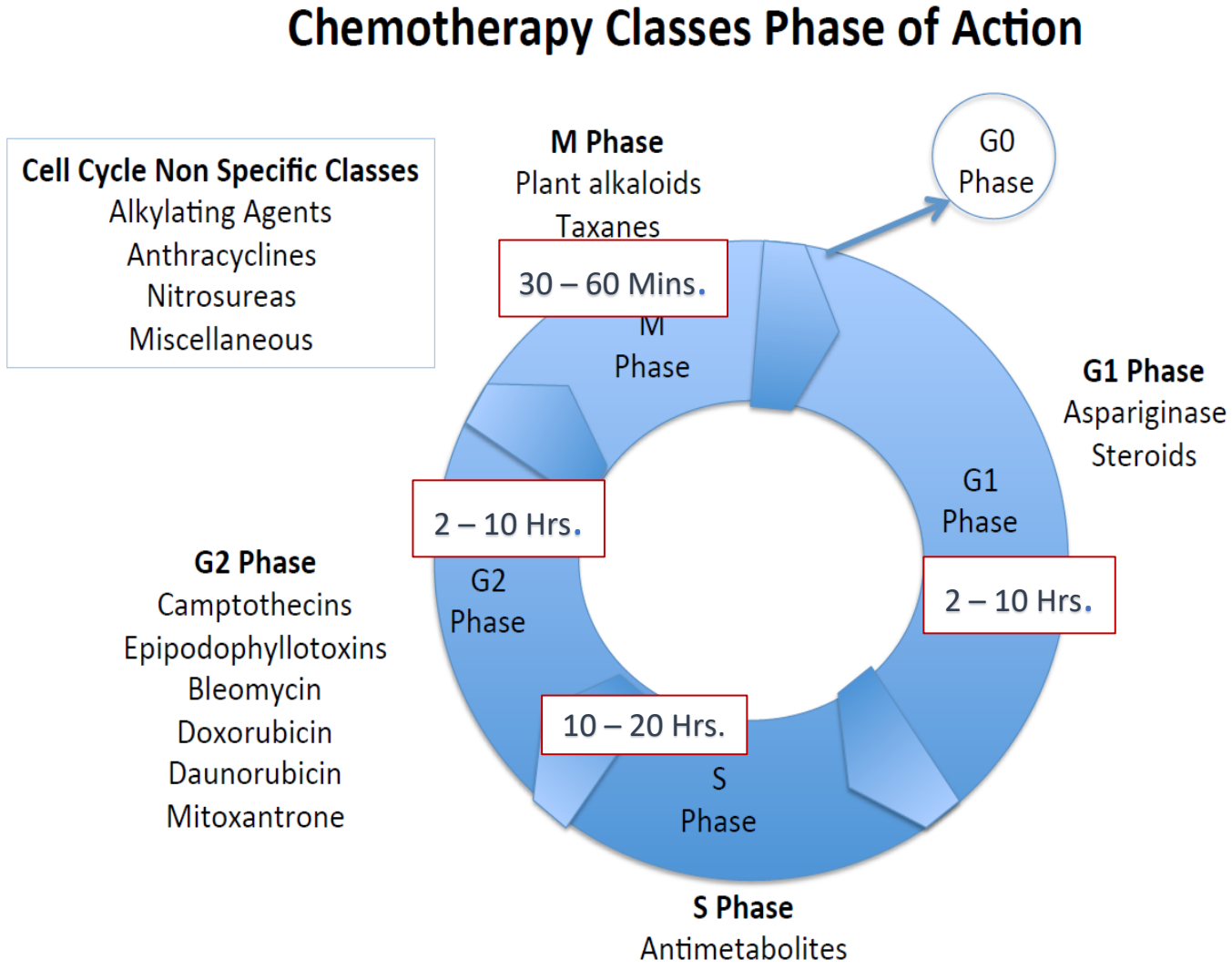
Alkylating Agents (Nitrosureas = sub-category) (DNA BINDING)	Antitumor Antibiotics (DNA BINDING)	Antimetabolites (Prevent synthesis of DNA – S Phase)	Plant Alkaloids	Miscellaneous (Indeterminate/ usual activity, unlike other classifications)
Platinum Agents • Carboplatin • Cisplatin * • Oxaliplatin	Anthracyclines • Doxorubicin • Daunorubicin • Epirubicin • Idarubicin • Liposomal doxorubicin • Valrubicin	Anti-Pyrimidines • Gemcitabine * (caution with hepatic insufficiency) • Fluorouracil • Capecitabine • Azacitdine • Decitabine	Mitotic Inhibitors – • Vinca Alkaloids: ○ Vinblastine ○ Vincristine ○ vinorelbine • Taxanes ○ Docetaxel ○ Paclitaxel	Asparaginase Pegaspargase
• Cyclophosphamide • Ifosfamide	Bleomycin	Anti-Purines • Clofarabine • Fludarabine • Mercaptopurine	Topoisomerase I inhibitors ** • Irinotecan • Topotecan	Arsenic Trioxide
Nitrosureas: • BCNU (BiCNI) ** • Lomustine **	Mitomycin	Anti-Folates • Methotrexate • Premetrexed	Topoisomerase II Inhibitors • Daunorubicin • Doxorubicin	Hydroxyurea

Cell Cycle Activity

All cells go through a cell division process.

- **CELL CYCLE PHASES:**
  - **G_o** – Non-dividing cells (G_0), can be recruited back into the cell cycle
  - **G1** – prepares the cell for cell division
  - **S** – (Synthesis) replicates DNA and forms a set of chromatids (DNA daughter strands)
  - **G2** – prepares for mitosis and synthesizes materials for mitotic spindles
  - **M** –chromosomes line up at centromere and are attached by mitotic spindle fibers.



Cell Circle Classifications

Cell Cycle-Specific Agents

- Exert effect within a specific cell cycle phase
  - Usually, S and M phase

Greatest tumor cell kill when given

- Frequent divided doses
- Continuous infusion with short cycle time

Examples:

- Antimetabolites
- Plant alkaloids
  - Epipodophyllotoxins
  - Taxanes
  - Vinca alkaloids
- Miscellaneous

SCHEDULE DEPENDENT

Cell Cycle Non-specific Agents

- Drug acts at any point in the cell cycle (including G0)
- Effective in slow-growing tumors
- Cytotoxicity is expressed when the cell replicates

Example:

- Alkylating
- Antitumor Antibiotics
- Nitrosoureas
- Hormone Treatment

DOSE DEPENDENT

Cell Cycle Specific Agents: Antimetabolites

Examples- (Gemcitabine, Fludarabine, and Methotrexate)

- Prevent synthesis of complementary DNA Strands during "S" Phase
- **Common Side Effects:**
  - Bone marrow depression with nadir in 7 – 10 days and recovery within 21 days
  - Bone marrow suppression (Dose Limiting Toxicity)
  - Mucositis: oral, esophagitis, intestine (diarrhea)
  - Nausea/vomiting
  - Flu-like Symptoms
- **Gemcitabine (Gemzar®)**
  - Inhibits DNA Synthesis
  - Metabolized by liver
  - Use cautiously in patients with renal or hepatic insufficiency
  - Toxicity is schedule-dependent.

Cell Cycle Non-Specific Agents:
Alkylating Agent: Examples

Nitrogen Mustard	Alkylating-like Compounds	Alkyl Sulfonates	Triazenes	Non-Classical
Bendamustine	Cisplatin	Busulfan	Dacarbazine	Thiotepa
Cholarambucil	Carboplatin		Temozolomide	Procarbazine
Cyclophosphamide	Oxaliplatin			
Ifosfamide				
Melphalan				

Alkylating Agents-Side Effects

Acute

- Nausea and vomiting
- Anemia, leukopenia, thrombocytopenia
- Mucositis
- Alopecia and nail damage

Long term

- Infertility
- Neuropathy with platins
- Secondary malignancy

Side Effects of Chemotherapy

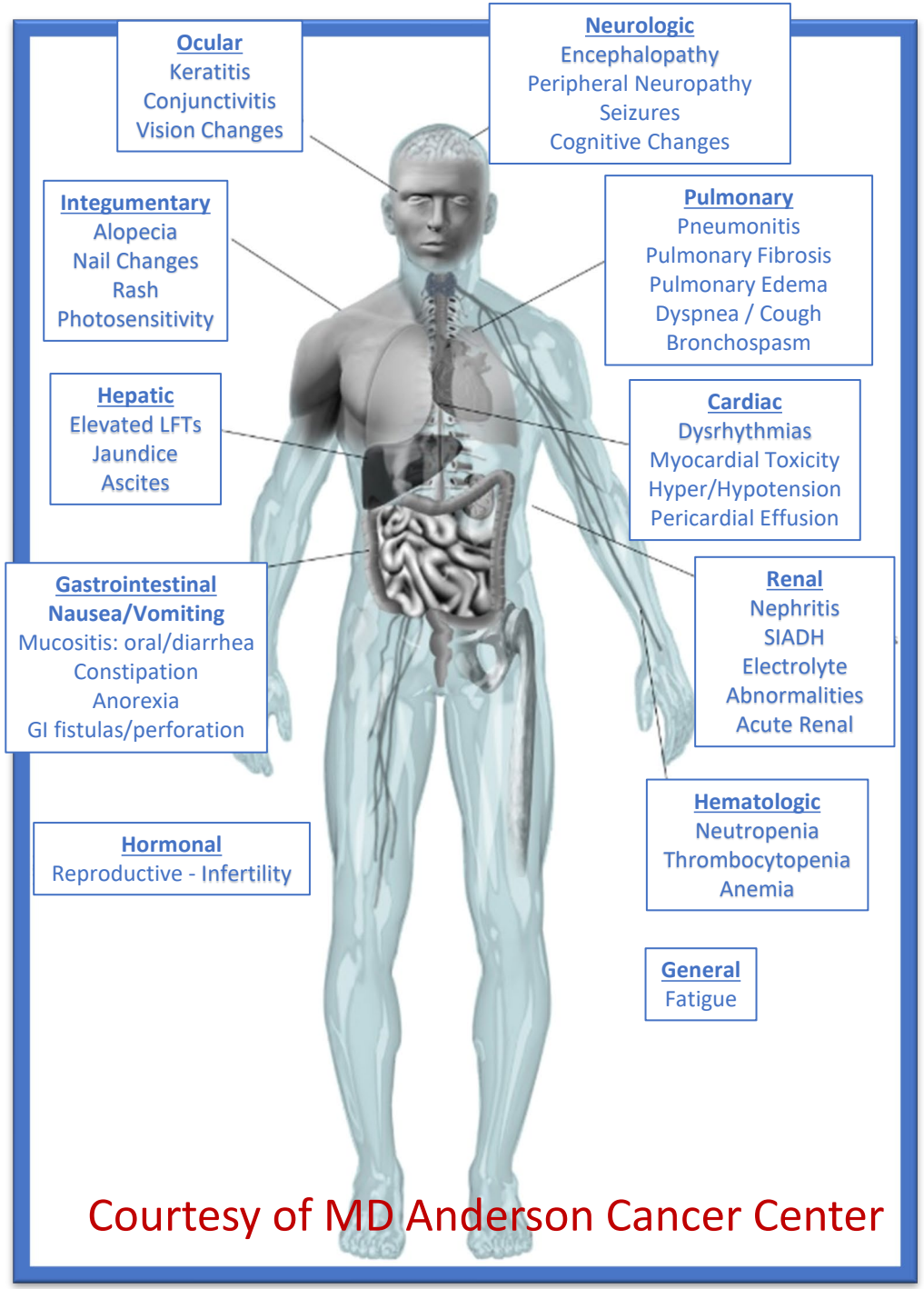
Potential Effects of Chemotherapy

Some adverse effects are due to action on rapidly dividing cells:

- Integumentary
- GI
- Hematologic
- Reproductive issues

Some adverse effects are due to drug metabolism:

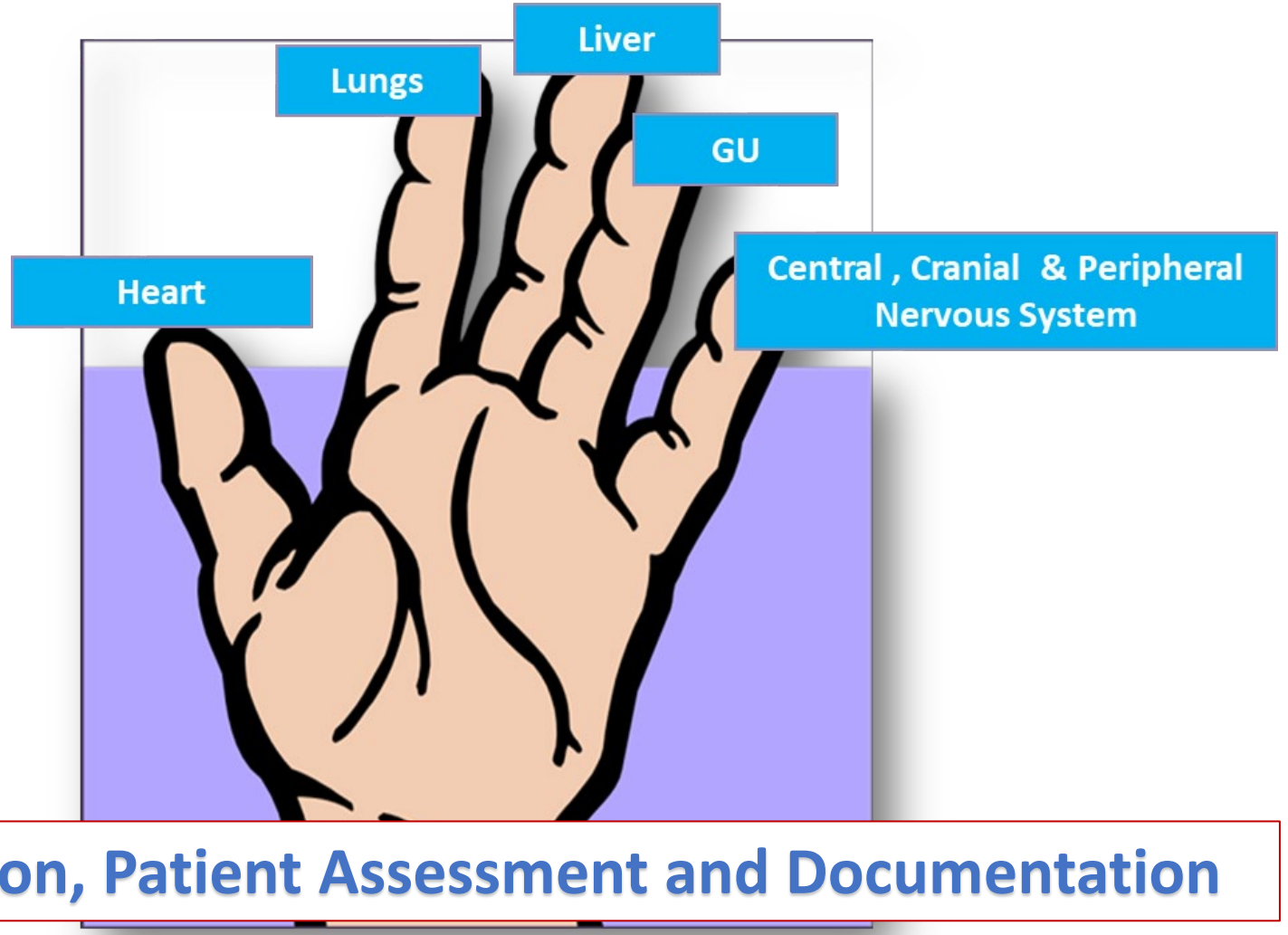
- Neurologic
- Pulmonary
- Cardiac
- Renal
- Liver



SIDE EFFECTS OF CHEMOTHERAPY

FAST DIVIDING CELLS

ORGAN TOXICITIES



Good Resource for Patient Education, Patient Assessment and Documentation

Managing Adverse Effects of Chemotherapy

Potential adverse events (AEs), that are not anticipated and managed using an evidence-based approach, may result in poor clinical outcomes, including treatment non-adherence and/or treatment cessation.

The Advanced Practice Oncology Nurse must:

- Have a good understanding of which chemotherapeutic agents are known to place patients at risk for adverse events.
- Be able to determine appropriate prophylactic medications to employ for AE prevention

Pre-medications to minimize the potential for common AEs related to systemic cancer therapies is essential

Addressing Common Adverse Events of Chemotherapy

CINV Risk Categories

CINV RISK CATEGORIES	ACRONYM	PERCENTAGE	CHEMOTHERAPY EXAMPLES
Highly Emetogenic Chemotherapy	HEC	90%	AC (combo. Doxorubicin or epi + cyclophosphamide) Cisplatin Cyclophosphamide ($\geq$ 1,500 mg/m^2) Epirubicin (> 90 mg/m^2) Ifophamide ($\geq$ 2 g/m^2 per dose)
Moderately Emetogenic Chemotherapy	MEC	30 – 90%	Amifostine (> 300 mg/m^2) Cytarabine ($\geq$ 200 mg/m^2) Irinotecan Oxaliplatin Temozolomide
Low Emetogenic Chemotherapy	LEC	10 – 30 %	Docetaxel Doxorubicin (liposomal) Etoposide Topotecan
Minimally Emetogenic Chemotherapy	Minimal	$\leq$ 10%	Cytarabine ($\leq$ 100 mg/m^2) Decitabine Valrubicin Vincristine

Common Adverse Events of Chemotherapy:
TYPES OF CINV

TYPES	DESCRIPTORS
ACUTE	Within 1st 24 hours of chemotherapy
DELAYED	24 hours after chemotherapy
ANTICIPATORY	Conditioned/learned response occurs before chemotherapy begins
BREAKTHROUGH	Occurs within 5 days of prophylactic antiemetics and requires rescue therapy
REFRACTORY	Occurs when patients develop CINV during subsequent cycles of chemotherapy when antiemetic prophylaxis has not been successful in controlling CINV in earlier cycles.
CHRONIC CINV	In advanced cancer patients. Poorly understood etiologies

KEY PRINCIPLES OF ANTIEMETICS FOR CINV

- Initiate prophylaxis for chemotherapy treatment plans >10% risk for CINV
- Continue prophylaxis long enough to cover the duration of emetic risk
- Highest emetogenic potential should guide the selection of antiemetic prophylaxis
- Reevaluate emetic risk for breakthrough CINV and add antiemetic with different MOA than those used in the previous cycle
- Olanzapine is a first-line agent for the management of breakthrough CINV

Sequence of Chemotherapy Agent Administration

- Taxanes should be administered before platinum
  - May reduce the severity of myelosuppression
- Considerations with camptothecins and cisplatin
  - Cisplatin before irinotecan (better tumor response without increasing toxicity)
  - Topotecan before cisplatin (reduces myelosuppression)
- If there is no evidence to support a specific sequence:
  - Follow institutional policy & safety considerations
  - Sequence should be stated in the orders
  - Administer according to a clinical trial or standard of care ordering sequence

Rescue / Modulating Medications (Offset Toxicities)

Chemo Protectant (use prophylactically)

- Mesna (Uromitexan®)-bladder protectant. Utilized with all Ifosfamide dosing & high doses of Cyclophosphamide
- Amifostine (Ethyol®) - to prevent Cisplatin induced nephrotoxicity & radioprotectant in H&N Patients
- Dexrazoxane- 2 formulations
  - Zinecard®- cardioprotective after cumulative doses of anthracycline
  - Totect® - anthracycline extravasation
- Anticonvulsants to prevent seizures r/t HD Busulfan
- Folic acid & vitamin B-12- reduce hematologic toxicity. Supplementation with Pemetrexed (Alimta®)

Rescue

- Uridine triacetate (Vistogard®) at the initial signs of early-onset, severe, or serious 5-FU toxicity
- Folic acid (Leucovorin®) given following high dose methotrexate to rescue the patient from severe toxicities
- Glucarpidase (Voraxaze®) when impaired renal function delays Methotrexate clearance despite leucovorin rescue

Immediate Complication

Hypersensitivity & ANAPHYLACTIC Reactions: OCCURRENCE

Common Occurrence:

- **Initial exposure**: often the highest risk (e.g., Taxanes, Rituximab)
- **Multiple exposures**: some have a higher risk with more exposure (e.g., Carboplatin, Oxaliplatin, L-Asparaginase)

- **Timing with the infusion**:
  - **Acute reaction**: maybe minutes to hours into the infusion
  - **Delayed reaction**: maybe 10-12 hours after exposure

Hypersensitivity & Anaphylactic Reactions: SYMPTOMS

Airway compromise	• Stridor • Hoarseness • Tongue or throat swelling
Breathing difficulty	• Shortness of breath • Drop in O_2 Saturation • Wheezing • Cyanosis • Respiratory arrest
Cardiac compromise	• Tachycardia • Hypotension • Myocardial ischemia • Cardiac arrest

Hypersensitivity & Anaphylactic reactions: SYMPTOMS

Neurologic changes	• Agitation • Altered mental status • Confusion • Loss of consciousness
Skin and mucosal changes	• Erythema • Urticaria • Periorbital or facial edema
GI symptoms (less common)	• Abdominal cramping • Diarrhea • Nausea • Vomiting

Common Terminology criteria for adverse event grading for allergic reaction and anaphylaxis

Adverse Event	1	2	3	4	5
Allergic Reaction	A systemic intervention is not indicated	An oral intervention is indicated	Bronchospasm; Patient will need intravenous intervention; and Hospitalization is indicated for clinical sequelae	There is life threatening consequences; urgent intervention is indicated	Death
Anaphylactic Reaction	-	-	Symptomatic Bronchospasm is noted with or without urticarial; Parenteral intervention needed; hypotension; Allergy- related type of edema	There is life threatening consequences; urgent intervention is indicated	Death

CTCAE, v.5.0

Definition: A disorder characterized by an adverse reaction to the infusion of pharmacological or biological substances

Hypersensitivity Reaction (HSR) Management

- Stop the infusion
- Open normal saline line
- Call for help
- Obtain vital signs
- Activate HSR orders
- Pull hypersensitivity algorithm to guide practice
- Administer appropriate medications
- Notify the provider to provide further instruction
    - If HSR orders indicate to restart at half rate after symptoms resolve, restart at half rate
- Order HSR in Smart sets
- Document HSR and place medication in allergies
- Place Safety Report

Definition of Terms

- **Vesicant:** A medication that can cause tissue necrosis or blistering when it accidentally infuses into tissue outside of a vein.
- **Extravasation:** administration of a vesicant solution or medication into surrounding tissue. Blood return will Not be present
- **Infiltration:** administration of a non-vesicant solution or medication into surrounding tissue. Blood return may or may not be present.

Signs and symptoms of Extravasation

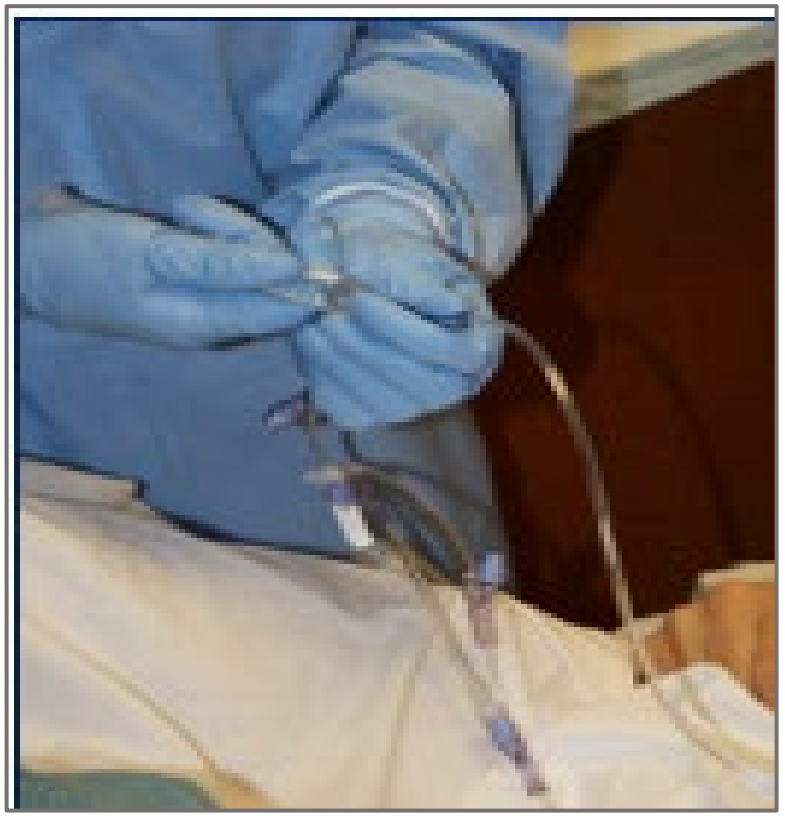
Sign	Immediate and Delayed Symptoms
Pain	▪ **Immediate**: burning, stinging, or sensation of coolness at and around the site. Some patients may not experience pain ▪ **Delayed**: intensity may increase over time
Redness	▪ **Immediate**: may occur but not always present. May be difficult to detect if it is in deep tissue ▪ **Delayed**: may intensify over time
Swelling/ Erythema	▪ **Immediate**: usually present especially with superficial extravasation; harder to detect if extravasation is in deep tissue ▪ **Delayed**: may increase over time
Blood return	• **Immediate**: loss of blood return may be first sign of possible extravasation
Ulceration	▪ **Immediate**: none may be detected ▪ **Delayed**: increased erythema, blistering and soughing may occur 1 – 2 weeks after event. May be followed by necrosis and require surgical consult.

Common Terminology Criteria for Adverse Events Grading for Infusion Site Extravasation

Adverse Event	1	2	3	4	5
Extravasation of infusion site	Edema - Painless	Erythema with symptoms such as pain, edema, phlebitis, induration	Necrosis, or ulceration with severe tissue damage; requires operative intervention	Severe life-threatening consequences, intervention requires urgent care	Death

CTCAE, v.5.0

Management of Extravasation



S Stop

L Leave (IV in place)

A Aspirate (attempt to aspirate any residual fluid)

P Pull Needle

P Provider notification

Extravasation Guidelines

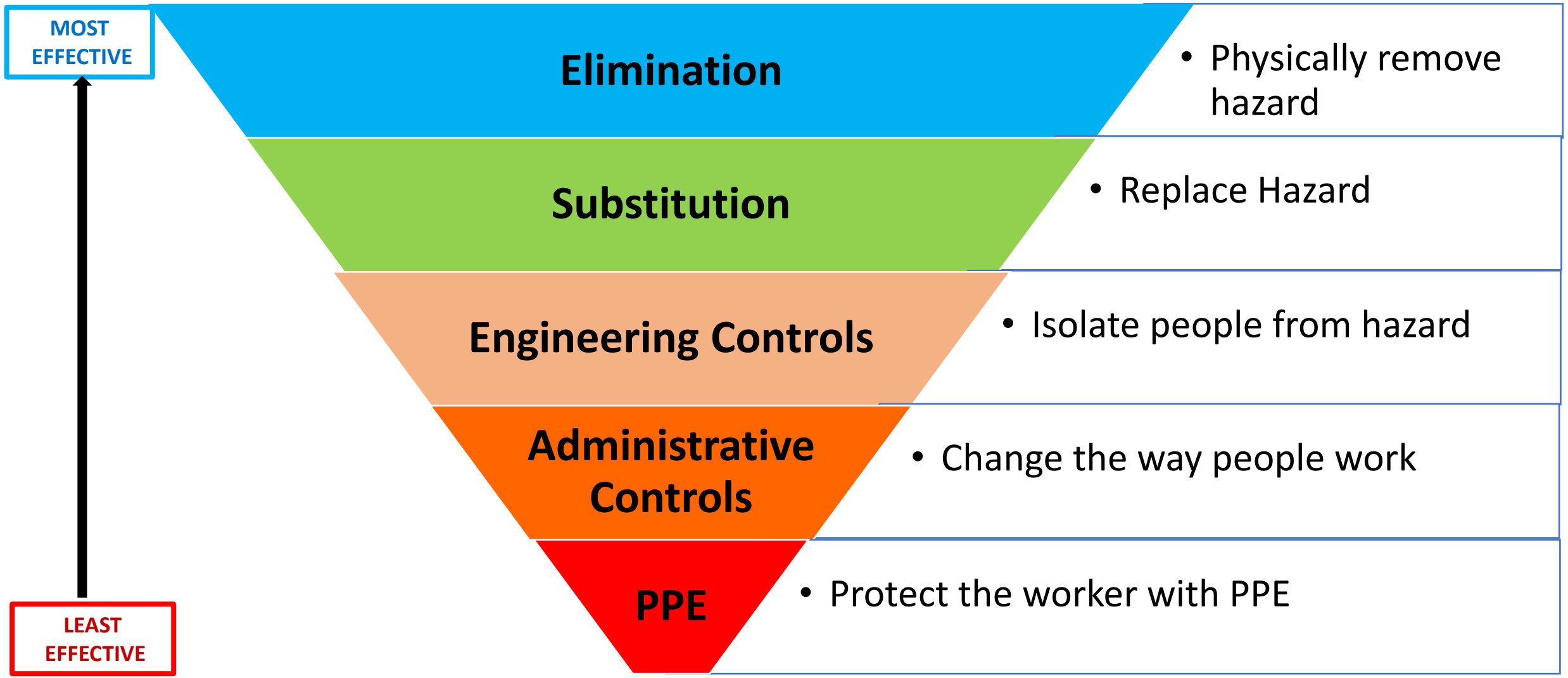
Agent	Topical Therapy	Antidote	Antidote or Treatment to be Administered
Alkylating: Mechlorethamine	Place ice for 6-12 hours following sodium thiosulfate	Sodium thiosulfate	Inject 2ml of sodium thiosulfate for every milligram extravasated using a 25 gauge or smaller needle into the subcutaneous
Alkylating: OXALIplatin	Warm Compress	Dexamethasone 8mg twice a day for 14 days	
Anthracyclines: DAUNOrubicin, DOXOrubicin, EPirubicin, IDArubicin	Place ice, remove 15 minutes prior to Dexrazoxane	Dexrazoxane	Dexrazone infusion within 6 hours of extravasation; infused over 1-2 hours for 3 days in any area other than the extravasation site
Antibiotics: Mitomycin, DACTINomycin	Place ice for 15-20 minutes four times a day for 24 hours	None	
Plant Alkaloids: VinBLAStine, VinCRIStine, Vindesine, Vinorelbine	Place warm pack for 15-20 minutes four times a day for 24-48 hours, keep extremity elevated	Hyaluronidase	Administer 1 ml (150 units) of hyaluronidase SQ in 5 separate injections, each containing 0.2 ml of solution using 25-gauge or smaller needle
Taxanes: DOCEtaxel, PACLitaxel	Place ice for 15-20 minutes 4 times a day for 24 hours		

Safe Patient Handlining

Safe Handling of Hazardous Drugs

- **NIOSH and the American Society of Health-System Pharmacists (ASHP) consider agents known to have one or more of the following toxicities as Hazardous:**
  - Carcinogenicity
  - Teratogenicity / developmental toxicities
  - Reproductive toxicities (e.g. infertility, low sperm count, miscarriages, low birth weights)
  - Organ toxicities (e.g. cardiac, renal, hepatic) at low doses
  - Genotoxicity (e.g. mutagenicity)
  - Structure & toxicity profiles of new drugs that mimic existing drugs determined hazardous in #s 1 - 5

NIOSH Primary Prevention recommendations



Hazardous Drug Spill Kit

PPE

- Gown
- Double gloves
- Respirator mask
- Goggles
- Shoes covers

Signage

- Outside room to alert of spill

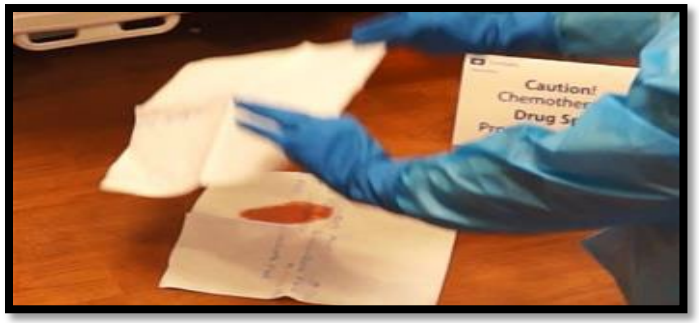
Absorbent materials- absorbent pad, material to crystallize liquid spill

Hazardous waste disposal bag/liner

Photo Courtesy of MDACC

Hazardous Drug Spill Steps 1-7

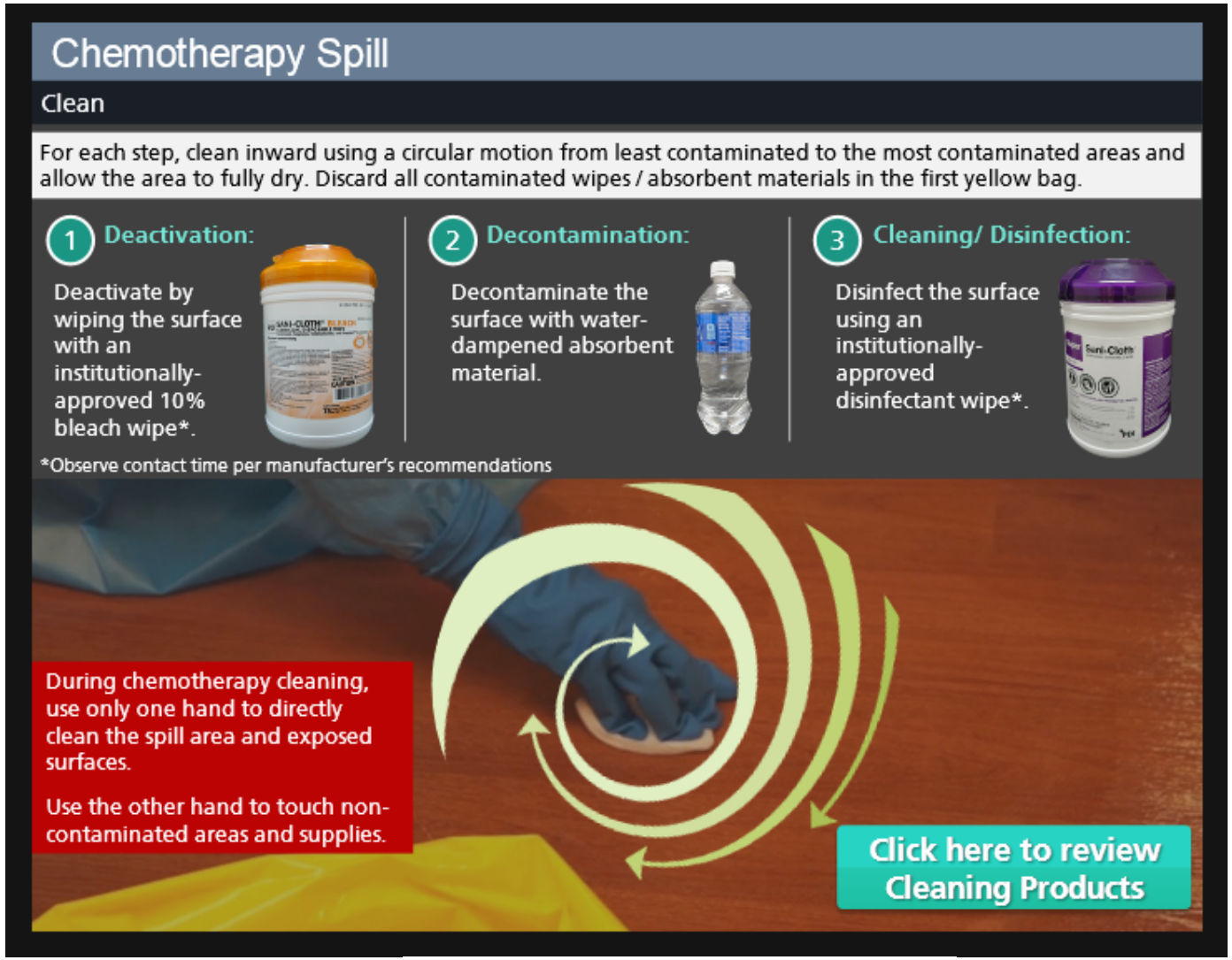
1. Assess	Assess exposure of individuals and isolate them from spill
2. Evacuate	Evacuate patients and personnel from area
3. Retrieve	Have Spill Kit retrieved
4. Place	Place signage
5. Don	All involved must don HD-Tested PPE (double gloves, gown, respiratory & face protection)
6. Contain	Contain the spill using plastic-backed absorbent sheets or spill pads.
7. Dispose	Place pads or towels into the waste disposal bag, avoiding contamination of the opening of the bag.



Photos Courtesy of MDACC

Hazardous Drug Spill Steps 8-10

8. Deactivate	10% Bleach solution OR other approved solution per your organization
9. Decontaminate	Rinse area with adequate dilution of HD residue. Such as water dampened absorbent pad
10. Disinfect/Clean	With an institutionally approved disinfectant wipe/liquid



Courtesy of MDACC

Accidental Exposure

- Skin
- Eye(s)
- Inhalation
- Ingestion

- Obtain emergent treatment after exposure
- Refer to SDS specific to the agent
- Report exposure to the employee health department for follow-up

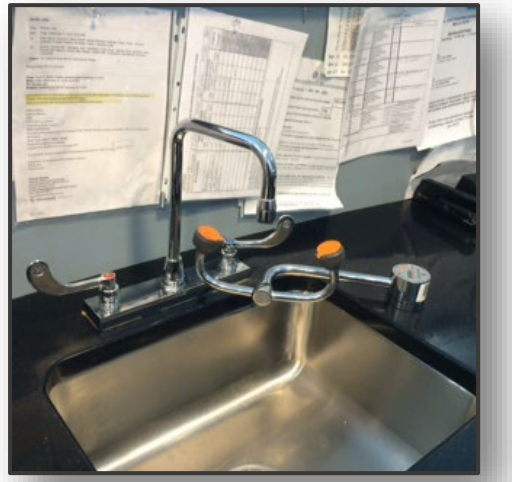


Photo courtesy of MD Anderson Cancer Center

Chemotherapy Administration: Key Points

Verification Elements

- Confirm informed consent has been obtained.
- The treatment plan has been reviewed for completeness and accuracy, including:

  - Patient name/DOB/MRN- NOT room or chair numbers
  - Allergies
  - Height/weight/BSA calculation
  - Drug/dose
  - Route of administration
  - Date/time of administration
  - Rate/volume of infusion
  - Start date/frequency/cycle
  - Supportive care treatments (hydration, premeds)
  - Provider signature(s) and date
  - Gender Identity

Pregnancy Screening

It is the RN's responsibility to ensure that a negative pregnancy screening is documented in the chart within the appropriate timeframe

Eligible:

- All female patients who are between the onset of menses and menopause must be screened and have their test results available in the medical record within the last 30 days before receiving treatment with systemic chemotherapy/biotherapy

- Screening should be checked at least 7 days before the treatment

Excluded:

- Postmenopausal
- History of hysterectomy or bilateral salpingo-oophorectomy.
- Ovarian failure
- History of bilateral tubal ligation or another surgical sterilization procedure

Treatment Schedule Dose Determination

To increase the accuracy of doses stated weight and height are not part of practice.

- Milligrams per kilogram of body weight (mg/kg)
- Body Surface Area (BSA) mg/m2
- Area under the Curve (AUC)
- Flat Dosing
- Dosage Variation
  - > 15% for **Carboplatin** notify MD
- BSA Variation- 5%
- 10% variation in weight
- Cumulative Dose/Lifetime Dose
- Pharmacokinetics
- Pharmacodynamics

Image Courtesy of MD Anderson Cancer Center

Dose Determination

Body Surface Area (BSA) mg/m2

$$\text{Formula} = \sqrt{\frac{\text{Height X Weight}}{3600}}$$

Total Dose =

BSA X mcg, mg, or gm/m^2

Calvert Formula to Calculate Area Under the Curve for Carboplatin

Carboplatin Dose ____mg = (AUC= _____) x (GFR _____+25)

Factors to Remember

- Advanced Practice RNs Must Consider:
  - Patient safety: cancer therapies are high-risk drugs
  - Confirm the stage of disease and identify patients' preferred goals of care
  - Confirm patient's allergies, document patient education and informed consent
  - Complete a chemotherapy plan, identify dosage, and treatment duration, and monitor the patient.
  - Implement ongoing patient and family education and monitor for adverse events (AE)/toxicities
  - NP should take the lead on assessing (CTCAE Grade), managing and documenting AEs and adjustments in therapy

Thank you!

Questions

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