

# DIFFERENCES IN CANCER TREATMENT BETWEEN CHILDREN AND ADULTS

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# DISCLOSURES

Presenter has no financial disclosures or conflicts of interest



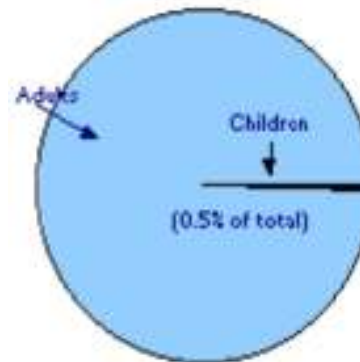
# OUTLINE

- Determine how oncologic disease states differ between adult and pediatric patients based on presentation, treatments, and outcomes
- Review calculations commonly used in dosing for pediatric oncology patients
- Examine potentially dangerous drug-drug interactions (DDIs) unique to chemotherapy agents

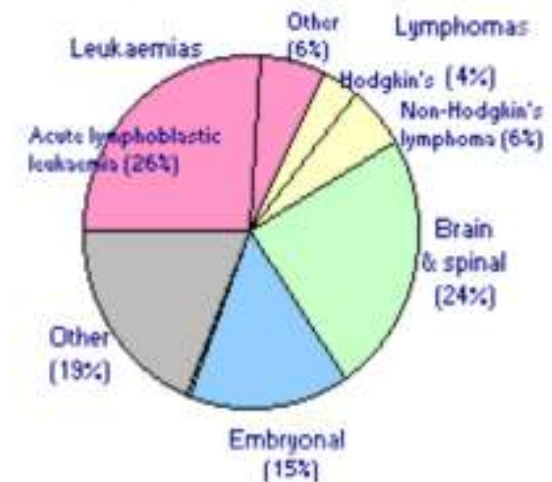
# ADULT VS PEDIATRICS BA0

- Kids get different cancers
- Second leading cause of death in children (accidents)
- Less patients (Children's Oncology Group, COG)
- **Kids are healthier** when starting treatment
- **Higher cure rate**
- Late effects
- Kids can't speak for themselves (supportive care)

All cancers



Childhood cancers



## Slide 4

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**BA0**

[@Kang, Jinjoo] I see you changed the format on this slide, did you want all future slides to reflect this format?

Bevinetto, Angelica, 2022-11-01T19:51:14.109

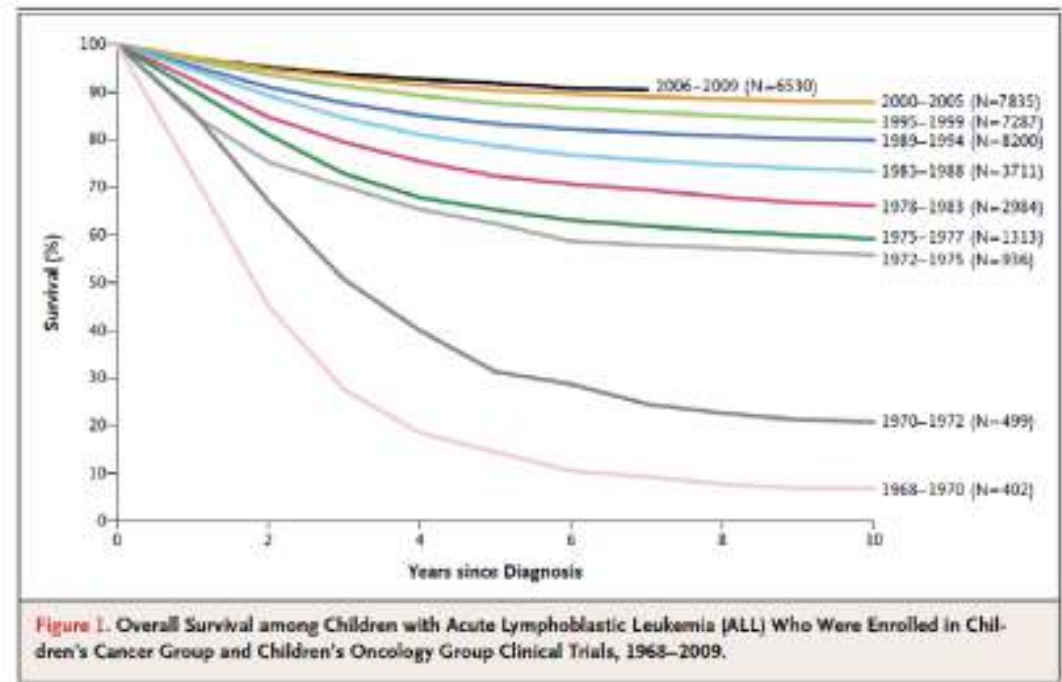
# ORGANIZATIONS FOR PONC

CHILDREN'S  
ONCOLOGY  
GROUP

The world's preeminent  
pediatric oncology

## COG - Children's Oncology Group

- Clinical trials group supported by the National Cancer Institute (NCI)
- Devoted exclusively to pediatric cancer research
- More than 200 centers around the world are part of COG



## Slide 5

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**BA0** Hunger SP, Mullighan CG. Acute Lymphoblastic Leukemia in Children. N Engl J Med. 2015 Oct 15;373(16):1541-52.  
Bevinetto, Angelica, 2022-09-14T15:21:01.949

# ORGANIZATIONS FOR PONC

NCCN - National Comprehensive Cancer Network

- Clinical practice guidelines (CPGs) for oncologic disease states and supportive care
- Specializes in mostly adult cancers



POGO - Pediatric Oncology Group of Ontario

- CPGs for supportive care related to pediatric oncology (fatigue, febrile neutropenia, etc)



IDSA - Infectious Diseases Society of America

- CPGs for management of infections – many focus on the immunocompromised population





# COG PROTOCOLS BA0

How are protocols named?

By Disease Type

All Types | ADM | **ALL** | AML | BRC | BTR | CCL | CNS | DAT | DVL | EPI |  
EWS | GCT | HEP | HOD | IND | LTC | LTE | MEL | NBL | NFM | NHL | NUR  
| OST | PHM | PSY | RAD | RARE | REN | RET | RST | SCT | SMN | SUP

# AALL1732

## Slide 7

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**BA0** While reviewing, please look at "slide view" to see animations  
Bevinetto, Angelica, 2023-08-02T19:34:46.956

# PONC OUTCOMES

After accidents, cancer is the second leading cause of death in children ages 1 to 14

About 10,470 children in the United States under the age of 15 will be diagnosed with cancer in 2022. About 1,050 children under the age of 15 are expected to die from cancer in 2022

Because of major treatment advances in recent decades, **85% of children with cancer now survive 5 years or more.** However, survival rates can vary depending on the type of cancer and other prognostic factors.



## Slide 8

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**BA0**

American Cancer Society. Cancer Facts & Figures 2022. American Cancer Society. Atlanta, Ga. 2021.

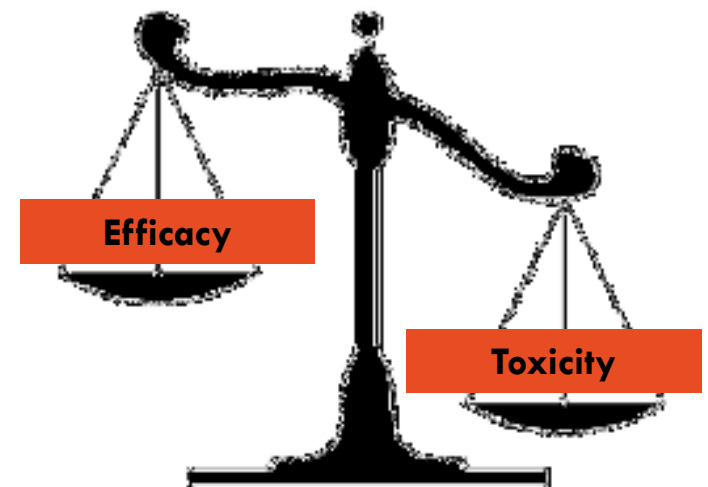
Bevinetto, Angelica, 2022-09-14T15:52:22.056

# PONC OUTCOMES

There are an estimated >500,000 childhood cancer survivors in the United States

More than 95% of survivors will have a significant health related issue by the time they are 45 years of age

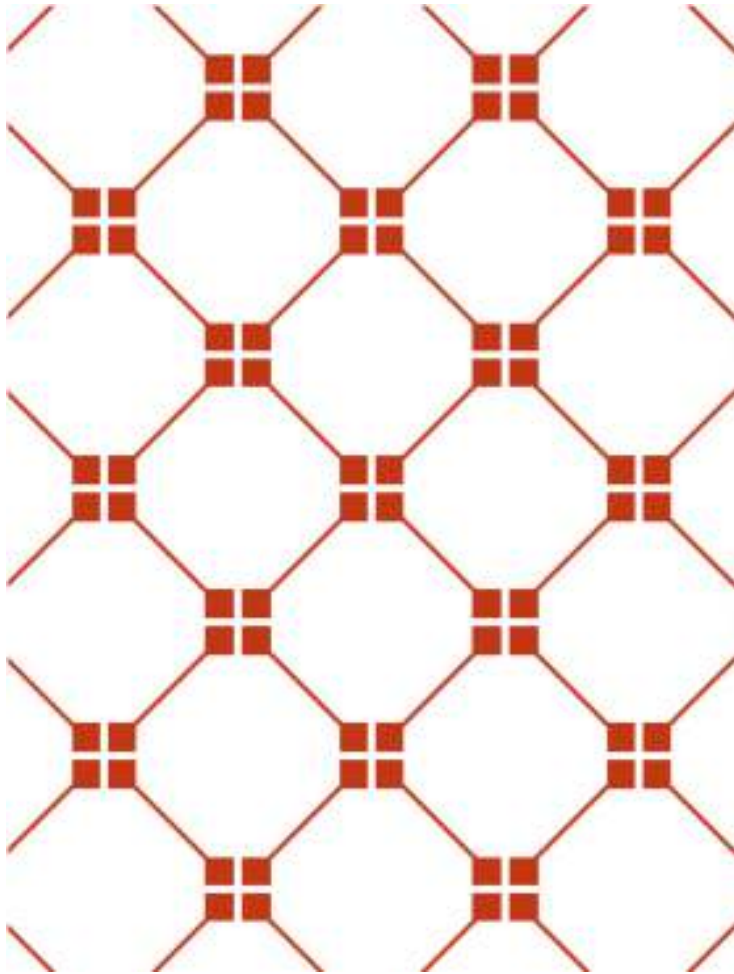
These issues are results from either the cancer or commonly from the treatment



**Slide 9**

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**BA0** COG. Parenteral And Oral Chemotherapy Administration Guidelines. May 2020  
Bevinetto, Angelica, 2022-09-14T17:21:53.607



# CHEMOTHERAPY AND CALCULATIONS OVERVIEW

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# WHAT IS CHEMOTHERAPY?

## Conventional

- Utilizes chemicals to destroy existing cancerous cells
- Types of chemotherapy include alkylating agents, antimetabolites, anti-tumor antibiotics, topoisomerase inhibitors, mitotic inhibitors, and plant alkaloids



## Biologics

- Derived from living organisms or their products and used as diagnostic, preventive, or therapeutic agents
- Types of biologics include colony stimulating factors (CSF), monoclonal antibodies (MABs), interferons, and interleukins (ILs)



Targeted therapy: Cancer treatment that targets proteins that control how cancer cells grow, divide, and spread. Most targeted therapies are either small-molecule drugs or monoclonal antibodies.

BA0



## Slide 11

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**BA0** I think this would look better as a venn diagram?

Bevinetto, Angelica, 2022-09-14T18:35:17.398

**BA1** Baudino TA. Targeted Cancer Therapy: The Next Generation of Cancer Treatment. *Curr Drug Discov Technol.* 2015;12(1):3-20.

Bevinetto, Angelica, 2022-09-14T18:48:37.708

# STAYING SAFE: PREPARATION AND ADMINISTRATION

"The National Institute for Occupational Safety and Health (NIOSH) considers a drug to be **hazardous** if it exhibits one or more of the following characteristics in humans or animals:

- **Carcinogenicity**
- **Teratogenicity**
- **Developmental toxicity**
- **Reproductive toxicity**
- **Organ toxicity at low doses**
- **Genotoxicity**
- or structure and toxicity profiles of new drugs that mimic existing hazardous drugs."

## Slide 12

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### **BA0**

Connor TH, MacKenzie BA, DeBord DG, et al. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication Number 2016-161 (Supersedes 2014-138)

Bevinetto, Angelica, 2022-09-14T18:50:32.415

# STAYING SAFE: PREPARATION AND ADMINISTRATION

## United States Pharmacopoeia (USP) Chapter 800: Hazardous Drugs – Handling in Healthcare Settings

- Guide for the handling of hazardous drugs and protect health care personnel, patients, and the environment during the transport, storage, preparation, dispensing, and administration of these medications.

### USP <800> REQUIREMENTS AT A GLANCE

Gloves	Double chemotherapy gloves (American Society for Testing and Materials D5878-05) for all hazardous drugs (HDs), including reproductive only HDs
Gowns	Disposable, with ability to resist chemotherapy, long sleeves, elastic or knit cuffs, closed front, and without seams or closures that could allow HD exposure Cloth lab coats, smocks, and isolation gowns are specifically prohibited Gown gowns must not be worn outside of HD handling areas
Respiratory protection	Full-face respirator equipped with a P100 filter or equivalent for respiratory exposure when cleaning spills in "larger than what can be contained with a spill kit" and/or "a known or suspected airborne exposure to personnel or patient" occurs
Face protection	Face shields and goggles for risk of splash (e.g., working above eye level, cleaning spills, surgery)
Waste disposal	Place in special containers designated for HDs
Closed system transfer devices	Required for HD administration when route allows (suggested for compounding)
Education	Training required prior to handling HDs and annually thereafter
Medical surveillance	Specific recommendations: <ul style="list-style-type: none"> <li>- Obtain baseline assessment, including medical and reproductive history and prior exposure to HDs; history should include estimated quantity of HDs handled per year and number of hours spent handling HDs.</li> <li>- Conduct physical exam and perform lab tests, such as a complete blood count.</li> <li>- Develop a follow-up plan for workers who have shown health changes suggesting toxicity of HDs have been involved in a spill.</li> <li>- Assess medical, reproductive, and exposure histories for employees who leave the facility.</li> <li>- Biologic monitoring (i.e., urine and blood tests for specific HDs) is not recommended but may be appropriate after spill exposure.</li> </ul>

**Slide 13**

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**BA0** Gabay M. USP <800> : Handling Hazardous Drugs. Hosp Pharm. 2014 Oct;49(9):811-2.  
Bevinetto, Angelica, 2022-09-15T15:48:04.990

# STAYING SAFE: INCLUDING THE PATIENTS!



Follow standardized processes as recommended by national guidelines:

- ASCO/ONS 2016 Updated Chemotherapy Administration safety standards, including standards for pediatric oncology
- ASHP 2014 Guidelines on Preventing Medication Errors with Chemotherapy and Biotherapy
- ISMP Targeted Medication Safety Best Practices for Hospitals

## EX. VINKA ALKALOIDS

Since January 2019, four children received vin**CRIS**tine erroneously by the intrathecal route of administration, each suffering a very painful death

***BEST PRACTICE #1:*** Dispense vinCRISTine (and other vinca alkaloids) in a minibag of a compatible solution and not in a syringe.

# REVIEWING ORDERS FOR ONCOLOGY PATIENTS

Drug interactions also happen with chemotherapy agents!

Some chemotherapy agents continue to cause interactions days after the day of administration

Common pediatric chemotherapy agents leading to interactions:

- **Methotrexate:** penicillins, sulfonamides, proton pump inhibitors, NSAIDs, phenytoin, probenacid
- **Doxorubicin:** CYP3A4 inhibitors/inducers
- **Ifosfamide:** CYP3A4 inhibitors/inducers
- **Vincristine:** CYP3A4 inhibitors/inducers
- **Busulfan:** acetaminophen, metronidazole, azole antifungals, phenytoin
- **Dasatinib:** CYP3A4 inhibitors/inducers

Common medications often used in oncology patients leading to interactions:

- **Tacrolimus:** CYP3A4 inhibitors/inducers
- **Fosaprepitant:** CYP3A4 inhibitors/inducers



# EX. METHOTREXATE INTERACTION CHECK

## HIGH DOSE METHOTREXATE (HD-MTX)

- Commonly used for ALL, brain tumors, and osteosarcoma
  - ex. 4 hr infusion for osteosarcoma

**methotrexate IV Intermittent w/additives - Peds -**  
5600 milliGRAM(s)  
with sodium bicarbonate additive 19.2 milliEquivalent(s) in dextrose 5% 396.8 milliLiter(s), IV Intermittent. once; infuse over 4 Hour(s); Stop After 1 Doses  
Administration Instructions: CAUTION: HAZARDOUS DRUG  
This is a High Alert Medication.  
Provider's Contact #: (631) 758-1910  
(Calc Info: 5,600 milliGRAM(s)/DOSE x 1 = 5,600 milliGRAM(s)/Dose (Requested dose was 5,600 milliGRAM(s) per Flat Dose)

- High dose methotrexate typically requires 2 or more days to adequate clearance
- Interacting medications should be avoided until clearance parameters are met!

# COMMON DDI WITH CHEMOTHERAPY

## HIGH DOSE METHOTREXATE DRUG INTERACTIONS

Common drug interactions that are contraindicated while awaiting MTX clearance:

- Trimethoprim/sulfamethoxazole**
- PPIs**
- NSAIDs**
- Penicillins**
- Phenytoin/fosphenytoin
- Probenecid
- IV contrast

# REVIEWING ORDERS FOR ONCOLOGY PATIENTS

The screenshot shows the Lexicomp Interactions tool interface. The top navigation bar includes links for Home, Triselle's IV Compatibility, Interactions, Drug I.D., Patient Education, Calculators, and More Clinical Tools. The main content area is titled "Interactions" and features a "Selected Items" sidebar on the left with a list of drugs: CeftRIAXone, DOXOrubicin (Conventional), Ondansetron, Pantoprazole, and Posaconazole. The main panel, "Interaction Analysis", contains filters for "Jump to Section", "Filter Item", and "Filter Risk Ratings". A legend defines risk ratings: A (No known interaction), B (No action needed), C (Monitor therapy), D (Consider therapy modification), and X (Avoid combination). The analysis results list the drugs and show two interactions: DOXOrubicin (Conventional) - Posaconazole (P-glycoprotein/ABCBI inhibitors) with a red X icon, and Pantoprazole (Inhibitors of the Proton Pump (PPIs and PCABs)) - Posaconazole with a yellow D icon and a note "Depends on Dosage Form".

Lexicomp® Search Lexicomp

Home Triselle's IV Compatibility Interactions Drug I.D. Patient Education Calculators More Clinical Tools

Interactions

Selected Items

Drugs

Enter drug name Add

- ⊗ CeftRIAXone
- ⊗ DOXOrubicin (Conventional)
- ⊗ Ondansetron
- ⊗ Pantoprazole
- ⊗ Posaconazole

Allergies

Enter allergy name Add

None

Interaction Analysis

Jump to Section Filter Item Filter Risk Ratings

Jump to Section All Items All Risk Ratings Reset Filters

A = No known interaction C = Monitor therapy X = Avoid combination  
B = No action needed D = Consider therapy modification

Drugs in this analysis: CeftRIAXone, DOXOrubicin (Conventional), Ondansetron, Pantoprazole, Posaconazole  
View interaction detail by clicking on link.

- > Drug-Allergy Interactions
- ∨ Drug-Drug Interactions

- X DOXOrubicin (Conventional) - Posaconazole (P-glycoprotein/ABCBI inhibitors)
- D Pantoprazole (Inhibitors of the Proton Pump (PPIs and PCABs)) - Posaconazole *Depends on Dosage Form*

# GEN PEDS VS PHO CALCULATIONS: HYDRATION



4-2-1  
Rule!

\*\*Reference General Pediatrics Review  
for 4-2-1 calculation explanations

## Ex. 1 Male 66kg 170 cm

- 1-10 kg =  $10\text{kg} \times 4 = 40 \text{ ml/hr}$
- 11-20 kg =  $10 \text{ kg} \times 2 = 20\text{ml/hr}$
- 20-66 kg = 46 kg →  $46 \text{ kg} \times 1 = 46 \text{ ml/hr}$
- Total maintenance =  $40 + 20 + 46 = 106 \text{ ml/hr}$

## Ex. 2 Female 17 kg 96 cm

- 1-10 kg =  $10\text{kg} \times 4 = 40 \text{ ml/hr}$
- 11-20 kg =  $7 \text{ kg} \times 2 = 14 \text{ ml/hr}$
- Total maintenance =  $40 + 14 \text{ ml/hr} = 54 \text{ ml/hr}$
- 1.5M =  $75\text{ml/hr}$ ; 2xMaintenance =  $100 \text{ ml/hr}$

# PEDIATRIC HYDRATION IN ONCOLOGY



4-2-1  
Rule!

Chemotherapy can be nephrotoxic and require prophylaxis by hyperhydration

- Based on 4-2-1 rule
  - 1.5-2 x maintenance
- Based on BSA (for chemo associated hydration)
  - Standard: 125 mL/m<sup>2</sup>/hr
  - Hyperhydration: 200 mL/m<sup>2</sup>/hr

Hydration orders in oncology will always follow 125 or 200 ml/m<sup>2</sup>/hr (unless following 4-2-1). If hydration rate does not follow either of these rules, order should be clarified with the ordering provider prior to verification.



# GEN PEDS VS PHO CALCULATIONS: HYDRATION

## BSA Calculation

Mosteller Formula

$$\text{BSA (m}^2\text{)} = \sqrt{\frac{[\text{height (cm)} \times \text{weight (kg)}]}{3600}}$$

### Ex. 1 Male 66kg 170 cm

- 4-2-1 rule: Maintenance = 106 ml/hr
- BSA= 1.76 m<sup>2</sup>
- 125 ml/m<sup>2</sup>/hr = 220 ml/hr
- 200 ml/m<sup>2</sup>/hr = 350 ml/hr

### Ex. 2 Female 17 kg 96 cm

- 4-2-1 rule: Maintenance = 54 ml/hr
- BSA= 0.67 m<sup>2</sup>
- 125 ml/m<sup>2</sup>/hr = 84 ml/hr
- 200 ml/m<sup>2</sup>/hr = 134 ml/hr

QUESTIONS?

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# REFERENCES

1. Hunger SP, Mullighan CG. Acute Lymphoblastic Leukemia in Children. N Engl J Med. 2015 Oct 15;373(16):1541-52
2. American Cancer Society. Cancer Facts & Figures 2022. American Cancer Society. Atlanta, Ga. 2021.
3. COG. Parenteral And Oral Chemotherapy Administration Guidelines. May 2020
4. Baudino TA. Targeted Cancer Therapy: The Next Generation of Cancer Treatment. Curr Drug Discov Technol. 2015;12(1):3-20.
5. Connor TH, MacKenzie BA, DeBord DG, et al. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication Number 2016-161 (Supersedes 2014-138)
6. Gabay M. USP <800> : Handling Hazardous Drugs. Hosp Pharm. 2014 Oct;49(9):811-2.



# QUESTION 1

Which of the following is true?

- A) ALL is the most common type of cancer in children; Pediatric brain tumors have the highest mortality rates**
- B) Brain tumors are the most common type of cancers in children; Pediatric ALL has the highest mortality rates
- C) Neuroblastoma is the most common type of cancer in children; Pediatric brain tumors have the highest mortality rates
- D) ALL is the most common type of cancer in children; Hodgkin lymphoma has the highest mortality rates

## QUESTION 2

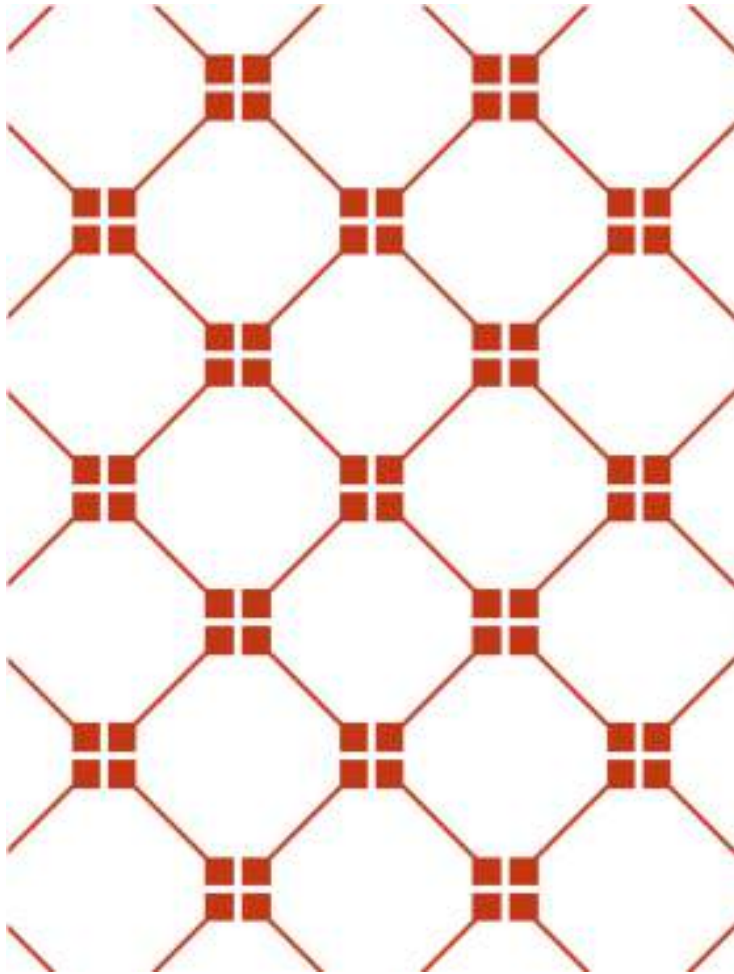
Which chapter of United States Pharmacopoeia (USP) focuses on hazardous drugs?

- A) USP <700>
- B) USP <797>
- C) USP <800>**
- D) USP <850>

## QUESTION 3

Which of the following medications causes delayed clearance of methotrexate due to a drug-drug interaction?

- A) Meropenem
- B) Pantoprazole**
- C) Ondansetron
- D) Famotidine



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