AN OUTPATIENT PHARMACY APPROACH TO PEDIATRIC ONCOLOGY

Jason Koury, Pharm.D., RN
Pediatric Hematology/Oncology Pharmacist
University of New Mexico Hospitals

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Disclosures

- No relationships to disclose

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Pharmacist Objectives

- Discuss considerations relating to pediatric medication dosing and administration
- Identify the most common types of pediatric cancer
- Identify treatment regimens for chemotherapy induced nausea and vomiting
- Develop an overall understanding of oral chemotherapy agents
- Discuss the safety of over-the-counter medications in a pediatric oncology patient
- Be able to recognize when to recommend a pediatric oncology patient to the emergency department

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Technician Objectives

- Discuss considerations relating to pediatric medication dosing and administration
- Be able to recognize appropriate oral chemotherapy dosing
- Develop an understanding of handling and dispensing oral chemotherapy agents
- Identify appropriate over-the-counter medications for pediatric oncology patients
- Be able to recognize a pediatric oncology patient who needs emergency care

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Pediatric Dosing and Administration

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Pediatric Dosing Considerations

- Age
- Weight
- BSA
- Indication
- Max dose
- Renal or hepatic adjustments
- Interactions
- Continuously changing

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Routes of Administration

- Oral
  - G-tube, etc.
- IV
- IM
- SQ
- IO
  - Emergency only

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Absorption[1,2,3]

- Gastric pH neutral then falls to pH 2-3 around 3 year
- Gastric emptying time slower during first week of life
- Gastro-enteral transit time reduced an of adults about 3 years of age
- Diet
- Pediatric formulations
- IM absorption
  - Volume of administration based on age and weight
- Topical absorption

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Distribution[1,2,3]

- Based on body composition
  - Water vs. fat
- Composition of medication
- Protein binding
  - Amount of protein
  - Decreased affinity for medications
- Drug transporters

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Pediatric Volume of Distribution[1,2,3]

Age	Total Body Water (%)	Extracellular Fluid (%)	Adipose Tissue (%)
Premature Neonate	92	50	1 – 5
Term Neonate	75	35	12 – 16
3 mo.	73	35	35
1 yr.	59	25	30
Adult	60	19	20

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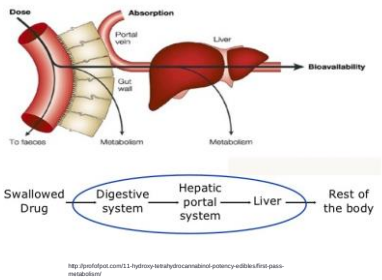

http://profofpot.com/11-hydroxy-tetrahydrocannabinol-potency-edibles/first-pass-metabolism/

11

Metabolism: CYP Enzymes[1,2,3]

	CYP1A2	CYP2D6	CYP2C19	CYP3A4	CYP3A7
Effect	Minimal fetal activity; exceeds adults in infancy then tapers down	Polymorph Rapid vs Slow Metabolism	Activity increase in first 2 weeks	Low at birth, Rapid 1month increase, in gut mucosa	High in Fetal and Newborns Lower efficiency than CYP3A4
Targets	Caffeine, Theophylline	Codeine and many others (psych)	AEDs and PPIs	~40% of all drugs	Similar to CYP3A4

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Phase II Metabolism[1,2,3]

- Inactivates compounds → increases water solubility and excretion
- Phase II enzymes found in mostly in liver but also in kidneys and lungs
- Glucuronidation accomplished by UGT
  - Mostly decreased in infants
  - Potential toxicity of APAP, morphine, zidovudine

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Elimination[1,2,3]

- Renal blood flow is lower at birth
  - Increases during first year of life
- Bedside Schwartz (1-18yr)
  - GFR (mL/minute/1.73 m) = 0.413 x length/SCr

https://www.123rf.com/photo_41118632_healthy-cartoon-kidney.html

https://www.123rf.com/photo_86146784_vector-cartoon-kidney.html

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Pharmacodynamics[1,2,3]

- How the drug affects the body
- Greater affinity for medications
- May have fewer receptors
- Paradoxical drug effects
- Growth and development
  - Tetracyclines, corticosteroids
- Adverse drug reactions
  - Aspirin, propylene glycol, cough products

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Pediatric Cancers

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Acute Lymphoblastic Lymphoma (ALL)[4]

- Most common malignancy in childrent between birth and 14 years
- Abnormal proliferation of precursor B cell or T cell lymphocytes
- Diagnosis based on evaluation of blood and bone marrow
- Genetic component
- Nonspecific signs/symptoms
  - Fever, bleeding, bone pain, lymphadenopathy, hepatosplenomegaly
- Corticosteroids important part of therapy among many other chemotherapy agents
- Depending on factors 5 year Overall Survival (OS) > 90%

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Acute Myeloid Leukemia (AML)[5]

- Less common than ALL
- Proliferation of abnormal myeloid, erythroid, monocytic, megakaryocytic cell precursors
- Fever, malaise, bone pain, cytopenia, coagulopathies
- Diagnosis on pathology of blood and bone marrow
- Event free survival and overall survival
  - 50% and 60-70%, respectively

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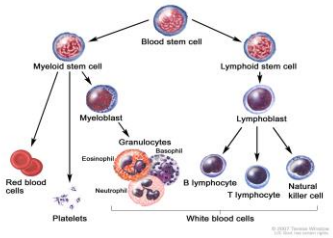
ALL vs. AML[4]



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Neuroblastoma[6]

- Most common extracranial solid tumor of childhood
- Peaks <4 years and median age of 19 months
- Begins in nerve tissue of adrenal glands (most common), neck, chest, abdomen, pelvis
- Genetic component
- Signs and symptoms
  - Fever, SOB, petechiae, high blood pressure, uncontrolled muscle and eye movements, droopy eyelids
- Increase in catecholamine release

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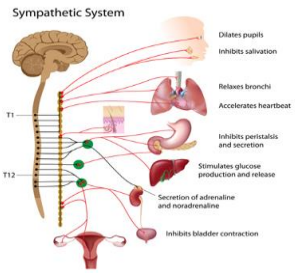

https://curesearch.org/Neuroblastoma-in-Children

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Oral Chemotherapeutic Agents

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Chemotherapy Dosing

- Dose by BSA (m^2) or weight (kg)
  - Less than 1 year old is weight
  - Greater than 1 year can be weight or BSA
- Should wear appropriate gear when manipulating medication
- Handle with caution if pregnant
- Standard doses may not be available
- Liquids are better in many cases due to dose variation

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NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings

- https://www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf?id=10.26616/NIOSHPUB2016161
- Reduction in occupational hazards and safe-handling precautions
- Medications that pose reproductive and developmental toxicity
- Take caution with medication preparation
  - Crushing
  - Splitting tablets
- Use already prepared liquid, if available
- Appropriate PPE and manipulated in appropriate engineering controls
- Check literature if a medication is not on this list

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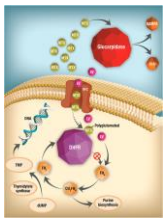
Methotrexate[7,10]

- Essential treatment for leukemia, lymphoma, osteosarcomas
  - Maintenance in ALL protocols
- Adverse effects
  - Acute Kidney Injury
  - Nausea/Vomiting
  - Myelosuppression
  - Mucositis
- Avoid drugs that will increase levels
- Requires hydration and rescue therapy
  - Mainly IV and large doses
- Liquid and tablet formulations



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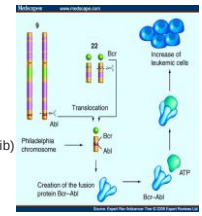
Tyrosine Kinase Inhibitors[8,10]

- Imatinib and Dasatinib
- BCR-ABL inhibitor
  - Ph+ ALL, CML
- Adverse effects
  - Myelosuppression
  - Elevated LFTs
  - Nausea, rash, edema, muscle cramps
- Drug interactions
- Avoid PPI or H2 blockers (dasatinib)
- Take with food and water for GI irritation (imatinib)
- Tablets
- Extemporaneous preparation(imatinib)
- Dissolve in apple juice



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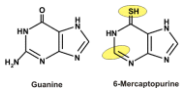
6-Mercaptopurine[9,10]

- Purine analog that incorporates itself into DNA and inhibits synthesis
  - ALL
- Adverse effects
  - Myelosuppression
  - Mucositis
  - Rash, photosensitivity
  - Hepatotoxicity
- Drug interactions
- Dose adjust for TMPT-deficiency
  - Homozygous deficiency
- Tablet, suspension, or extemporaneous preparation
- Take on empty stomach
- Ok to crush



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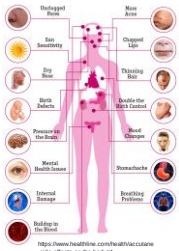
Isotretinoin[10]

- Decreases cell proliferation and induces differentiation
- Recurrent neuroblastoma
- Adverse effects
  - Skin reactions
  - Growth effects
  - Neutropenia
  - LFT elevation
  - Pancreatitis
  - Photosensitivity
- REMS Program – teratogenic defects
- Capsules
- Extemporaneous preparation
- Swallow whole with a meal



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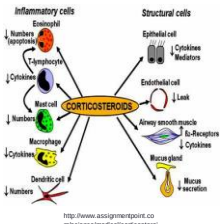
Corticosteroids[10]

- Dexamethasone and prednisone
- Inhibition of inflammatory mediators and suppression of immune system
- Used in ALL
  - Dexamethasone has better CNS penetration and is more potent
  - Dexamethasone in < 10 y/o and prednisone in > 10 y/o
- Adverse effects
  - Cardiovascular
  - CNS
  - Endocrine
  - Osteoporosis
  - Adrenal suppression
  - **Infection**



http://www.assignmentpoint.com/science/medical/corticosteroid.html

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Corticosteroids[10]

- Tablets, liquid, injections
- Taper down
- Be aware with concomitant administration of live vaccinations and high doses
- Dexamethasone is longer acting
- Can be a problem if given to a new diagnosis of ALL prior to diagnosis

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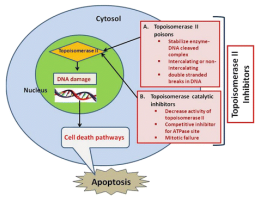
Etoposide[10]

- Topoisomerase II inhibitor
  - Cause DNA strand breaks
- Oral used for comfort care
- Adverse effects
  - Myelosuppression
  - Nausea and vomiting
- Oral capsules and extemporaneous preparation
- Counsel on comfort care measures



https://link.springer.com/chapter/10.1007/978-3-319-12253-3_20

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Chemotherapy Induced Nausea Vomiting (CINV)

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CINV Guidelines

- National Comprehensive Cancer Network (NCCN): Clinical practice guidelines in oncology for antiemesis (2017)
- Pediatric Oncology Group of Ontario (POGO): Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients
- Children's Oncology Group (COG): Guidelines on Chemotherapy-induced Nausea and Vomiting in Pediatric Cancer Patients

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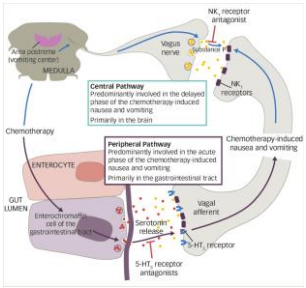

https://www.researchgate.net/figure/Pathophysiology-of-chemotherapy-induced-nausea-and-vomiting_fig2_321932045

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Emesis Definition[12]

- Acute emesis
  - Occurs within first 24 hours after chemotherapy
  - In absence of effective prophylaxis it can occur within a few hours of chemotherapy initiation
- Delayed emesis
  - Greater than 24 hours after chemotherapy delivery
  - Cisplatin, cyclophosphamide are offenders
- Anticipatory emesis
  - Conditioned response to previous administration of chemotherapy
  - Association between chemotherapy and nausea

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Table 1: Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients Given as Single Agents

High Level of Emetic Risk (> 90% frequency of emesis in absence of prophylaxis)		
Altretamine *Carmustine *Cisplatin > 250 mg/m² *Cisplatin *Cyclophosphamide > 1 g/m²	*Cytarabine ≥ 1 g/m²/dose Dacarbazine Mechlorethamine (nitrogen mustard) Streptozotocin	*Methotrexate ≥ 12 g/m² Procarbazine (oral) *Ramustine *Thiotepa ≥ 300 mg/m²
Moderate Level of Emetic Risk (30–90% frequency of emesis in absence of prophylaxis)		
Aldesleukin > 12 to 15 million units/m² Amifostine > 300 mg/m² Arsenic trioxide Azacitidine Bendamustine Busulfan *Carboplatin ≤ 250 mg/m² *Cytarabine *Cyclophosphamide < 1 g/m² Cyclophosphamide (oral)	Cytarabine > 200 mg/m² ≤ 1 g/m² *Daunorubicin *Doxorubicin Epirubicin Etoposide (oral) Idarubicin Ifosfamide Irinotecan (oral) *Intrathecal therapy (methotrexate, hydrocortisone & cytarabine)	Irinotecan Lomustine Methotrexate > 50 mg/m² Methotrexate ≥ 250 mg/m² to < 12 g/m² Oxaliplatin < 75 mg/m² Temozolomide (oral) Vinorelbine (oral)
Low Level of Emetic Risk (10–30% frequency of emesis in absence of prophylaxis)		
Amifostine ≤ 300 mg/m² Bexarotene Bleomycin *Busulfan (oral) Capecitabine Cytarabine ≤ 200 mg/m² Docetaxel Doxorubicin (liposomal) Etoposide	Fludarabine (oral) Fludarabine IV Gemcitabine Ixabepilone Methotrexate < 50 mg/m² > 250 mg/m² Mitomycin C Mitoxantrone Nilotinib	Paclitaxel Paclitaxel albumin Pemetrexed Temsirolimus Thiotepa < 300 mg/m² Topotecan Vinblastine
Minimal (10% frequency of emesis in absence of prophylaxis)		
Alemtuzumab Alpha interferon Asparaginase (IM or IV) Bevacizumab Bleomycin Bortezomib Cetuximab Chlorambucil (oral) Cladribine (2-chlorodeoxyadenosine) Clofarabine Denileukin diftitox Dasatinib Everolimus	Erlotinib Fludarabine Gefitinib Gemtuzumab ozogamicin Hydroxyurea (oral) Lapatinib Lenalidomide Methotrexate (low-dose) Mercaptopurine (oral) Methotrexate ≤ 50 mg/m² Nelarabine Panitumumab Pemetrexide Rituximab	Sorafenib Sunitinib Temozolomide Thalidomide Thioguanine (oral) Trastuzumab Valrubicin Vemurafenib Vincristine Vindesine Vinorelbine

* Pediatric evidence available — Note: All agents given intravenously (IV) unless stated otherwise.

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Table 2: Classification of the Acute Emetogenic Potential of Specific Antineoplastic Medication in Pediatric Cancer Patients Given in Combination

High Level of Emetic Risk (> 90% frequency of emesis in absence of prophylaxis)	
Cyclophosphamide + anthracycline	*Cytarabine 300 mg/m² + etoposide
*Cyclophosphamide + doxorubicin	*Cytarabine 300 mg/m² + teniposide
*Cyclophosphamide + epirubicin	*Doxorubicin + ifosfamide
*Cyclophosphamide + etoposide	Doxorubicin + methotrexate 5 g/m²
*Cytarabine 150-200 mg/m² + daunorubicin	*Etoposide + ifosfamide

* Pediatric evidence available Note: All agents given intravenously (IV) unless stated otherwise.

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Non-pharmacological[11]

- Eat small, more frequent meals
- Odor control
- Avoid spicy, fatty, high salty foods
- Use measures that have helped in past

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Highly Emetogenic Chemotherapy[11]

- Aprepitant used in patients > 6 months old!
  - NK1-receptor antagonist
  - Monitor drug interactions
- 5-HT3 antagonist + dexamethasone
- Ondansetron, granisetron, palonosetron
- Do not use dexamethasone for CINV in ALL
- Anti-emetic drip (inpatient)
  - Dexamethasone, diphenhydramine, metoclopramide, lorazepam if anticipatory

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Moderate-Low Emetogenic Chemotherapy[11]

- Moderate
  - 5-HT3-receptor antagonist + dexamethasone
  - Ondansetron, granisetron, palonosetron
  - If > 6 months and cannot receive dexamethasone then ok to use aprepitant
- Low
  - 5-HT3 antagonist
  - Ondansetron, granisetron, palonosetron

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Anticipatory CINV[11]

- Hypnosis, acupuncture?
- Use same agents as listed above
- Lorazepam

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Breakthrough CINV

- Metoclopramide (> 1 y/o)
  - Extrapyramidal reactions
- **Olanzapine**
- Diphenhydramine
- Promethazine
- Lorazepam
- Scopolamine patches
- Dronabinol

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Olanzapine[10]

- Second generation antipsychotic
  - Antagonism of serotonin, dopamine, histamine, and alpha1-adrenergic receptors
- Drug interactions
- Adverse effects
  - Hyperprolactinemia
  - Gynecomastia
  - Hyperlipidemia
  - Hyperglycemia
  - Restlessness
  - Somnolence
  - Q-T prolongation

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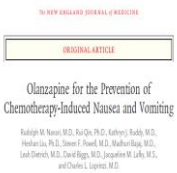
Olanzapine for Prevention of CINV[14]


THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting

Rudolph M. Navari, M.D., Rui Qin, Ph.D., Kathryn J. Ruddy, M.D., Heshan Liu, Ph.D., Steven F. Powell, M.D., Madhuri Bajaj, M.D., Leah Dietrich, M.D., David Biggs, M.D., Jacqueline M. Lafky, M.S., and Charles L. Loprinzi, M.D.

- Randomized, double-blind, phase 3 trial
- Patient 18 + with malignant disease who had not received chemotherapy
- 5-HT3-receptor antagonist, dexamethasone, NK1-receptor antagonist + olanzapine(10mg x 4 days)or placebo
- Stratified by sex, chemotherapy regimen (cisplating vs. anthracycline + cyclophosphamide containing), and 5-HT3-receptor antagonist
- Primary outcome – no nausea during assessment period of 120 hour

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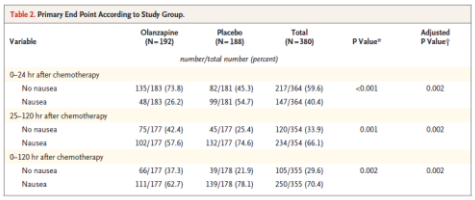
Table 2. Primary End Point According to Study Group.

Variable	Olanzapine (N = 192)	Placebo (N = 188)	Total (N = 380)	P Value*	Adjusted P Value†
	number/total number (percent)				
0–24 hr after chemotherapy					
No nausea	135/183 (73.8)	82/181 (45.3)	217/364 (59.6)	<0.001	0.002
Nausea	48/183 (26.2)	99/181 (54.7)	147/364 (40.4)		
25–120 hr after chemotherapy					
No nausea	75/177 (42.4)	45/177 (25.4)	120/354 (33.9)	0.001	0.002
Nausea	102/177 (57.6)	132/177 (74.6)	234/354 (66.1)		
0–120 hr after chemotherapy					
No nausea	66/177 (37.3)	39/178 (21.9)	105/355 (29.6)	0.002	0.002
Nausea	111/177 (62.7)	139/178 (78.1)	250/355 (70.4)		

* P values were calculated with the use of the chi-square test.
† P values were calculated according to the Simes gatekeeping procedure.

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Olanzapine in Adults[13]

- Meta-analysis (Cochrane Review)
  - Highly and moderate emetogenic
  - Olanzapine vs. placebo
  - Likelihood of being free from nausea or vomiting during chemotherapy (RR 1.98, 95% CI 1.59 to 2.47; participants = 561; studies = 3; $I^2 = 0\%$)
  - About 5 days of treatment
  - Probably reduces delayed nausea with acute nausea and vomiting being uncertain

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Olanzapine in Pediatrics: Multi-center, prospective, open-label, feasibility[15]

- Flank, J., Schechter, T., et al.
  - English speaking; 4-18 y/o; ≥ 14kg
  - Olanzapine 0.14 mg/kg/dose (max 10 mg/dose; 2.5 mg increments) x 4 doses (max) + standard of care
  - Dose decreased if patient experienced undesirable sedation
  - Feasibility of recruitment, compliance, and adverse effects for endpoints
  - Endpoints were met
  - Free of vomiting and retching on 86 ± 21%of acute phase days
    - All but 1 patient experienced nausea
  - free of vomiting and retching on 75 ± 32% and free of nausea on 50 ± 33% of delayed phase days
  - Mild sedation was main adverse effect

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Olanzapine in Pediatrics: Retrospective, Multi-Center Review[16]

- Flank, J., Thackray, J.,et al.
- Patients < 18 y/o who received olanzapine for CINV in acute phase of chemotherapy block
- Primary outcome - # times vomited in acute phase


TABLE II. Description of 158 Chemotherapy Blocks During Which Olanzapine Was Given for CINV Control

Characteristic	
Chemotherapy	
Median duration of chemotherapy block (days; range)	4 (1–42)*
Chemotherapy emetogenicity (number of blocks; %)	
High	128 (81)
Moderate	26 (16)
Low	2 (1)
Minimal	0
Number of chemotherapy blocks containing cisplatin (%)	32 (20)
Antiemetic prophylaxis provided	
Antiemetic agents given on a scheduled basis (number of blocks; %)	
Ondansetron or granisetron	154 (97)
Dexamethasone	99 (57)
Aprepitant	39 (25)
Nabilone or dronabinol	21 (13)
Lorazepam	15 (9)
Scopolamine	7 (4)
Prometheazine	4 (3)
Diphenhydramine	2 (1)
Antiemetic agents given on an as needed basis (number of blocks; %)	
Lorazepam	105 (65)
Hydroxyzine	65 (41)
Ondansetron or granisetron	15 (9)
Prometheazine	8 (5)
Diphenhydramine	4 (3)
Dronabinol or nabilone	4 (3)

*One patient received daily oral temozolomide for 42 days.

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Olanzapine in Pediatrics: Retrospective, Multi-Center Review[16]

TABLE III. Description of Olanzapine Use During 158 Chemotherapy Blocks

Characteristic	
Reason for olanzapine use (number of blocks; %)	
History of uncontrolled CINV in previous chemotherapy block	94 (59)
Unknown	37 (23)
Uncontrolled CINV in current chemotherapy block	27 (17)
Median number of chemotherapy blocks per patient during which olanzapine was given (range)	2 (1–10)
Olanzapine dose frequency (number of blocks; %)	
Once daily	151 (96)
Twice daily	7 (4)
Mean initial single olanzapine dose (±standard deviation; range)	
mg/kg/dose	0.10 ± 0.051 (0.026–0.256)
mg/m²/dose	3.0 ± 1.45 (0.81–6.42)

TABLE IV. Vomiting Control and Adverse Events Reported in 158 Chemotherapy Blocks During Which Olanzapine Was Given

Characteristic	
Acute CTV control when olanzapine was initiated on the first day of chemotherapy[a] (number of blocks; %)	
Highly emetogenic chemotherapy (106 chemotherapy blocks)	
Complete CTV control	72 (68)
Partial CTV control	23 (22)
Uncontrolled CTV	11 (10)
Moderately emetogenic chemotherapy (20 chemotherapy blocks)	
Complete CTV control	9 (45)
Partial CTV control	5 (15)
Uncontrolled CTV	8 (40)
Low emetic risk chemotherapy (two chemotherapy blocks)	
Complete CTV control	2 (100)
Partial CTV control	0
Uncontrolled CTV	0
Reported adverse events (number of blocks; %)	
Sedation	11 (7)
Increased transaminase concentrations[b]	5 (20)
Dizziness	2 (1)
Dystonia	1 (0.6)
Constipation	1 (0.6)
Excessive hunger	1 (0.6)
Fainting	1 (0.6)
Hypertension	1 (0.6)
Hyperglycemia	1 (0.6)
Increased plasma creatinine concentration	1 (0.6)
Stomach pain	1 (0.6)
Mean change in weight between chemotherapy blocks[c] (%)	0 (−22 to +16)

[a]Assessed in 128 chemotherapy blocks. [b]Assessed in 25 chemotherapy blocks during which transaminase concentrations were assessed at least twice. [c]Assessed in 26 patients who received olanzapine during more than one chemotherapy block (6 weeks or less apart).

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Over-The-Counter (OTC) Safety

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OTC Safety Considerations

- Drug-drug interactions!!
- Drug-disease interaction
  - NSAIDs
- Herbals
  - Some families believe that herbals will work better than western medicine
  - Limited data
  - Including homeopathic
- CBD oils

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Mucositis

- Inflammation and ulceration of oral mucosa
- Secondary to immunosuppression, chemotherapy, and radiatrion
- Decreased quality of life
- Increase risk of bacterial and fungal infection
- Decrease nutritional status
- Pain management
  - Narcotics
  - Magic mouthwash
- Oral hygeine

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Honey for Mucositis

Elsass, FT.	Al Jaouni, SK., et al.	Bulut, HK., et al.	Badr, IK., et al.
Case series	Open-label, RCT	Quasi-experimental with experiment and control group	Double blind, RCT Ongoing: NCT03399331
Pediatrics: 9 mo - 17 yr; 3 cases	Pediatric oncolgy: 40 patients	Pediatric oncology: 83 patients	Adults and pediatric
AML, ALL, HLH	Hematological and non-hematological cancers	Leukemia, lymphoma	Leukemia
Leptospermum honey paste	Apply hosptial provided honey 4-6x/day or honey + standard of care	Honey group bewtween 7th and 14th day of induction compared to routine mouth care	Honey or olive oil compared to standard of care
Oral nucositis improved at 5 days in all cases	Reduction of oralmucositis development, fungal, and bacterial infections	Reduction in oral mucositis incidence in honey group	Outcome is severity of oral mucositis

* All trials outside of US

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Probiotics in Pediatric Oncology

- Insufficient data
- Which strains of probiotics are most beneficial?
- Outcome of probiotics?
  - Decrease in diarrhea
  - Improved overall health
  - Preserve gut function
- Infectious in immunocompromised patients?
- Lot's of research and data both supporting and refuting probiotics
- Dosing?

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Safety and Feasibility of Probiotics in Hematopoietic Cell Transplantation (HCT)[21]

- *Lactobacillus plantarum* 1 × 10^8 colony-forming units/kg/day
  - Examined to ensure they were free of bacteria and fungal contamination
- Pilot study for safety and feasibility of RCT
  - Primary objective was safety
- Thirty children and adolescents between 2 and 17 years undergoing HCT
- Started day -8 or -7 through + 14
- Ninety-seven percent received at least 50% of dose
- No episodes of lactobacillus bacteremia

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Lactobacillus acidophilus Sepsis[22]

- Case study
- Sixty-nine year old male with stage IIIA mantle cell lymphoma
  - Underwent autologous hematopoietic SCT
- Became septic with *Klebsiella pneumonia* and was treated for 3 days
- Then developed severe mucositis, vomiting, diarrhea on day 10
- Colonoscopy and biopsy showed chronic inflammation
- Repeated blood cultures that grew *Lactobacillus acidophilus*
- Eating 6-8 cups/day of probiotic enriched yogurt
- Improved once yogurt was stopped

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Febrile Neutropenia

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Guidelines

- Guideline for the Management of Fever and Neutropenia in Children With Cancer and Hematopoietic Stem-Cell Transplantation Recipients: 2017 Update
- Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America
- Children's Oncology Group (COG): Guideline for the Management of Fever and Neutropenia in Children with Cancer and/or Undergoing Hematopoietic Stem-Cell Transplantation

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Oncologic Fever

- Fever without neutropenia
- Fever with neutropenia
- Fever
  - Temperature > 38.3°C
  - Oral or axillary
  - Avoid rectal – risk of mucosal trauma and bacteremia
- Neutropenia
  - Mild: ANC 1000 to 1500/microL
  - Moderate: ANC 500 to 1000/microL
  - Severe: **ANC < 500/microL**

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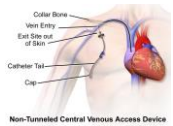
Over the Counter & Supportive Care

- Fever control
  - Acetaminophen (10-15 mg/kg; 5-6 doses/day)
  - Ibuprofen??
- Avoid vaccines at this time
- Avoid fresh flowers
- Daily inspection of vascular site
- Neutropenic diet
  - Well-cooked foods
- All people preform hand hygiene
- Daily shower
- Avoidance of tampons



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Outpatient Pharmacy Evaluation

- Look at the patient
  - Sick vs. non-sick
- Vital signs
- Medical history
- **Refer to ED Immediately!!**

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Inpatient Evaluation

- Vital signs
- Labs
- Cultures
- H&P
- Respiratory virus panel
- C-diff PCR if frequent, watery stools
- Lumbar puncture
- Radiology

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Inpatient Empiric Treatment[20]

- Administer antibiotics within 1 hour or sooner
- UNM Hospital
  - Ceftriaxone: fever, non-neutropenic
  - Cefepime: fever, neutropenic
- Alternatives
  - Zosyn, meropenem
- Add vancomycin (q6h dosing) for suspected gram + organism
- Add vancomycin + gentamicin + cefepime for hemodynamic instability

https://www.european-coatings.com/Raw-materials-technologies/Technologies/Anti-bacterial-coatings-combat-hospital-acquired-infections

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Antibiotic Duration[20]

- De-escalate and treat accordingly to blood cultures
- High risk:
  - Discontinue empiric treatment in patients with neg. blood cultures for 48 hours + afebrile for at least 24 hours + marrow recovery
- Low risk:
  - Discontinue empiric treatment in patients with neg. blood cultures for 48 hours + afebrile for at least 24 hours
- Fungal management for prolonged febrile neutropenia ≥ 96 hours

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