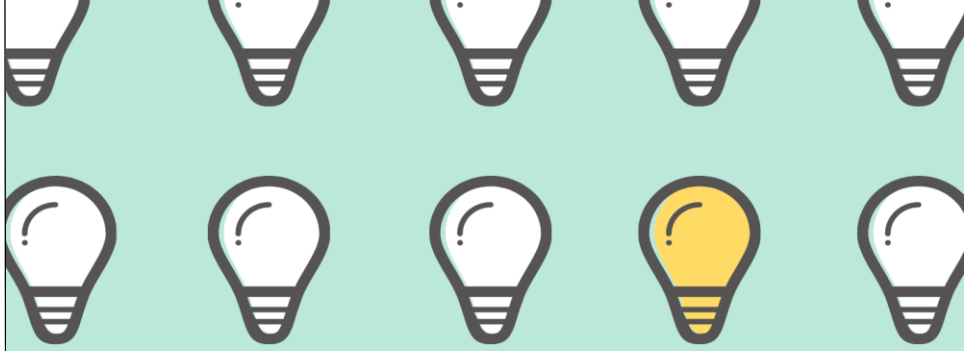

2021 WARDS MANUAL

HEMATOLOGY AND ONCOLOGY

UCLA-Olive View Medical Center

WRITTEN BY: JADE LAW, MD
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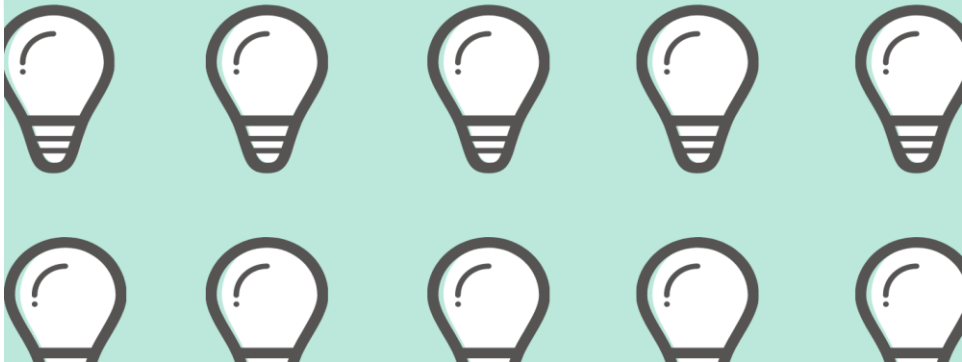

Hematology-Oncology
2021 Wards Manual
UCLA – Olive View Medical Center

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"The art of medicine is to cure sometimes, to relieve often, to comfort always." - Ambroise Paré

Structure of hematology/oncology wards

Introduction
- Welcome to OVMC's hematology/oncology wards!
- The team: 2 residents w/ separate patient lists, supervised by 1 fellow + 1 attending.
- Days off: Either Sat. or Sun., you will cover the other resident's patients on their day off.

Admissions
- Admissions are scheduled (chemo) + unscheduled (chemo complications, onc emergencies).
- For scheduled admissions, the fellow will have chemotherapy orders
- Write the other admission orders, see section on supportive care (i.e., pain control, anti-emesis, constipation, VTE prevention).

Presentations (general format)
- New patients:
    - ID: Type of disease, stage of disease, date of diagnosis
    - Chief complaint (complication, induction, consolidation, maintenance)
    - Initial presentation of malignancy (e.g., mass, B-symptoms, bruising, etc.)
    - Diagnosis (imaging, biopsy, IHC, molecular studies)
    - Treatment, response, complications, relapses in chronologic order
    - ROS, physical exam, labs, radiology
    - Assessment and Plan, goals of therapy
- Daily updates:
    - Identification/Summary statement
    - Cycle x, Day y of ___ chemotherapy
- Signout: include contingencies as discussed w/ attending:
    - Fevers: diagnostics (e.g. cultures), changes in antibiotics
    - Bleeding: need for scans (e.g. CTs), threshold for blood products
    - Chemotherapy reactions: when to stop infusion, antidotes

Radiation therapy
- Some patients have radiation therapy off-site while hospitalized for chemotherapy
- Fellow sets up transportation prior to admission
- Patients don't have to be NPO; OK to hold chemo until they return if continuous infusion
- Patients will not have pain meds during sessions. Especially for 1st session, consider giving usual/extra opioid dose prior to departure.

Discharges:
- Write d/c instructions and d/c summary.
- The fellow will write a summary note, and set up outpatient f/u + labs
- Anti-emetic regimen, anti-constipation regimen, GCSF, PICC line supplies
- Weekly PICC line dressing appts to be scheduled by fellow

Palliative care
- Pager: 818.313.1036, Room 5D129
- Monday-Friday 8:30am-5:00pm
- Referrals: refractory sx (e.g., pain, anxiety/depression, nausea, dyspnea), GOC, transition to hospice, prolonged ICU stay w/ poor prognosis or no evidence of improvement

Useful phone numbers for finding fellow/attendings
- Clinic C: 73133
- Fellows' workroom: 73149
- STC (outpt chemo): 73540
- STC fellow: 73875

ECOG Grade	Description
0	Fully active
1	Restricted in physically strenuous activity, ambulatory, able to carry out light work
2	Ambulatory, does all self-care but not work activities, out of bed/chair > 50% of waking hr
3	Does only limited self-care, confined to bed/chair > 50% of waking hr
4	Completely disabled, cannot carry on any self-care, totally confined to bed/chair
5	Deceased

Supportive Care

Pain management
- Stepwise approach:
    - Non-opioid (NSAID, tylenol) + adjuvant
    - Opioid + non-opioid
    - Opioid + non-opioid + adjuvant
- Adjuvant:
    - TCAs: Neuropathic pain (e.g., amitriptyline 25mg daily, up to 100mg/day)
    - AEDs: Brachial/lumbosacral plexopathies (e.g. gabapentin 100-1200 mg TID)
    - Misc: SNRI, benzos, steroids, muscle relaxants, lidocaine, capsaicin, nerve blocks
- Avoid NSAIDS if thrombocytopenia anticipated (esp leukemia, lymphoma, small cell)
- Avoid Norco/Tylenol for pain if neutropenic, as Tylenol may mask fevers
- Opioid side effects:
    - Sedation, N/V, constipation, urinary retention, respiratory depression, cognitive impairment, pruritus
    - **Always** start bowel regimen if receiving standing opioid regimen (see next page)
- Consider PCA if unknown pain medication requirements, then transition to long-acting scheduled regimen + short-acting PRN
- Breakthrough pain:
    - Chronic cancer pain generally requires long acting opioid around the clock w/ short acting agent for breakthrough pain
    - Cover w/ short-acting opioids using ~10% of total 24h standing opioid dose available q1-2h.
    - e.g., MS-Contin 60mg PO q12h + morphine 12mg PO q2h PRN BTP
- Converting between opioids:
    - For calculating equivalence, rectal=oral route, SQ=IV route
- Low-potency opioid agonists: Codeine, hydrocodone, tramadol
- High-potency opioid agonists: Morphine, oxycodone, hydromorphone, fentanyl, methadone

Constipation
- Common causes:
    - Medications: opioid use, anticholinergics (TCA, antipsychotics), iron, CCB, Zofran
    - Obstruction: cancer causing stricture, extrinsic compression
    - Metabolic/endo: hypercalcemia, hypokalemia, hypomagnesemia
    - Other: immobility, dehydration
- Suggested treatment:
    (1) Colace 100mg BID, senna 2 tabs BID if on standing long-acting opioid
    (2) Add Miralax 17g PO BID or bisacodyl 5-15mg PO qday
    (3) Consider lactulose 30cc q6h until BM (can be nauseating to oncology patients)
    (4) Add bisacodyl suppository 10mg, tap water enema (unless neutropenic)
    (4) Proximal impaction may require magnesium citrate
    (5) If hard stools in vault, may need manual disimpaction
- Methylnaltrexone subq for opiate induced constipation

Supportive Care cont.

Opioid conversion chart

Opioid agonist	Parental dose	Oral dose	Factor (IV→PO)
Morphine	10 mg	30 mg	3
Hydromorphone (Dilaudid)	1.5 mg	7.5 mg	5
Oxycodone	-	15-20 mg	-
Hydrocodone	-	30-45 mg (Norco 5/325 x 6tabs)	-
Codeine	-	200 mg	-

Adapted from Cancer pain management with opioids:: Optimizing analgesia., UpToDate accessed 03.09.2021

Opioid starting dose, half-life, duration of analgesia

Drug	Initial dose for opioid-naïve adult	Half-life (hours)	Duration of analgesia (hours)	Notes
Morphine	2-5 mg IV q 2-4h	2-3	3-4	Hepatically converted to active metabolites M3G/M6G which are excreted by kidney, beware in renal failure
	15-30 mg PO q4h	2-3	3-6	
Morphine, extended (MS-Contin)	15 mg PO BID		8-12	
Hydromorphone (Dilaudid)	0.3-1 mg IV q2-4h	2-3	3-4	
	2-4 mg PO q3-4h	2-3	3-6	
Codeine	15-60 mg PO q4-6h	3	4-6	Hepatically converted to morphine; beware of hypermetabolizers
Oxycodone	5-15 mg PO q4-6h	2-3	3-6	
Oxycodone, extended (Oxycontin)	10 mg PO BID	4.5	8-12	
Hydrocodone	5-10 mg PO q3-4h	3-4	4-8	Limited by formulation w/ acetaminophen
Methadone	2.5-10 mg PO q4-8h, not for opioid-naïve	12-150	3-4 initially use; 6-8 chronic use	Long T1/2 (0.5 to 7 days), watch for accumulation. ↑QTC, interacts w/ CYP3A4. Consider palliative consult before initiation.
Fentanyl transdermal	Not for opioid-naïve, may need to pass OVMC intranet test to prescribe	17 after removal	48-72 per patch, up to 12 after removal	Useful if stable pain, unable to take PO. Patch changed q72h. Dose based on avg daily opioid req. over 7d. If switching to fentanyl, overlap w/ previous opioid by 12h for fentanyl to reach therapeutic levels
Tramadol (Ultram)	50-100 mg PO q4-6h	~6-9	6	Weak mu agonist. Caution if taking SSRI or TCA given risk of serotonin syndrome! Avoid if renal insufficiency, risk for seizures or depression

Adapted from Cancer pain management with opioids;: Optimizing analgesia., UpToDate accessed 03.09.2021
Adapted from NCCN Guidelines Version 1.2021 Adult Cancer Pain

Anti-emesis: (see Appendix 1)

- *Acute-onset N/V:* within minutes to hours after drug administration
- *Delayed-onset N/V:* >24 hrs after chemo. Common w/ cisplatin, carboplatin, doxorubicin, cyclophosphamide.
- *Other causes of emesis:* bowel obstruction, vestibular dysfunction, brain mets, electrolyte imbalance (hypercalcemia, hyperglycemia, hyponatremia), uremia, gastroparesis
- Consider H2 blocker or proton pump inhibitor to prevent dyspepsia (can mimic nausea).
- Initial regimen ordered by fellow based on emetogenic potential of chemo (see Appendix 5)

Anti-emetic Medications:

Drug	Main Receptor	Main Indication	Starting PO Dose/Route	Side Effects
Metoclopramide (Reglan)	D2	Opioid-induced, gastric stasis	10 mg q4h PO, SC, IV (up to 2mg/kg)	EPS (akathisia, dystonia, dyskinesia, diarrhea
Prochlorperazine (Compazine)	D2	Opioid-induced	10 mg q6h PO, IV	EPS, NMS, sedation
Promethazine (Phenergan)	H1	Vestibular, motion sickness, obstruction	12.5 mg q4h PO, PR, IV	EPS, NMS, sedation
Ondansetron (Zofran)	5-HT3	Chemotherapy, less effective for delayed emesis	8-16 mg q12h PO, IV	Headache, constipation, ↑QTc
Diphenhydramine (Benadryl)	H1, Ach	Intestinal obstruction, vestibular, ICP	25 mg q6h PO , IV, SC	Sedation, dry mouth, blurred vision
Scopolamine	Ach	Intestinal obstruction, colic, secretions	0.2-0.4 mg q4h SL, SC, TD	Dry mouth, urine retention, agitation
Lorazepam (Ativan)	BZD	Anxiety, anticipatory N/V	0.5-2 mg q4-6h PO, IV, SL	Sedation
Dexamethasone (Decadron)	Corticosteroid	Chemotherapy	4-12 mg PO/IV daily	Hyperglycemia, agitation, AI, myopathy, leukocytosis
Aprepitant (Emend)	Neurokinin-1 (substance P)	Chemotherapy	150mg IV on day 1	Fatigue, weakness, hiccups, GI sx
Olanzapine (Zyprexa)	5-HT3, Ach, D, BZD	Delayed N/V from chemo, use w/ 5-HT3 antagonist + steroid	5-10 mg PO daily	Sedation, EPS, fatigue, insomnia, hyperglycemia

Adapted from Elsayem A, Driver LC, Bruera E. The MD Anderson Palliative Care Handbook. Houston, TX: MD Anderson Cancer Center; 2002.
Adapted from NCCN Guidelines Version 1.2021 Antiemesis

OVMC Anti-Emesis Guidelines

- Minimal risk: No routine premeds
- Low risk premeds: Choose one –
  - (1) Zofran 16mg PO→ 8mg BID PRN, (2) Decadron 8mg PO, (3) Reglan 10mg PO→PRN, or (4) Compazine 10mg PO→PRN
- High risk/moderate risk: see chart
- Breakthrough N/V: Add agent from different drug class
  - Ex. Olanzapine 5-10mg qday, Zofran 8mg PO q8-12h, Ativan 0.2-2mg PO/IV q6h, Dronabinol 5-10mg PO TID, Haldol 0.5-2mg q4-6h, metoclopramide 10-20mg PO/IV q4-6h, Prochlorperazine 10mg PO/IV q6h
- Radiation-induced N/V (esp abdomen):
  - Zofran 8mg PO Bid w/ XRT +/- Decadron 4mg qday, +/- Ativan +/- PPI/H2R blocker

Emetogenic Potential of IV chemo agent:	High Risk	Moderate Risk
Initial premeds:	Zofran 16mg IV/PO + Dexamethasone 12mg IV/PO + Olanzapine 5-10mg PO +NK1 RA (ex. Fosaprepitant 150mg IV)	Zofran 16mg IV + Dexamethasone 12mg IV/PO
Delayed Emesis Prevention:	Recommended (D2-4): *Dexamethasone 8mg PO qday + Olanzapine 5-10mg PO qday	Optional (D2-3): Zofran 8mg PO BID, OR Dexamethasone 8mg PO qday
Continued issues w/ delayed emesis:	Olanzapine (Zyprexa) 5-10mg PO D1-2 + Zofran 16mg PO BID D1-2 (max 32mg/day)	
Oral Chemo: (High/Mod Risk)	Start before chemo & cont daily w/ chemo: Zofran 16mg PO qday/BID ± Ativan 1mg SL Q4-6 PRN ± PPI or H2 Blocker	

*Adapted from NCCN Guidelines Version 1.2021 Antiemesis. **Watch blood sugars carefully in diabetics on dexamethasone***

Supportive Care cont.

Mucositis
- Viscous lidocaine 2% 15cc gargled (max q3h)
- Artificial saliva (e.g., Biotene spray)
- Magic mouthwash (1:1:1 Maalox, Benadryl, lidocaine) 5-10cc swish/swallow qAC
- For candidal superinfection: Nystatin 500,000 units swish/swallow q6h

Venous thromboembolism prevention
- Mechanisms: venous stasis (immobility), hypercoagulability 2/2 cancer, intimal injury (catheters, surgery), chemo (esp. tamoxifen, cisplatin, cyclophosphamide, MTX, 5-FU, high dose steroids)
- LMWH superior to warfarin in CLOT trial (9% vs. 17% HR for **recurrent** VTE at 6 mo)
- Xarelto superior to LMWH in SELECT-D trial in decreasing risk of recurrent VTE in cancer-associated VTE, though increases rate of bleeding esp. GI cancer
- Apixaban noninferior to LMWH
- Warfarin ineffective in cancer pts w/ active clot, use UFH/LMWH
- Pharmacologic prophylaxis: UFH vs. LMWH vs. fondaparinux, none w/ superior efficacy.
    - Heparin 5,000 units sq q8-12h
    - Lovenox 40mg sq daily (30mg daily if CrCl<30)
    - Fondaparinux 2.5mg sq daily (consider if HIT, but contraind. if CrCl<30, <50kg)
- Other:
    - As outpt, surgical onc pt will need VTE ppx for 4 weeks after surgery.
    - Multiple myeloma patient receiving thalidomide/lenalidomide will need ASA 81-325 daily (low risk) vs. LMWH or warfarin if high risk for VTE.
    - Consider Khorana Predictive Model for VTE ppx as outpatient (Appendix 3)

Transfusions

Transfusion Goals
- *pRBC:* Hgb>7 in general, Hgb >8-9 if receiving chemo/BMT/PSCT due to decreased marrow production, Hgb >8 if coronary ischemia
- *Platelets*: >10k in general, >20k if increased risk for bleed (febrile, infection, concurrent coagulopathy, DIC, liver/renal failure, significant splenomegaly), >50k if active bleeding/procedure, >100k if neurologic/cardiac surgery
- *Cryoprecipitate*: Fibrinogen>100

Ordering
- *Premedication:* Tylenol 650mg PO x1, Benadryl 25-50mg PO/IV x 1
- *Type and cross:* Transfusion likely, verifies ABO-Rh status of donor+recipient, screens for unexpected Ab to common RBC Ag, mixes donor RBCs + recipient serum to exclude immediate hemolysis
- *Type and screen:* No immediate need for transfusion, tests ABO, Rh, routine Ab screen (indirect Coombs')
- *Type O, Rh-negative:* Universal donor, used in emergent transfusion
- *Leukocyte-reduced:* Removes WBCs (chief cause of alloimmunization to HLA antigens), use if long-term transfusions needed, recurrent febrile reactions. (Done for all RBCs at OVMC)
- *Irradiated:* kills donor stem cells which can cause rare GVHD. Use in BMT candidates/recipients, immunosuppressed patients, if donor+recipient are blood relatives, patients receiving HLA matched platelets
- *CMV negative:* Use if patient CMV seronegative + candidates/recipients of bone marrow/solid organ transplants, SCID, AIDS or pregnant. Test CMV if status unknown
- *Saline washed RBC:* Removes plasma proteins, electrolytes, Ab. Use if hx of severe transfusion reactions, hyperkalemia, PNH, IgA deficiency

Blood product characteristics

	Packed RBC	Platelets	Fresh frozen plasma	Cryoprecipitate
Shelf-life	21-42 d	5 d	1 yr frozen, 24hr thawed	1 yr frozen
Volume/unit	250-350 mL	250-350 mL	200-250 mL	20-50 mL
Approximate contents	Red cells: 65-80% Plasma: 20-35%	Platelets + plasma	All factors + Protein C/S (200-250U), fibrinogen (400-500mg)	Factor VIII: 80 units Fibrinogen: 225 mg vWF: variable
Typical dose	1 unit	1 pharesis pack = 6 units of pooled donor plt	4 units or 15mL/kg	10 units or 1 units/5 kg
Typical dosage effect	↑Hgb by 1g/dL	↑ Plt by 30-60,000/μL	↑Most coag factors by 20-25% (level needed for effective hemostasis)	↑ fibrinogen by 75 mg/dL
Notes	- CBC 2 hrs after transfusion to assess response - If cardiomyopathy, can run as splits (1/2 unit over 4 hours) + Lasix IV - Watch Ca, K, Plt, coags if massive transfusion	- CBC 1 hr after transfusion to assess response - If refractory may have allo-ab, try ABO-matched platelets. If still refractory check for HLA-Ab. - Not indicated in TTP/HUS, HELLP, HIT	- Max effect declines after 2-4 hrs, transfuse 1 hr before procedure - INR of FFP ~1.3 -Acellular so does not transmit intracellular infections (e.g., CMV)	- Consider if massive transfusion

Adapted from Strecker-McGraw M. Chapter 41. Hematologic Emergencies. In: Humphries RL, Stone C, eds. CURRENT Diagnosis & Treatment Emergency Medicine. 7th ed. New York: McGraw-Hill; 2011.

Complications
- *Acute hemolytic:* fever, hypotension, flank pain, renal failure <24hr after transfusion. 2/2 ABO incompatibility (preformed Abs against donor RBCs).
    - Tx: maintain UOP w/ IVF, diuretics.
- *Delayed hemolytic:* less severe than acute hemolytic, 5-7d after transfusion. Undetected allo-Abs against minor antigens. No specific tx.
- *Febrile non-hemolytic:* fevers, rigors 0-6hr after transfusion. Due to Ab against donor neutrophils + cytokines released from cells in blood product.
    - Tx: acetaminophen, r/o infection.
- *Allergic:* urticaria, rarely anaphylaxis (bronchospasm, laryngeal edema, hypotension). Reaction to transfused proteins; anaphylaxis in IgA-deficient pts w/ anti-IgA Abs.
    - Tx: Benadryl, epinephrine, glucocorticoids
- *Transfusion-related acute lung injury (TRALI):* non-cardiogenic pulmonary edema within 6 hours. Hypoxia, PaO2:FIO2<300. Donor Abs bind recipient neutrophils, aggregate in pulmonary vasculature, release mediators causing ↑ capillary permeability
    - Treat as ARDS.
- *Transfusion-associated circulatory overload (TACO)*: ↑ volume → pulm edema, ↑ BP.
    - Tx: slow transfusion rate, diuretics, O2, ±nitrates, ±positive pressure ventilation

If reaction (except minor allergic): fever, tachycardia, dyspnea, back pain, hemodyn. instability
(1) Stop transfusion
(2) Check ABCs, cardiac/O2 monitoring
(3) Recheck patient name, typing. Send remaining blood + fresh blood sample to blood bank for analysis. Steps 4-7 if acute hemolytic reaction suspected (as indicated):
(4) Medications: hydrocortisone 100mg IV, diphenhydramine 50mg IV, acetaminophen 650mg PO, epinephrine 0.3 mL of 1:1000 dilution subq
(5) IV fluids to keep UOP >30-50cc/hr
(6) Lab tests: CBC, coombs test, urine free Hgb, haptoglobin, coags, fibrinogen, bilirubin, LDH
(7) Leukocyte-reduced blood for future transfusions

Transfusions cont.

Transfusion complication risks			
Non-infectious	**Risk (per unit)**	**Infectious**	**Risk (per unit)**
Febrile	1:100	CMV	Common
Allergic	1:100	Hepatitis B	1:220,000
Delayed hemolytic	1:1,000	Hepatitis C	1:1,600,000
Acute hemolytic	<1:250,000	HIV	1:1,800,000
Fatal hemolytic	<1:100,000	Bacteria (pRBC)	1:500,000
TRALI	1:5,000	Bacteria (plt)	1:12,000

From Transfusion 5-13. Pocket Medicine 6th ediation., adapted from NEJM 1999;340:438; JAMA 2003; 289:959

Vitamin K: (condensed/rearranged)

- Deficiency: malnutrition, liver disease (↓ stores), ↓ absorption (antibiotic suppression of vit K-producing intestinal flora or malabsorption – needs bile salts for absorption), warfarin
- Vit K deficiency → ↓ factor II, VII, IV, X, protein C&S
- 1st line: 10mg PO x 3d if bilirubin normal
- 2nd line (or if rapid reversal needed): 1-2.5mg IV. Small risk of anaphylaxis to diluent (1 in 3000 doses), reduced if infused over 1 hr. Will see effect 6-12 hrs later, maximal at 36hr.

Oncologic emergencies

Neutropenic fever

- Definitions:
    - Fever: single T>38.3°C, T>38.0°C over 1h OR T>1.5°C from baseline
    - Neutropenia: <500 neutrophils/μL OR <1,000 neutrophils/μL and predicted decline to 500/μL over next 48h.
- WBC nadir from chemo typically at 10-14d, recovery heralded by monocytes
- Previously mostly GN (e.g., P. aeruginosa, generally more severe infection), now GP more common (staph epi, staph aureus, strep)
- Dx: Blood cx x2 (include all catheter sites, also consider anaerobic/fungal), urine cx, U/A, CXR
- **Empiric coverage:** Monotherapy w/ cefepime 2g IV q8h.
    - Other single agents: imipenem, meropenem, piperacillin/tazobactam, ceftazidime
    - If penicillin allergy and cannot tolerate cephalosporins: aztreonam + vancomycin
- Add vancomycin IF you suspect catheter-related infection, skin/soft tissue infection, PNA, or hemodynamic instability. Discontinue in 2-3d if no source identified requiring vancomycin.
- Broaden anaerobic coverage for aspiration, GI or oral source
- Add aminoglycoside if septic. Has good urinary concentration, synergistic w/ beta-lactams
- If still febrile after 5d, consider fungal coverage, VRE, anaerobes (*Bacteroides, prevotella, fusobact.* not covered by cefepime). Consider re-imaging if new or worsening site of infx

GCSF

- *Prophylactic use:* assess risk of neutropenia. Use associated w/ less reduction in chemo dosage, and reduction in risk/severity of febrile neutropenia.
    - Start 1-3d after completion of chemo, tx through post-nadir recovery.
- *Therapeutic use:* less certain, 1 study showed ↓ LOS + neutropenia, but no mortality benefit.
- *Filgrastim (Neupogen):* 5 mcg/kg/d (rounding to 300mcg or 480mcg subq) until post-nadir ANC recovery to normal or near-normal.
- *Pegfilgrastim (Neulasta):* 1 dose of 6 mg subq/cycle of chemo. Given as outpatient in STC only

Additions to empiric coverage based on local symptoms

Site	Evaluation	Additions to empiric treatment
Mouth/mucosal	Gram stain, cx of suspicious lesions. HSV/VZV	Anaerobic, HSV, fungal
Esophagus	Cx oral lesions (HSV, fungal), endoscopy	Fungal, HSV, CMV
Sinus/nasal	High res sinus CT/orbit MRI, ENT/ophtho eval, biopsy/cx	Vanco if periorbital cellulitis, amphotericin B for aspergillosis/mucormycosis if CT/MRI findings
Abdominal pain	CT abdomen, LFTs, lipase	C.diff, anaerobic
Perirectal pain	Perirectal inspection **(avoid DRE!)**, consider CT a/p	Anaerobic, local care (ex. sitz baths, stool softener)
Diarrhea	C.dif stool antigen, stool Cx, OxP	C.diff
Urinary tract symptoms	Ucx, U/A	None additional until ID/sensitivitiy
Lung infiltrates	Blood/sputum cx, nasal wash for resp. virus, legionella urine Ag, B-D-glucan if risk for mold infx, CT chest, BAL, PJP DFA	Azithromycin/FQ for atypical coverage, mold-active fungal agent, viral, TMP-SMX if PJP possible, vancomycin/linezolid for MRSA
Cellulitis/skin and soft tissue	Aspirate/biopsy	MRSA
Vascular access devices	Swab/blood culture from ports	Vanco, removal of catheter
Vesicular lesions	Aspiration/scraping for DFA VZV/HSV, cx	VZV/HSV
Disseminated papules/lesions	Aspiration/bx for bacteria/fungal/mycobacterial cultures, histopathology	Vanco, mold-active antifungal
CNS symptoms	CT +/- MRI, lumbar puncture, neuro consult	Meningitis coverage (Pseudomonas, GP like Listeria, MDR GNR). High dose acyclovir with hydration if encephalitis

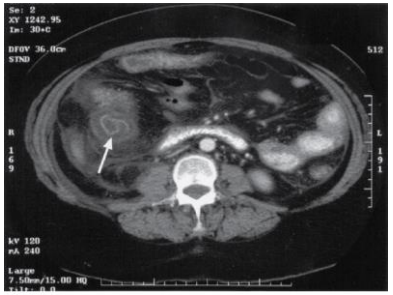
Adapted from NCCN Guidelines Version 2.2020 Prevention and Treatment of Cancer-Related Infections

Commonly used antimicrobials in neutropenic fever:

Agent		Dose	Coverage, comments
Antibacterial Pseudomonal activity	Imipenem/cilastatin	500 mg IV q6h	Most GP, GN, anaerobic. Preferred in ESBL and serious Enterobacter infections. Meropenem > imipenem for CNS infx. Carbapenems may lower seizure threshold
	Meropenem	1 gram IV q8h (2 g IV q8h for meningitis)	
	Piperacillin/tazobactam	3.375g IV q6h or extended infusion q8h	Most GP, GN, anaerobic. Use for suspected intra-abdominal source, not for meningitis.
	Cefepime	2 grams IV q8h	Most GP, GN. Not active against most anaerobes and Enterococcus spp (add Flagyl).
Antibacterial Gram-positive activity	Vancomycin	15 mg/kg IV q12h For C.diff: 125 mg PO q6h	GP except VRE + some rare GP.
	Linezolid	600 mg PO/IV q12h	GP + VRE. ↓plt, rare serotonin syndrome, peripheral/optic neuropathy w/ long-term use.
	Daptomycin	6 mg/kg/d IV	GP, in vitro activity vs. VRE but not FDA-approved for this indication. Weekly CK for rhabdo. Not for PNA due to inactivation by pulmonary surfactant.
Antibacterial Other	Ciprofloxacin + Augmentin	500-750 mg PO q8-12h + Augmentin 875 mg q12h	GN + atypicals with cipro; add Augmentin for anaerobic coverage and aerobic GP
	Levofloxacin	500-750 mg PO or IV daily	GN + atypicals, not anaerobes.
	Aminoglycosides	Dosing individualized, monitor levels	GN + ESBL. Nephrotoxicity, ototoxicity.
Antifungals	Fluconazole	400 mg IV/PO daily	Candida, Histo, Cocci, Crypto. Inactive against C. galbrata, C. krusei, Aspergillus, zygomycetes.
	Itraconazole	400 mg PO daily (measure trough after 7d)	Candida, Aspergillus, Histo, Cocci, Crypto. Negative inotropic, contraindicated in cardiomyopathy
	Voriconazole	Invasive aspergillosis: 6mg/kg q12h x 2doses, then 4 mg/kg q12 h OR 200mg PO BID.	Candida, Aspergillus, Histo, Cocci, Crypto. Not zygomycetes. Primary tx of invasive aspergillosis.
	Posaconazole	Prophylaxis: 300mg PO bid on day 1 then maintenance 300mg PO qday	Candida, Aspergillus, Histo, Cocci, Crypto, Zygometes. PPI lowers levels. Administer with food; avoid If pt cannot eat a full meal or tolerate nutritional supp.
	Liposomal amphotericin	3mg/kg/d IV	Candida, Aspergillus (except terreus), Zygomycetes, Histo, Cocci, Crypto.
	Caspofungin	70mg IV x1 dose, then 50mg IV daily	Primary tx for candidemia, salvage for Aspergillus. Echinocandins have poor CNS and eye penetratino
	Micafungin	100mg IV/d	
Antiviral	Acyclovir	Variable dosing depending on indications (HSV, VZV, CMV; prophylaxis vs. treatment)	HSV, VZV. Hydration to avoid crystal nephropathy w/ high doses. Dosing based on ideal body weight.
	Valacyclovir		HSV, VZV.
	Ganciclovir		CMV, HSV, VZV, HHV-6. May cause myelosuppression.
	Valganciclovir		CMV. May cause myelosuppression.
	Foscarnet		HSV, VZV, CMV, HH-6. Drug of choice for HSV/VZV resistant to acyclovir, and CMV resistant to ganciclovir. Nephrotoxic, monitor electrolytes.

Adapted from NCCN Guidelines Version 2.2020 Prevention and Treatment of Cancer-Related Infections

Typhlitis/Neutropenic enterocolitis



Source: Kantarjian HM, Wolff RA, Koller CA: *The MD Anderson Manual of Medical Oncology, 2nd Edition*: www.accessmedicine.com

- Bowel inflammation, wall thickening, ulcers, hemorrhage, necrosis involving proximal large bowel
- Cecum most often affected (decreased vasculature, increased distensibility).
- Breakdown of gut mucosal integrity from cytotoxic chemo, impaired host defense
- Often seen 10-14d s/p chemo in neutropenic pts
- Present w/ fever, RLQ pain, diarrhea (can be bloody).
- Mucositis (somatitis, pharyngitis) may be present, indicates diffuse gut involvement.
- Clostridium, GNR most commonly isolated, but also GPC, candida.
- Ddx: Appendicitis, pseudomembranous colitis, ischemic colitis, colonic obstruction
- Dx: CT preferred; plain film often inconclusive unless perforation
- Tx:
    - Bowel rest, IVF, broad-spectrum abx including anaerobic coverage
    - Add empiric c. diff coverage if pseudomembranous colitis has not been excluded
    - If febrile >72hr, consider antifungal (voriconazole/amphotericin B will cover aspergillus and fluconazole-resistent candida).
    - Surgery if peritonitis, free perforation, GI bleed.

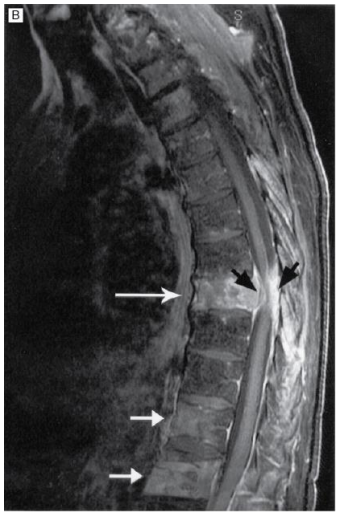
Increased intracranial pressure

- Causes: hemorrhage, brain mets (vasogenic edema, mass effect), hydrocephalus from obstruction, radiation therapy
- Sx: commonly headache that is present on waking, recur throughout day, increased w/ Valsava, associated w/ N/V, AMS, visual changes, seizures, neurologic deficits.
- If brain mets, seizures are presenting symptom in 15-20% of patients.
- Brain mets:
    - Most common are lung, breast, melanoma
    - Also colorectal, kidney, prostate, testicular, ovarian, sarcomas
    - Pelvic tumors have ↑ propensity for mets to posterior fossa.
- Tx: initial steroids, neurosurgical intervention or palliative XRT if multiple mets

Leptomeningeal disease (LMD)

- Invasion of brain, spinal parenchyma, nerve roots, blood vessels of nervous system
- Occurs in 0.8-8% of all cancer pt
- Spreads hematogenously, via direct extension, or through bone marrow mets
- Most common malignancies: lung, breast, melanoma, NHL, leukemia
- Variable sx depending on location (H/A, AMS, CN palsy, incontinence, back pain, sensory changes, seizures, stroke-like presentation)
- Dx: MRI better than CT, but not diagnostic. May see leptomeningeal enhancement, hydrocephalus, cortical nodules.
    - CSF analysis = gold standard, may need multiple LP as 50% of pt have positive cytology on 1st evaluation. Other findings are high OP, low glucose, high protein, mononuclear pleocytosis
- Tx: chemo through LP instillation vs. implanted Ommaya reservoir. Use methotrexate, thiotepa, cytarabine. Radiation tx for localized LMD or areas of nerve root involvement not likely to reach adequate concentration
- Once leptomeningeal disease detected: median survival 3-6mo, 15-25% surviving >1yr

Spinal cord compression

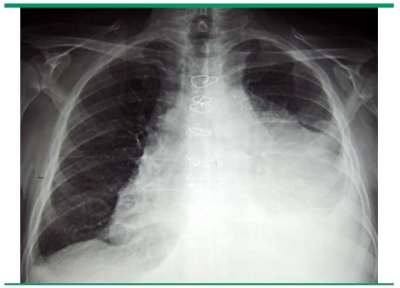


Source: Kantarjian HM, Wolff RA, Koller CA: *The MD Anderson Manual of Medical Oncology, 2nd Edition*: www.accessmedicine.com

67-yo man w/ melanoma + back pain. Post-contrast T1-weighted MR image of thoracic cord compression at T8 level produced by an epidural tumor from vertebral body metastasis (large arrow). Smaller arrows point to other sites of bony metastasis. The epidural tumor is visualized better w/ contrast (black arrows).

- Affects 2.5% of oncology pts
- Metastases in vertebral body extend and cause epidural spinal cord compression
- Most commonly seen: prostate, breast, and lung cancers, followed by renal cell carcinoma, NHL, and myeloma
- Sx: pain first (precedes neuro sx!), weakness, urinary retention, ↓ anal sphincter tone, sensory loss
- Imaging:
    - Urgent whole-spine MRI with contrast
    - CT myelography "gold standard" but invasive, time-consuming, painful
    - XR has false neg in 30%+ of cases as 30-50% of bone must be destroyed before lesions seen.
- Tx: Dexamethasome 10mg IV STAT then 4mg IV or PO q6h)
    - Emergent radiotherapy and/or surgical decompression
    - Discuss with neurosurgery through MAC
- General surgical indications: recurrent/progressive disease at area w/ previous max radiotherapy, spinal mechanical instability, unknown tissue dx of malignancy, compression of spinal cord by bony structure/fragment.
- If ambulatory upon presentation, ¾ regain strength w/ tx. 10% presenting paralyzed able to walk again
- Median survival ~3mo (but dependent on underlying malignancy)

Pericardial disease – Cardiac tamponade



Cardiomegaly due to a massive pericardial effusion. At least 200 mL of pericardial fluid must accumulate before the cardiac silhouette enlarges.

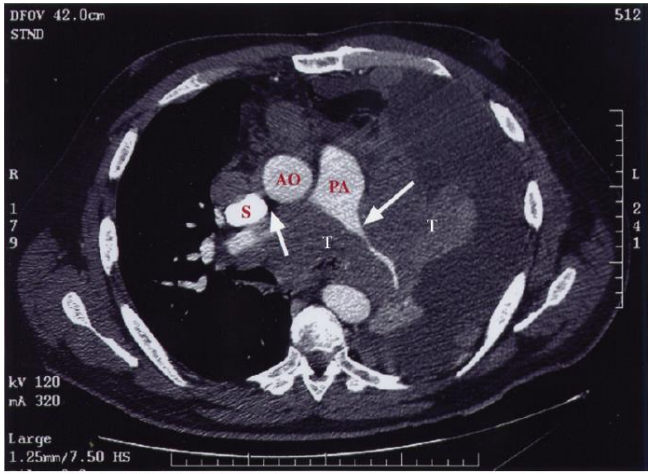
Courtesy of Massimo Imazio, MD, FESC.

Source: http://www.uptodate.com/contents/images/CARD/57640/CXR_perieff.jpg?title=Chest+x-ray+of+a+pericardial+effusion. Accessed 6/1/21.

- Most neoplastic pericardial involvement seen in mets from lung cancer; then breast, esophageal cancer, melanoma, lymphoma, and leukemia
    - Pericarditis, pericardial effusion, constrictive pericarditis
- Pericardial effusions can be due to chemo, chest radiation, or infx (esp related to fungal infx)
    - Chemo associated w/ pericardial effusion: fludarabine, cytarabine, doxorubicin, docetaxel, cyclophosphamide, dasatinib
- Sx: SOB, cough, cardiogenic shock, epigastric pain, chest pain worse w/ lying down/leaning forward
- Signs of tamponade:
    - Beck's triad: JVD, hypotension, ↓ heart sounds
    - Pulsus paradoxus, ↓ pulse pressure
- Dx: EKG, CXR, TTE
- Tx: O2, cautious IV fluids, + inotropes (avoid BB)
    - Pericardiocentesis (daily drainage catheter until <50cc/day).
    - Pre-load dependent, avoid diuretics.
- Prevent reaccumulation: Pericardial window, radiation, chemo, sclerosis of pericardium

SVC syndrome

- Low blood flow from SVC to RA
- Extrinsic compression by tumor, intrinsic compression by tumor/clot, fibrosis
- Lung cancer most common cause (bronchogenic carcinoma, small cell), followed by lymphoma, breast, GI, sarcoma, melanoma, prostate, mediastinal tumor
- Sx: UE/face/neck swelling, SOB, dysphagia, H/A, dizziness, confusion. Chest wall collateral vessels on exam.
- Dx: CT w/ contrast, biopsy of tumor if unknown type
- Tx: diuretics, lytics for thrombosis, chemo (e.g., small cell lung cancer), radiation, intravascular stenting, angioplasty, corticosteroids for elevated ICP.



Source: Kantarjian HM, Wolff RA, Koller CA: *The MD Anderson Manual of Medical Oncology, 2nd Edition:* www.accessmedicine.com

Large arrow indicates compression of the left pulmonary artery; small arrow indicates obliteration of the right pulmonary artery. T, tumor; AO, aorta; PA, main pulmonary artery; S, superior vena cava.

Toxic lung injury

- ATRA: Retinoic acid syndrome (RAS) causing ARDS in 26% of patients 2-47d after tx
- Cytarabine: diffuse lung injury, capillary leakage, pulmonary edema after 6d of therapy
- Pulmonary edema: mitomycin C, gemcitabine, cyclosporine, interferon, TNF, IL-2, GMCSF
- ILD: bleomycin (hypersensitivity pneumonitis, dose related, usually >450 units), carmustine, lomustine, busulfan (3 wk - 3 yr, high mortality), cyclophosphamide (early onset = pneumonitis responsive to steroids, late onset = progressive fibrosis not responsive to steroids), methotrexate (days to years), doxorubicin (pulmonary fibrosis "recall" effect after radiation therapy), actinomycin D (see note on doxorubicin), tyrosine kinase inhibitors
- Pulmonary veno-occlusive disease: bleomycin, mitomycin C, busulfan

Hemorrhagic cystitis

- Inflammation, bleeding of bladder
- Causes:
    - Radiation (3mo-yrs after)
    - Viral infection (BK in BMT patients)
    - Chemo (cyclophosphamide, ifosfomide)
- Tx: hydration, diuresis, Mesna to bind cyclophosphamide/ifosfomide metabolites (acrolein, chloroacetaldehyde) during administration, consider Urology evaluation
- Other tx: gentle bladder irrigation to remove clots, decompress bladder.

Hyperviscosity

- ↑ concentration of paraproteins→ ↑ viscosity, RBC sludging, low O2 delivery to tissues
- Occurs in 15% of pt w/ Waldenstrom macroglobulinemia (IgM)
    - Also seen in other myelomas, polycythemia vera, essential thrombocythemia
    - Present w/ bleeding 2/2 abnormal platelet function, thrombosis, headache, AMS, dizziness, visual complaints), CHF (increased plasma volume), weakness, fatigue
- Avoid transfusions, as may worsen hyperviscosity
- Dx: CXR, serum viscosity (normal 1.4-1.8, sx when >5), fundoscopic exam
- Tx: IV fluids, plasma exchange with saline, chemotherapy.

Leukostasis

- Hyperleukocytosis: WBC > 100k/μL. Can be seen w/ blasts > 50-80k/μL or rapid increase
- WBC poorly deformable, lodged in microvasculature of kidneys, lungs (ARDS vs. V/Q mismatch), brain
- Seen in AML and CML w/ blast crisis. Less commonly ALL/CLL (lymphocytes smaller).
- Sx: H/A, dizziness, vertigo, SOB, AMS, hemoptysis, retinopathy (vascular engorgement, exudates, hemorrhage), CNS bleed
- If untreated, 1-week mortality 20-40%
- Tx: leukopharesis via HD line, chemotherapy, hydration

Tumor lysis

- Result of excessive tumor breakdown, generally w/ chemotherapy (but also radiation, hormonal agents, corticosteroid)
- Causes ↓calcium, ↑phosphate, ↑potassium, ↑uric acid, renal failure (generally reversible)
- Risk factors: high tumor burden, high-grade lymphomas (Burkitt's) and leukemias (ALL, AML, CML in blast crisis); rare with solid tumors
- Prophylaxis: IV fluids, allopurinol 300 daily (dose renally)
- Treatment:
- If uric acid >8mg/dL:
    - BMP, Ca, phosphate, uric acid, LDH q8h
    - IV fluids 200-300 cc/hr if no contraindications, maintain UOP >100cc/hr
    - Allopurinol 100mg/m^2 q8h (max 800mg/day, dose renally)
    - Rasburicase: 0.15-0.2 mg/kG IV (needs H/O attending approval)
        - Recombinant urate oxidase, converts uric acid to allantoin rapidly.
        - Contraindicated if G6PD, methemoglobinemia, pregnancy.
    - Hemodialysis if persistent hyperuricemia
- Hyperkalemia: kayexalate, lokelma, calcium gluconate, albuterol, insulin + D50, Lasix
- Hyperphosphatemia: diet restriction, sevelamer 800-1600 TIDWM
- Hypocalcemia: if asx → NO tx; if symptomatic, treat hyperphos first prior to calcium

Chemotherapy–induced extravasations (See Appendix 2)

- Can cause skin irritation/ulceration, tissue necrosis, nerve damage
- Can be avoided by using central venous catheters
- Most severe reactions:
    - Alkylating agents (mechlorethamine, cisplatin, mitmoycin C)
    - DNA intercalating agents (doxorubicin, daunarubicin)
    - Plant alkaloids (vincristine, vinblastine, vinorelbine)
- Tx: Mitomycin, anthracyclines: Topical DMSO (dimethylsulfoxide) in 50% solution, 1.5cc applied to site q6h x 7-14d
    - If still symptomatic w/ anthracyclines, will need plastic surgery consultation for excision/skin grafting.
    - Apply cool or warm packs

Hypercalcemia

- Causes: PTHrP, ↑ Vitamin D 1,25 (lymphoma), bony mets (most common)
- Symptoms: AMS, polyuria, polydipsia, N/V, anorexia, constipation, seizures
- Treatment: Ca > 14mg/dL requires treatment, consider if 12-14 and symptomatic
    - IV fluids 200-300cc/hr if no contraindications w/ goal UOP 100-150cc/hr
    - Zoledronic acid: used for long-term lowering of Ca+ by inhibiting bone resorption.
    - Dialysis if unable to tolerate hydration
    - Calcitonin: rapid lowering of Ca+ by ↑ renal excretion of Ca + ↓ bone resorption.

Chemotherapy toxicities

Common chemotherapy toxicities: Direct DNA-interacting agents

Drug	Toxicity	Interactions, Issues
Alkylators		
Cyclophosphamide	Marrow (relative platelet sparing), cystitis, alopecia, pulm., infertility, teratogenesis	Liver metabolism required to activate to phosphoramide mustard + acrolein. MESNA protects against "high-dose" bladder damage.
Bendamustine	N/V, hyperbilirubinemia, cough, N/V	CLL, NHL
Ifosfamide	Myelosuppressive, bladder, neurologic, metabolic acidosis, neuropathy	Isomeric analogue of cyclophosphamide. More lipid soluble, ↑ activity vs testicular neoplasms and sarcomas. Must use MESNA.
Cisplatin	Nausea, neuropathy, auditory, marrow (plt >WBCs), renal (Mag, K wasting)	Maintain high urine flow; osmotic diuresis, monitor intake/output K+, Mg2+. Emetogenic—prophylaxis needed. Full dose if CrCl > 60 mL/min + tolerate fluid push.
Carboplatin	Marrow (plt > WBCs), nausea, renal (high dose)	↓ dose according to CrCl: to AUC of 5–7 mg/mL per min [AUC = dose/(CrCl + 25)]
Oxaliplatin	Nausea, anemia	Acute reversible neurotoxicity, chronic sensory neurotoxicity cumulative w/ dose. Reversible laryngopharyngeal spasm (avoid cold).
Antitumor Antibiotics and Topoisomerase Inhibitors		
Bleomycin	Pulm., skin effects, Raynaud's, hypersensitivity, allergic reactions	Deactivated by bleomycin hydrolase (decreased in lung/skin). O2 ↑ pulm. toxicity. Cisplatin-induced decrease in CrCl may increase skin/lung toxicity, reduce dose if CrCl < 60 mL/min. Radiation recall.
Etoposide (VP16-213)	Marrow (WBCs > platelet), alopecia, hypotension, hypersensitivity (rapid IV), nausea, mucositis (high dose)	Hepatic metabolism—renal 30%, reduce doses w/ renal failure. Schedule-dependent (5 day better than 1 day). Late leukemogenic. Accentuates antimetabolite action.
Irinotecan (CPT II)	Diarrhea: "early onset" w/ cramping, flushing, vomiting; "late onset" after several doses, marrow, alopecia, N/V, pulmonary	Prodrug requires enzymatic clearance to active drug "SN 38." Early diarrhea likely 2/2 biliary excretion. Late diarrhea: use "high-dose" loperamide (2 mg q2–4 h).
Doxorubicin and daunorubicin	Marrow, mucositis, alopecia, cardiovascular (acute/chronic)	Vesicant. Heparin aggregate; coadministration ↑clearance. Acetaminophen, BCNU ↑ liver toxicity. Radiation recall.

Adapted from Table 85-1 of Sausville EA, Longo DL. Chapter 85. Principles of Cancer Treatment. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw-Hill; 2012. http://www.accessmedicine.com/content.aspx?aID=9114487. Accessed July 31, 2013.

Grading Toxicity

Grade	Description
1 (Mild)	Asymptomatic or mild symptoms. Clinical or diagnostic observation only. No intervention indicated.
2 (Moderate)	Minimal, local, or noninvasive intervention indicated. Limiting age-appropriate IADLs (preparing meals, shopping for groceries/clothes, using telephone, managing money.
3 (Severe)	Hospitalization or prolongation of hospitalization indicated. Disabling, limiting ADLs (bathing, dressing/undressing, feeding self, using toilet, taking medications)
4 (Life-threatening)	Urgent intervention indicated
5 (Death)	Death

Of note, specific parameters for each grade are available for each organ system. Please see UpToDate's article on "Common terminology criteria for adverse events for detailed grading for each organ system.

Common chemotherapy toxicities: Indirect DNA-interacting agents

Drug	Toxicity	Interactions, Issues
Antimetabolites		
6-Mercaptopurine	Marrow, liver, nausea	Variable bioavailability. Metabolized by xanthine oxidase, decrease dose w/ allopurinol. ↑ toxicity w/ thiopurine methyltransferase deficiency.
Azathioprine	Marrow, nausea, liver	Metabolizes to 6MP, therefore reduce dose w/ allopurinol. ↑ toxicity w/ thiopurine methyltransferase deficiency.
Hydroxyurea	Marrow, nausea, mucositis, skin changes. Rare renal, liver, lung, CNS.	Decrease dose w/ renal failure. Augments antimetabolite effect.
Methotrexate	Marrow, liver/lung, renal tubular, mucositis	Rescue w/ leucovorin. Excreted in urine, start alkalinization upon admission. ↓ dose in renal failure. NSAIDs ↑ renal toxicity. Hold omeprazole/Bactrim when on MTX.
5-Fluorouracil (5FU)	Marrow, mucositis, neurologic, skin changes, vasospasm	Toxicity enhanced by leucovorin. Dihydropyrimidine dehydrogenase deficiency ↑ toxicity. Metabolizes in tissues.
Capecitabine	Diarrhea, hand-foot syndrome	Prodrug of 5FU
Gemcitabine	Marrow, nausea, hepatic, fever ("flu syndrome")	
Antimitotic Agents		
Vincristine	Vesicant, marrow, neurologic, GI (ileus/constipation; bladder hypotoxicity), SIADH, cardiovascular	Hepatic clearance. Dose reduction for bilirubin >1.5 mg/dL. Prophylactic bowel regimen.
Vinblastine	Vesicant, marrow, neurologic (less common but similar to other vincas), HTN, Raynaud's	Hepatic clearance. Dose reduction as w/ vincristine.
Paclitaxel	Hypersensitivity, marrow, mucositis, alopecia, sensory neuropathy, CV conduction disturbance, nausea (infrequent)	Premedicate w/ steroids, H1 and H2 blockers. Hepatic clearance. Dose reduction as w/ vincas.
Docetaxel	Hypersensitivity, fluid retention syndrome, marrow, dermatologic, sensory neuropathy, nausea (infrequent), stomatitis (some)	Premedicate w/ steroids, H1 and H2 blockers

Common chemotherapy toxicities: Molecularly-targeted agents

Drug	Toxicity	Interactions, Issues
Retinoids		
Tretinoin	Teratogenic, cutaneous	APL differentiation syndrome: pulm. dysfunction/infiltrate, pleural/pericardial effusion, fever
Tyrosine Kinase Inhibitors		
Imatinib	Nausea, periorbital edema	Myelosuppression not frequent in solid tumor indications
Dasatinib	Liver changes, rash, neutropenia, thrombocytopenia, pericardial/pleural effusions	
Sorafenib	Diarrhea, hand-foot syndrome, other rash	Tx RCC, multiple targets including RAF/VEGF
Anti-EGFR		
Trastuzumab (Herceptin)	Infusion reaction, cardiomyopathy, pulm. toxicity	Anti-HER2, tx breast ca
Pertuzumab	Cardiomyopathy, alopecia, diarrhea, cytopenia	Anti-HER2, tx breast ca
mTOR Inhibitors		
Everolimus	Stomatitis, fatigue	
Monoclonal antibodies		
Bevacizumab (Avastin)	Proteinuria, HTN, GI perforation, arterial embolism	Colon Ca, NSCLC, renal, breast
Rituximab (Rituxan)	Severe mucocutaneous reactions, infusion reaaction, PML, cytopenias	Hepatitis B reactivation
Immune Checkpoint Inhibitors		
Nivolumab, Pembrolizumab	Severe immune-mediated reactions (enterocolitis, hepatitis, dermatitis, neuropathy, endocrinopathy)	Monoclonal ab against PD-1
Atezolizumab, avelumab, durvalumab	Severe immune-mediated reactions (enterocolitis, hepatitis, dermatitis, neuropathy, endocrinopathy)	Monoclonal ab against PD-L1
Ipilumumab	Severe immune-mediated reactions (enterocolitis, hepatitis, dermatitis, neuropathy, endocrinopathy)	Monoclonal ab against CTLA-4
Other		
Arsenic trioxide	QTc prolongation, peripheral neuropathy, MSK pain, hyperglycemia, APL differentiation syndrome	

Adapted from Table 85-1 of Sausville EA, Longo DL. Chapter 85. Principles of Cancer Treatment. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw-Hill; 2012. http://www.accessmedicine.com/content.aspx?aID=9114487. Accessed July 31, 2013.

Appendix 1: Pathophysiology of nausea and vomiting

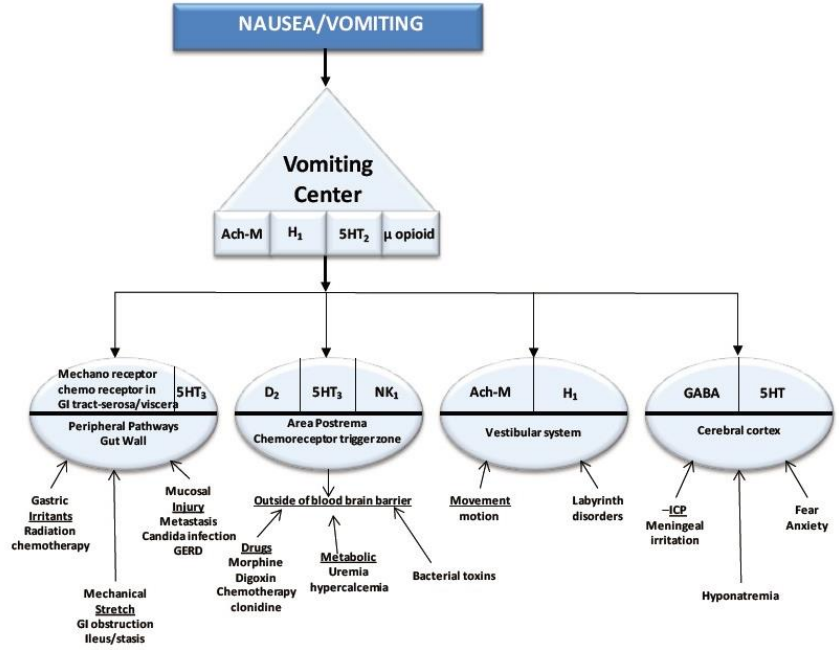


Figure 1. HS Smith, LR Cox, BR Smith. Dopamine Receptor antagonists. Annals of Palliative Medicine. Vol 1, No 2 (July 2012)

Appendix 2: Chemotherapeutic extravasations and their antidotes

Chemotherapy	Irritant vs. Vesicant	Sodium Thiosulfate	DMSO	Hyaluronidase	Cold Packs	Warm
Carboplatin	I	+			+	
Carmustine	I/V	+		+		Dry warm
Cisplatin		I/V	+			+
Cyclophosphamide	I	+			+	
Dacarbazine	I/V	+				
Dactinomycin	I/V				+	
Daunorubicin	I/V		+		+	
Docetaxel	I				+	Warm soaks
Doxorubicin	I/V		+		+	
Epirubicin	I/V		+		+	
Etoposide	I/V			+		+
Idarubicin	I/V		+		+	
Ifosfamide	I				+	
Mechlorethamine	I/V	+				
Mitomycin C	V		+		+	
Oxaliplatin	I/V	+				
Paclitaxel	I/V			+		
Plicamycin	I/V					
Streptozocin	I/V					
Teniposide	I/V			+		+
Topotecan					+	
Vinblastine	I/V			+		+
Vincristine	I/V			+		+
Vindesine	I/V			+		+
Vinorelbine	I/V			+		+

From: Yeung S, Manzullo EF. Chapter 46. Oncologic Emergencies. In: Kantarjian HM, Wolff RA, Koller CA. eds. The MD Anderson Manual of Medical Oncology, 2e. New York, NY: McGraw-Hill; 2011. http://accessmedicine.mhmedical.com/content.aspx?bookid=379&Sectionid=39902077. Accessed March 23, 2015.

Appendix 3

Khorana Predictive Model For Chemotherapy-Associated VTE[1]

Patient Characteristic	Risk Score
• Site of primary cancer	
➤ Very high risk (stomach, pancreas)	2
➤ High risk (lung, lymphoma, gynecologic, bladder, testicular)	1
• Prechemotherapy platelet count 350X10^9/L or higher	1
• Hemoglobin level less than 10 g/dL or use of red cell growth factors	1
• Prechemotherapy leukocyte count higher than 11X10^9/L	1
• BMI 35 kg/m^2 or higher	1

Total Score	Risk Category	Risk of Symptomatic VTE[2]
0	Low	0.8-3%
1, 2	Intermediate	1.8-8.4%
3 or higher	High	7.1-41%

Per NCCN: *"Consider patient conversation about risks and benefits of VTE prophylaxis in the Khorana score ≥3 patient population."*

Appendix 4: Oncology Conferences

- Bone Marrow Rounds - Friday at 1:30 PM
- Tumor Board - Weekly on Thursday at 1:00 PM
- Gyn Onc Tumor Board - Weekly on Monday 11:30 AM
- Lymphoma Conference - Monthly on Tuesday at 8:00 AM
- Heme/Onc Journal Club - Monthly on Thursday at 12:00 PM
- Thoracic Conference - Every other week on Thursday at 12:00 PM
- Hepatobiliary Conference - Monthly on Tuesday at 1 PM
- Heme/Onc Core Curriculum Conference - Monthly on Tuesday

Appendix 5: Emetogenic potential of chemo

High risk (>90% frequency of emesis)	Moderate risk (30-90% frequency of emesis)	Low emetic risk (10-30% frequency of emesis)	Minimal emetic risk (<10% frequency of emesis)
Doxorubicin or epirubicin + cyclophosphamide	Aldesleukin >12-15 million IU/m2	Amifostine ≤300mg	Alemtuzumab
Carmustine > 250mg/m2	Amifostine >300 mg/m2	Adlesleukin ≤12 million IU/m2	Asparaginase
Cisplatin	Arsenic trioxide	Brentuximab vedotin	Bevacizumab
Cyclophosphamide >1500 mg/m2	Azacitidine	Cabazitaxel	Bleomycin
Dacarbazine	Bendamustine	Capecitabine (oral)	Bortezomib
Doxorubicin >60mg/m2	Busulfan	Carfilzomab	Cetuximab
Epirubicin >90mg/m2	Carboplatin	Cytarabine 100-200mg/m2	Chlorambucil (oral)
Hexamethylmelamine (oral)	Carmustine ≤250 mg/m2	Docetaxel	Cladribine
Ifosfamide ≥2 g/m2 per dose	Clofarabine	Doxorubicin (liposomal)	Cytarabine <100mg/m2
Mechlorethamine	Cyclophosphamide ≤ 1500 mg/m2	Eribulin	Decitabine
Procarbazine (oral)	Cytarabine >200 mg/m2	Etoposide	Denileukin diftitox
Streptozocin	Dactinomycin	Everolimus (oral)	Dexrazoxane
	Daunorubicin	5-FU	Erlotinib (oral)
	Doxorubicin ≤60 mg/m2	Fludarabine (oral)	Fludarabine
	Epirubicin ≤90 mg/m2	Floxuridine	Gefitinib (oral)
	Idarubicin	Gemcitiabine	Hydroxyurea (oral)
	Ifosfamide <2g/m2	IFN-α 5-10 million IU/m2	IFN-α <5 million IU/m2
	Imatinib (oral)	Ixabepilone	Ipilmumab
	Interferon alfa ≥ 10 million IU/m2	Lapatinib (oral)	L-phenylalanine mustard (oral)
	Irinotecan	Lenalidomide (oral)	Methotrexate <50mg/m2
	Melphalan	Methotrexate 50-250mg/m2	Nelarabine
	Methotrextate ≥ 250mg/m2	Mitomycin	Ofatumumab
	Oxaliplatin	Mitoxantrone	Panitumumab
	Temozolomide	Paclitaxel	Pegaspargase
	Vinorelbine (oral)	Paclitaxel-ablumin	Peginterferon
		Pemetrexed	Pertuzumab
		Pentostatin	Rituximab
		Pralatrexate	6-thioguanine (oral)
		Romidepsin	Sorafenib (oral)
		Thalidomide (oral)	Temsirolimus
		Thiotepa	Trastuzumab
		Topotecan	Valrubicin
		Sunitinib (oral)	Vinblastine
			Vincristine
			Vincristine (liposomal)
			Vinorelbine

Adapted from Grunberg SM, Warr D, Gralla RJ, et al. Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity--state of the art. Support Care Cancer. 2011 Mar;19 Suppl 1:S43-7.

Resources:

- **Accessmedicine.com** (use UCLA proxy):
  -- Williams Hematology
  -- MD Anderson Oncology
  -- Harrison's Internal Medicine

- **NCCN.org** (free account): Comprehensive management guidelines, see also free app

- **Chemotherapy regimens:**
  -- Chemoregimen.com
  -- Hemonc.org

- **Patient information (English + Spanish):**
  -- Cancer.net

- **American Society of Hematology Image Bank:**
  imagebank.hematology.org/

- **University of Utah Hematopathology slides**:
  library.med.utah.edu/WebPath/HEMEHTML/HEMEIDX.html

- **NEJM procedure videos**
  -- Lumbar puncture: www.nejm.org/doi/full/10.1056/NEJMvcm054952
  -- Paracentesis: www.nejm.org/doi/full/10.1056/NEJMvcm062234
  -- Thoracentesis: www.nejm.org/doi/full/10.1056/NEJMvcm053812
  -- Bone marrow biopsy: www.nejm.org/doi/full/10.1056/NEJMvcm0804634

- **California POLST forms in multiple languages**:
  CApolst.org/

- **Informed consent summary:**
  www.ama-assn.org//ama/pub/physician-resources/legal-topics/patient-physician-relationship-topics/informed-consent.page

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NCCN Guidelines:
NCCN Guidelines Version 1.2021 Adult Cancer Pain
NCCN Guidelines Version 1.2021 Antiemesis
NCCN Guidelines Version 2.2018 Myeloid growth factors
NCCN Guidelines Version 2.2020 Prevention and Treatment of Cancer-Related Infections
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