

Chemotherapy Drug Toxicities

Chemotherapy induced nausea:

- 3 subtypes: anticipatory, acute, delayed (48-72 hours after)
- Drugs are classified by how emetogenic they are, the highest include platinum, nitrogen mustard, DTIC (dacarbazine).
- Mainstay of treatment for acute chemotherapy induced nausea remains serotonin receptor antagonists (Zofran, Kytril) in combination with Decadron (IV and PO), Reglan or Compazine
- Delayed nausea and vomiting best addressed with similar agents plus the use of Aprepitant (Emend) which blocks the neurokinin 1 receptor responsible for delayed chemotherapy induced nausea.

INSERT REFERENCE TO TABLE ON EMETOGENIC POTENTIAL OF CHEMO AGENTS

Mucositis:

- Occurs most commonly with **5-FU**, but also with **Methotrexate**, **Adriamycin**, **Irinotecan** and oral **VP-16**
- Can sometimes be prevented by having patients chew on ice chips prior to and after infusions with bolus **5-FU**
- Symptomatic relief with Magic Mouthwash and Carafate

Diarrhea:

- Diarrhea is graded by severity from 1-4
- Grade 3 (7-9 stools/day, incontinence, or severe cramping) and Grade 4 (>10 stools/day, grossly bloody stool, or need for parenteral support) diarrhea sometimes seen with **5-FU + Leucovorin**, **Irinotecan** (in part by anticholinesterase effect) and **Eribitux**
- Usually mild to moderate cases respond to Imodium
- Monitor for signs of progressive dehydration and do not hesitate to admit for IV hydration
- Consider Flagyl because of high risk for C. diff colitis

Dermatologic manifestations:

- **Bleomycin**, **Eribitux** and **Tarceva** (90%) frequently will produce self limited skin rashes
- **Xeloda** and **Doxil** can cause palmar-plantar erythrodysesthesia (PPE) where patients present with red, hot, painful palms and soles after treatment, usually self limited, treat symptomatically
- See **Vesicant Extravasation Necrosis in Oncologic Emergencies** section

Peripheral Neuropathy:

- **Cisplatin**, **Taxanes** (acute neuromyopathy), **Oxaliplatin** (cold induced neuropathy), **Vinca** alkaloids
- Usually reversible unless had previous underlying condition i.e. diabetic neuropathy

- No preventative strategy

Bone Marrow Toxicity:

- see **Neutropenic Fevers in Oncologic Emergencies** section
- Most chemotherapy agents have some bone marrow toxicity, but with variations in which cell lines are affected and the timing of nadirs.
- Purine analogues result in a marked reduction in the CD4 count, often lasting 12 or more months and increasing the risk of OI, particularly PCP or Herpes zoster.

Cardiac toxicity:

- **Anthracyclines** can cause a cumulative dose dependent cardiomyopathy by free radical production. Damage begins at a cumulative dose of about 200mg per meter squared and above 450mg per m² risk increases steadily. **Zinecard** can be used to chelate ferric iron which is related the damage caused by anthracyclines and is recommended when doses exceed 300mg per m².
- **Herceptin** can cause a reversible cardiomyopathy, and monitoring of ejection fraction recommended while on treatment. Initiation of drug is contraindicated in those patients with a nuclear study first pass ejection fraction less than 50%. Research ongoing into the role of Brain Natriuretic Peptide (BNP) in risk stratification and follow up for patients on Herceptin.

Pulmonary Toxicity:

- **Bleomycin** causes a dose-dependent pulmonary fibrosis when total doses exceed 300 units. Patients need baseline pulmonary function studies and should be monitored for increasing cough or Dyspnea.
- **BCNU, Mitomycin C and Methotrexate** can also cause interstitial pulmonary disease but these are less common.

Renal Toxicity:

- **Cisplatin** causes both acute and chronic renal failure which can be prevented with adequate hydration. In addition one needs to monitor for severe magnesium wasting related to proximal tubule injury
- **Mitomycin C** can cause Hemolytic Uremic Syndrome (HUS) including renal failure, anemia and thrombocytopenia.

Hepatic Toxicity:

- **Gemcitabine** and **Xeloda** can cause reversible transaminitis.
- **Tamoxifen** can cause hepatic steatosis with occasional evolution to cirrhosis.

Genitourinary Toxicity:

- **Ifosfamide** can lead to hemorrhagic cystitis if **Mesna** is not given concurrently.

Common Combination Chemo Regimens:

- ABVD (Hodgkin) Doxorubicin(**Adriamycin**), **Bleomycin**, **Vinblastine**, **Dacarbazine**
- AC → T (Breast) Doxorubicin(**Adriamycin**), **Cyclophosphamide** followed by Paclitaxel (**Taxol**)
- BEACOPP (Hodgkin) **Bleomycin**, **Etoposide**, Doxorubicin(**Adriamycin**), **Cyclophosphamide**, Vincristine (**Oncovin**), **Procarbazine**, **Prednisone**
- CAF (Breast) **Cyclophosphamide**, Doxorubicin (**Adriamycin**), 5-**Fluorouracil**
- CHOP (NHL) **Cyclophosphamide**, **Hydroxydaunomycin** (doxorubicin), Vincristine (**Oncovin**), **Prednisone**
- CVP (NHL) **Cyclophosphamide**, **Vincristine**, **Prednisone**
- EPOCH (NHL) **Etoposide**, **Prednisone**, Vincristine (**Oncovin**), **Cyclophosphamide**, Doxorubicin
- ESHAP (NHL salvage) **Etoposide**, **Solumedrol**, **High dose** cytarabine(**Ara-C**), cis**Platin**
- FOLFIRI (CRC) 5-**Fluorouracil** + **Leucovorin**, **Irinotecan**
- FOLFOX (CRC) 5-**Fluorouracil** + **Leucovorin**, **Oxaliplatin**
- ICE (NHL salvage) **Ifosfamide**, **Carboplatin**, **Etoposide**
- MOPP (Hodgkin) **Mechlorethamine**, Vincristine (**O?**), **Procarbazine**, **Prednisone**
- hyper-CVAD-AM (ALL) high dose **Cyclophosphamide**, **Vincristine**, Doxorubicin(**Adriamycin**), **Dexamethasone** with high dose cytarabine (**Ara-C**) and **Methotrexate**