MSHP Annual Meeting 2016

Supportive Care of the Cancer Patient

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Common Toxicities of Cancer Treatment

- **Nausea and Vomiting**
- **Myelosuppression**
- **Mucositis/Diarrhea**
- **Tumor Lysis Syndrome**
- Alopecia
- Fatigue
- Pain

Nausea and Vomiting (N & V)

- Vomiting=Emesis
- Drugs used to **prevent**/treat nausea and vomiting=anti-emetics
- N & V can be associated with a variety of clinical conditions and drugs. This discussion will focus on Chemotherapy Induced Nausea and Vomiting (CINV)
- Approximately 70-80% of all cancer patients receiving chemotherapy experience nausea and vomiting. Patients often experience more nausea than vomiting.

Pathophysiology of N & V

- Vomiting is triggered by afferent impulses to the vomiting center, a nucleus of cells in the medulla.
- Vomiting center receives these impulses from multiple sites including the chemoreceptor trigger zone (CTZ), cerebral cortex, vestibular apparatus, pharynx and GI tract.
- Neurotransmitter receptors located in the vomiting center, CTZ, and GI Tract include dopaminergic, opiate, histaminic, cholinergic, neurokinin, serotinergic, and benzodiazepine receptors.
- Chemotherapy triggers the process of emesis through stimulation of one or more of these receptors.

Therapy Related Risk Factors for CINV

- Intrinsic emetogenicity of antineoplastic agent.
- Antiemetic regimens for multi-agent chemotherapy treatments should be based on the drug with the **highest** emetogenic risk.
- Dose, route, and administration rate of antineoplastic agent
- Multiple chemotherapy cycles
- Concomitant radiation

Emetogenic Potential of IV Antineoplastic Agents

Emetogenic Potential	Example Antineoplastic Agents
High emetic risk: >90% frequency of emesis	Cisplatin Cyclophosphamide >1500mg/m^2 Dacarbazine
Moderate emetic risk: 30-90% frequency of emesis	Azacitidine Bendamustine Carboplatin
Low emetic risk: 10-30% frequency of emesis	Docetaxel 5-Fluorouracil Paclitaxel
Minimal emetic risk: <10% frequency of emesis	Bleomycin Fludarabine Vincristine

NCCN Guidelines Version 2.2015 Antiemesis NCCN=

Patient Related Risk Factors for CINV

- Poor control with prior therapy
- Age <50
- Alcohol use history (<10 drinks/week or 1.5 oz. EtOH/day)
- Female
- History of motion sickness or morning sickness

Classifications of CINV

- Acute:
  - Occurs during the first 24 hour period following the administration of chemotherapy
- Delayed:
  - Occurs more than 24 hours after chemotherapy administration
  - Cisplatin one of the most "notorious" agents associated with delayed CINV
- Anticipatory:
  - Classically-conditioned response; a previously neutral stimulus (e.g. smells, sights, or sounds of the chemotherapy environment) elicits a conditioned response. Occurs prior to, or at other times without chemo agent being administered.

Treatment of CINV

- ***Prevention*** of nausea/vomiting is the goal. The risk of nausea/vomiting for persons receiving chemotherapy of high and moderate emetic risk lasts for at least 3 days after the last dose of chemotherapy for high, and 2 days for moderate. Patients need to be protected throughout the **full period of risk.**

NCCN Guidelines Version 2.2015 Antiemesis

5-HT3 Receptor Antagonists

- Serotonin is released by enterochromaffin cells in the GI tract after exposure to chemotherapy. These drugs block presynaptic serotonin receptors on sensory vagal fibers in the gut wall, thus blocking acute phase CINV.
- Also block serotonin stimulation centrally at the CTZ.
- All agents in this class are **equally effective** at equivalent doses for **acute** CINV
- Palonosetron has activity in preventing **delayed** CINV
- None of these agents are FDA approved for **treatment** of CINV once it occurs.

5-HT3 Receptor Antagonists

- **Ondansetron (Zofran®, Zuplenz®)**
  - **IV, oral tablet, oral solution, oral dispersible tablet, oral film (8-24mg p.o./IV)**
- **Granisetron (Kytril®, Sancuso®)**
  - **IV, oral tablet, oral solution, transdermal patch (1-2mg p.o./IV, 3.1mg patch)**
- **Dolasetron (Anzemet®)**
  - **IV, oral tablet (100mg p.o. for CINV)**
- **Palonosetron (Aloxi™)**
  - **IV only (0.25mg IV)**

5-HT3 Receptor Antagonists

- **Side effects**
  - **Headache**
  - **Constipation**
  - **Dose dependent QT prolongation**

Neurokinin-1 Receptor (Substance P) Antagonists

- Substance P is a peptide neurotransmitter, with NK1 (neurokinin 1) as its preferred receptor.
- In the GI tract, Substance P is considered a neuromuscular excitatory transmitter in intestinal motor activity resulting in emesis. Acute N & V is mediated by both serotonin and Substance P, while delayed N & V is primarily mediated by Substance P.
- Substance P binds to neurokinin (NK-1) receptors to elicit N & V.

Neurokinin-1 Receptor Antagonists

- Prevent delayed CINV by inhibiting the neurokinin 1 receptor.
- These agents augment the antiemetic activity of 5HT3 antagonists and corticosteroids to inhibit acute and delayed CINV.
- Recommended for use as part of a three drug cocktail for patients receiving chemotherapy of high emetic risk.
- Also recommended as optional therapy for patients receiving chemotherapy of moderate emetic risk.

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Neurokinin-1 Receptor Antagonists

- **Aprepitant/Fosaprepitant (Emend®)**
- Dosage: 125mg p.o. or 115mg IV (as fosaprepitant) 1 hour prior to chemotherapy on Day 1, then 80mg p.o. daily in the morning on Days 2 and 3.
- Fosaprepitant may also be given as a single 150mg IV dose.
- **Rolapitant (Varubi®)**
- Dosage: 180mg p.o. prior to chemotherapy on Day 1.
- **Netupitant 300mg/palonosetron 0.5mg (Akynzeo®)**
- Dosage: one capsule p.o. prior to chemotherapy on Day 1

Neurokinin-1 Receptor Antagonists

- Have potential for numerous drug interactions. Substrates, inducers and inhibitors of CYP3A4 and inducers of CYP2C9.
  - When dexamethasone is given with aprepitant/fosaprepitant or netupitant, the max dose is 12mg. (AUC of dexamethasone is increased 50% by these drugs.)
- Side Effects: asthenia, fatigue, diarrhea, hiccups, and dehydration.

Corticosteroids

- Antiemetic mechanism of action is not fully understood
- Steroids are sometimes used as single agents against low emetogenic chemotherapy
- Potentiates the antiemetic properties of 5-HT3 antagonists
- Can be administered orally, intramuscularly, or intravenously
- Equally efficacious at equivalent doses
- Most clinical trials use dexamethasone, thus most often used steroid for antiemesis

Olanzapine Containing Regimens

- Olanzapine 10mg p.o. once Day 1, 2,3,4
  - Antagonist of serotonin, dopamine, histamine and muscarinic receptors
- Palonosetron 0.25mg IV once Day 1
- Dexamethasone 20mg IV once Day 1

NCCN Guidelines Antiemesis

- High Emetic Risk Intravenous Chemotherapy-Acute and Delayed Emesis **Prevention** Day 1 prior to chemo:
  - A. Three drug cocktail:
    - NK-1 antagonist
    - 5HT3 antagonist
    - Steroid
  - B. Netupitant containing regimen
    - Netupitant/Palonosetron
    - Dexamethasone 12mg
  - C. Olanzapine containing regimen
    - Olanzapine 10mg p.o.
    - Palonosetron 0.25mg IV
    - Dexamethasone 20mg IV

NCCN Guidelines Version 2.2015 Antiemesis

NCCN Guidelines Antiemesis

- Moderate Emetic Risk Intravenous Chemotherapy-Acute and Delayed Emesis **Prevention** Day 1 prior to chemo:
  - A. Two or Three drug cocktail:
    - 5HT3 antagonist (palonosetron preferred)
    - Steroid
    - With or Without NK-1 antagonist
  - B. Netupitant containing regimen
    - Netupitant/Palonosetron
    - Dexamethasone 12mg
  - C. Olanzapine containing regimen
    - Olanzapine 10mg p.o.
    - Palonosetron 0.25mg IV
    - Dexamethasone 20mg IV

NCCN Guidelines Version 2.2015 Antiemesis

NCCN Guidelines Antiemesis

- Minimal Emetic Risk Intravenous Chemotherapy-Emesis **Prevention:**
  - Dexamethasone 12mg p.o./IV daily
  - Metoclopramide 10-40mg p.o./IV
  - Prochlorperazine 10mg p.o./IV
  - 5HT3 antagonists
- Low Emetic Risk Intravenous Chemotherapy: no routine prophylaxis used

NCCN Guidelines Version 2.2015 Antiemesis

Antiemetic Agents for *Breakthrough* CINV

- The general principle of breakthrough treatment is to add one agent from a different class to the current regimen.
- Dopamine 2 Antagonists
  - Metoclopramide
  - Phenothiazines
  - Butyrophenones
- Cannabinoids
- Benzodiazepines
- Other agents:
  - Olanzapine
  - Transdermal scopolamine
  - 5HT3 antagonists
  - Steroids

NCCN Guidelines Version 2.2015 Antiemesis

Benzodiazepines

- Treatment of choice for anticipatory CINV
- May be used for prevention and treatment of anxiety and anticipatory nausea and vomiting
- Act on higher CNS structures, the brainstem, and spinal cord
- Produce anxiolytic, sedative, and anterograde amnesic effects
- Decrease the severity of EPS, especially akathisia, associated with dopaminergic receptor antagonist antiemetics.
  - Lorazepam is the primary benzodiazepine used for CINV

Self Assessment Question

CB is a 40 y/o F with Stage III breast cancer. She is being treated with carboplatin/paclitaxel q 3 weeks. Her prophylactic anti-emetic regimen is:

Fosaprepitant 150mg IV, palonosetron 0.25mg IV, and dexamethasone 12mg IV on Day 1 prior to chemo.

Despite receiving this regimen, CB calls the clinic 5 days later with complaints of significant N & V.

Which of the following is most appropriate to add to her antiemetic regimen at this time?

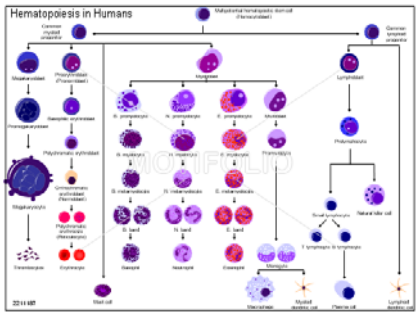
Self Assessment Question

- A. Aprepitant 80mg p.o. x 1
- B. Prochlorperazine 10mg p.o. q4-6 hrs prn
- C. Sancuso patch 3.1mg applied daily
- D. Akynzeo® 1 capsule p.o. daily

Self Assessment Question

- A. Aprepitant 80mg p.o. x 1
- B. **Prochlorperazine 10mg p.o. q4-6 hrs prn**
- C. Sancuso patch 3.1mg applied daily
- D. Akynzeo® 1 capsule p.o. daily

Hematopoesis



http://www.motifolio.com/2211187.html

Myelosuppression

- Chemotherapy-induced bone marrow suppression is the most common dose-limiting toxicity of traditional chemotherapeutic agents and a common toxicity of targeted therapies for hematologic malignancies
- The nadir is the lowest value the blood counts reach following a cycle of chemotherapy
- Occurs 10 - 14 days after chemotherapy administration and counts usually recover by 3 to 4 weeks after chemotherapy

Myelosuppression

- White blood cells (WBC): Normal range of 4.8 - 10.8 $x10^9$ /L. Half-life of 5.4 days
  - Absolute Neutrophil Count (ANC) = WBC x % granulocytes (Segs + Bands)
  - Decreased WBC = neutropenia (< 0.5 x 10^9 /L), leukopenia, or granulocytopenia
  - Neutropenia puts patients at risk for life-threatening infections
- Megakaryocytes (platelets). Normal range of 140,000 - 440,000 cells/mm^3. Half-life of 5 - 10 days
  - Decreased platelets = thrombocytopenia (< 10,000/mm^3)
  - Risk of life-threatening bleeding

Myelosuppression

- Red blood cells (RBC) Normal range of 4.6 - 6.2 $x10^6$ cells/mm^3. Half-life of 120 days.
  - Decreased RBC = anemia
  - Risks are hypoxia and fatigue

Granulocyte Colony Stimulating Factors (G-CSF)

- Short Acting: Dose is 5mcg/kg sq daily
  - Filgrastim (Neupogen®)
  - Tbo-filgrastim (Granix®)
  - Filgrastim-Sndz (Zarxio®)
- Long acting: Dose is 6mg sq q14 days
  - Pegfilgrastim (Neulasta®)
  - 1 dose of pegfilgrastim is equivalent to 11 doses of filgrastim.)

Use of White Cell Growth Factors

- Indicated to decrease the incidence of infection in patients receiving myelosuppressive chemotherapy associated with a significant incidence of neutropenic fever. (aka febrile neutropenia or FN)
- FN=ANC <0.5 x 10^9/L (or 500 cells/mm^3) and an oral temp of >38.5 degrees Celsius
- G-CSF benefits patients receiving chemo by decreasing the incidence of FN, length of hospitalization, and duration of antibiotic therapy.
- Must be administered 24 hours after chemotherapy.
- Should not be given > 72 hours after chemotherapy.

Mucenski, JW et.al. JMCP March/April 2003;vol 9. no.2

Use of White Cell Growth Factors

- Primary prophylaxis of FN:
  - In all patients receiving chemotherapy regimens administered at full dose expected to cause ≥ 20% incidence of FN
- Secondary prophylaxis of FN:
  - In patients who experienced neutropenic complication after prior chemotherapy given without CSF in which a dose reduction would compromise outcome or survival

ASCO guidelines Smith TJ et.al. J Clin Oncol. 2006;24:3187-205 ASCO=American Society of Clinical Oncology

Chemotherapy Induced Anemia

- Anemia is the most common hematologic complication of cancer chemotherapy.
- Red blood cell growth factors (Erythropoietic agents, Erythropoiesis stimulating agents, ESAs) correct chemotherapy induced anemias.
- Chemotherapy induced anemia is usually not life threatening as neutropenia can be.

Red Blood Cell Growth Factors

- There are two erythropoietic agents available in the U.S., produced through recombinant DNA technology. These two agents are considered to be equivalent in safety and efficacy when used at FDA approved doses.
  - Epoetin Alfa (Procrit®, Epogen®)
    - Dose is 20,000-40,000 units sq weekly
  - Darbepoetin Alfa (Aranesp®)
    - Dose is 100-500mcg sq q 2 or 3 weeks
- May be given same day as chemotherapy

Red Blood Cell Growth Factors

- **US Boxed Warnings:**
  - **ESAs increased the risk of serious cardiovascular events, myocardial infarction, stroke, venous thromboembolism, vascular access thrombosis, and mortality in clinical studies when administered to target Hb levels >11g/dL.**
  - **A shortened overall survival and/or increased risk of tumor progression or recurrence has been reported in studies with breast, cervical, head and neck, lymphoid and NSCLC patients.**

Aranesp (package insert) Thousand Oaks, CA: Amgen, 2001-2015

Red Blood Cell Growth Factors

- **US Boxed Warnings:**
  - **To decrease these risks, and risk of cardio and thrombovascular events use the lowest dose needed to avoid red blood cell transfusions. Use ESAs in cancer patients only for the treatment of anemia related to concurrent myelosuppressive chemotherapy; discontinue ESA following completion of the chemotherapy course. ESAs are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is curative.**

Aranesp (package insert) Thousand Oaks, CA: Amgen, 2001-2015

Red Blood Cell Growth Factors

- FDA labeling limits the indication for ESA use to patients receiving chemotherapy for palliative intent, weighing harms vs. benefits
- ASCO guidelines on ESAs:
  - ESA use is an option if anemia is chemo induced, and Hb < 10gm/dl with intent to decrease RBC transfusions
  - Increased rates of thromboembolism have been established with ESA use in cancer patients
- Class side effects:
  - Hypertension, fatigue, headache, fever, edema, N&V, arthralgias and diarrhea

Rizzo JD et.al. J Clin Oncol 2010;28:4996-5010

Platelet growth factors

- **Romiplostim (Nplate®)**
  - Currently only FDA approved for use in ITP
  - Given as a weekly sq injection
- **Eltrombopag (Promacta®)**
  - Currently only FDA approved for use in ITP, HCV,AA)
  - Given as a daily oral dosage form
- At the present time there is no FDA approved growth factor for chemo induced thrombocytopenia. We rely on platelet transfusions to correct this, and prevent life-threatening bleeding.

ITP=Immune Thrombocytopenic Purpura, HCV=Hepatitis C Virus, AA=Aplastic Anemia

Self Assessment Question

AC is a 69 year-old male undergoing his third cycle of carboplatin plus paclitaxel for Stage IV non-small cell lung cancer. At diagnosis, his Hb was 13 g/dl; however today his Hb is 8 g/dl. The patient has a history of chronic obstructive lung disease and today he complains of difficulty breathing and significant fatigue, which is interfering with his activities of daily living.

True or False, it would be appropriate per ASCO and FDA guidelines to start this patient on darbepoietin on Day 1 of his third cycle of chemo?

Self Assessment Question

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Self Assessment Question

- Since AC is receiving myelosuppressive chemotherapy,
- True or False, he can also receive pegfilgrastim on Day 1 of chemotherapy.

Self Assessment Question

- Since AC is receiving myelosuppressive chemotherapy,
- True or **False**, he can also receive pegfilgrastim on Day 1 of chemotherapy.

Mucositis/Diarrhea

- Mucositis is a morbid side effect of many anticancer treatments. The clinical sequelae of mucositis increase the morbidity and mortality associated with cytotoxic therapy and interfere with patient functioning and quality of life.
- The gastrointestinal (GI) mucosa is composed of epithelial cells with a high mitotic index, and a rapid turnover rate, making it a frequent site of chemotherapy and radiation therapy induced toxicity. The resulting inflammation, or mucositis, can lead to extremely painful ulcerations, local infections, and the inability to eat, drink, or swallow.
- Mucositis is divided into two classifications: oral and GI.

Mucositis Presentation

- Mucositis is inflammation of the mucosal surfaces throughout the body.
- It typically involves redness and ulcerative sores in the soft tissues of the mucosa.
- Oral mucositis manifests as erythema, inflammation, ulceration, and hemorrhage in the mouth and throat.

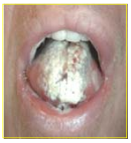


Image from: Spielberger, Ricardo; Kepivance™: A Breakthrough for Oral Mucositis Associated with Myeloablative Hematopoietic Stem Cell Transplantation; City of Hope National Medical Center, Department of Hematology and Bone Marrow Transplantation

Introduction

- The time course of development and resolution of mucositis usually ***follows that of neutropenia***. The most severe manifestation of mucositis is ulceration of the mucosa. This may be exacerbated by the colonization of the ulceration by bacterial flora which may be a source of systemic infection.
- Doses of chemotherapy may have to be reduced or delayed because of mucositis.
- There is no widely accepted treatment to prevent or reduce the severity of chemotherapy or radiotherapy induced mucositis.

Mucositis Incidence & Outcomes

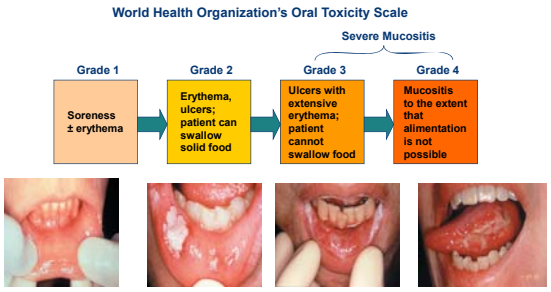
- Standard-dose chemotherapy:
- Severe mucositis may occur in 90% of patients treated for oropharyngeal cancer
- Approximately 35% of patients who develop grade 3 or 4 mucositis have a subsequent cycle of chemotherapy delayed
- Approximately 60% of patients have their doses of chemotherapy-reduced secondary to mucositis and 30% have their chemotherapy regimen discontinued
- 70% of patients who develop grade 3 or 4 mucositis require enteral or parenteral nutrition
- 60% of patients with mucositis develop fever and 62% require hospitalization
- Solid tumor patients receiving myelosuppressive chemotherapy who develop mucositis have an infection in 73% of their cycles versus 36% in patients without mucositis

Sonis ST, Elting LS, Keefe D et al. Perspectives on cancer therapy-induced mucosal injury. *Cancer.* 2004; 100(9): 1995-2025
Sonis ST. Oral mucositis. *Anticancer Drugs*. 2011; 22(7): 607-12.
Clarkson JE, Worthington HV, Furness S et al. Interventions for treating oral mucositis for patients with cancer receiving treatment. *Cochrane Database of Systematic Reviews*. 2010; (10).

The World Health Organization (WHO) grades mucositis based on degree of severity as follows:

- Grade 0= None
- Grade 1=Soreness ± erythema
- Grade 2=Erythema, ulcers, and patient can swallow solid food
- Grade 3=Ulcers with extensive erythema and patient cannot swallow solid food
- Grade 4=Mucositis to the extent that alimentation is not possible

WHO's Oral Toxicity Scale



Etiology

- Radiation therapy
- Chemotherapy
  - Methotrexate
  - 5-fluorouracil
  - Irinotecan
  - Anthracyclines
  - Etoposide
  - Cyclophosphamide
  - Melphalan

Pathophysiology

- Initially thought to only involve epithelium
- Involves various components of the GI mucosa
  - Epithelial
  - Endothelial
  - Microvascular

Mucositis Management – Oral Hygiene

- Toothbrush – soft nylon brush
- Flossing
- Foam toothbrushes
- Fluoride
- Most studies examining the use of oral care protocols for the prevention of oral mucositis reported a beneficial effect.

Cancer. 2014 May 15;120(10):1453-61.

Mucositis Management

- Bland rinses
  - 0.9% saline solution
  - Sodium bicarbonate/baking soda solution
- Topical anesthetics
  - Lidocaine: viscous, ointment, sprays
  - Benzocaine: sprays, gels
  - Gelclair ®
  - Diphenhydramine solution
- Mucosal coating agents
  - Mylanta
- Analgesics
  - Benzydamine hydrochloride topical rinse
  - **Opioid Drugs**

Mouthwash Formulations

- Magic Mouthwash
- Hawaiian punch
- Stomatitis cocktail
- Magic swizzle

- Most common formulation
  - Viscous lidocaine
  - Diphenhydramine
  - Maalox

Potential ingredients

- Diphenhydramine
- Glucocorticoids
- Lidocaine
- Maalox
- Nystatin
- Sucralfate
- Tetracycline
- Erythromycin

MASCC / ISOO Guidelines

- Oral Mucositis: Recommendations in Favor of:
  - 30 min. oral cryotherapy in patients receiving bolus 5-Fluorouracil
  - Patient Controlled Analgesia with morphine used to treat mucositis pain in patients undergoing HSCT
  - Benzydamine mouthwash in patients with head and neck cancer receiving radiation
  - Palifermin for patients receiving auto HSCT.

Abbreviations: HSCT, hematopoietic stem cell transplantation; MASCC/ISOO, Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology.
Cancer. 2014 May 15;120(10):1453-61.

MASCC / ISOO Guidelines

- GI Mucositis: Recommendations in Favor of:
  - IV Amifostine at a dose of ≥ 340mg/m^2 to prevent radiation induced proctitis.
  - Octreotide at a dose of ≥ 100mcg sq twice daily to treat diarrhea induced by standard or high dose chemo associated with HSCT, if loperamide is ineffective.

Abbreviations: HSCT, hematopoietic stem cell transplantation; MASCC/ISOO, Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology.
Cancer. 2014 May 15;120(10):1453-61.

Palifermin (Kepivance™)

- Recombinant keratinocyte growth factor
- MOA: Keratinocyte growth factor (KGF) is an endogenous protein in the fibroblast growth factor family that binds to the KGF receptor
  - Results in proliferation , differentiation, and migration of epithelial cells
- Indication: Indicated to decrease the incidence and duration of severe oral mucositis in patients with hematologic malignancies receiving myelotoxic therapy requiring hematopoietic stem cell support

Mucositis Summary

- Complex pathophysiology
- Mucosal damage can occur at any point along the entire length of the GI tract
- Therapeutic options
  - Prevention
  - Treatment is largely supportive
  - Limited data to support use of many agents

Mucositis Summary

- Cryotherapy and good oral hygiene are the mainstay of our current preventative measures
- Opioids and enteral/total parenteral nutrition are the mainstay of our current treatment regimens

Tumor Lysis Syndrome (TLS)

- **Tumor Lysis Syndrome (TLS)** is defined as a group of metabolic disorders that usually occurs after the treatment of a neoplastic disorder, due to the destruction of cancer cells. It manifests as:
- Hyperphosphatemia
- Hypocalcemia
- Hyperuricemia
- Hyperkalemia
- Acute renal failure
  - Acute uric acid nephropathy
  - Acute hyperphosphatemia (leading to Ca++/PO4- deposits intrarenally)

Tumor Lysis Syndrome (TLS)

Background of Tumor Lysis Syndrome:

- Life-threatening oncologic emergency resulting from abrupt release of intracellular contents overwhelming the body's ability to metabolize and excrete adequately
- May be spontaneously induced by tumor prior to anti-cancer therapy or as result of anti-cancer therapy
- Observed 12-72 hours after starting chemotherapy and may continue up to 3 days after start of chemotherapy
- Ideally, TLS prevention would begin 24-48 hours before starting anti-cancer therapy

Treatment of TLS

- IV hydration is the most important intervention in treatment and prophylaxis of TLS because it maintains renal blood flow and promotes urinary excretion of uric acid and phosphate.
- Begin 24-48 hours prior to induction chemotherapy
- Normal saline-containing intravenous fluids (IVF) serve as the backbone of both prevention and treatment
- IVF must be given at aggressive rate; at least 2.5-3 liters/m^2/24 hours in order to maintain urine output of at least 100 mL/hr

Drug Therapy for TLS

- **Rasburicase (Elitek™)**
  - Also known as urate oxidase.
  - Metabolizes uric acid to allantoin
  - FDA indication is: initial management of uric acid levels in pediatric and adult patients with leukemia, lymphoma, and solid tumor malignancies receiving chemotherapy expected to result in tumor lysis and elevation of plasma uric acid.
  - Dose: 0.2mg/kg IV once daily for 1-5 days.
    - A flat dose of 6mg may also be used, or 0.05mg/kg
    - Usually only one dose is given, but may need to be repeated based on uric acid levels

Drug Therapy for TLS

- **Allopurinol (Zyloprim®, Aloprim®)**
  - Inhibits xanthine oxidase
- Backbone of prevention and useful adjunct for treatment of TLS
- Allopurinol 300-900 (p.o. or IV) mg per day is recommended for adults, with higher daily doses given to those with high-risk disease and/or high uric acid levels
- Allopurinol dose SHOULD NOT be adjusted based upon renal function for indication of treatment of TLS
- Usually administered as q12h or q8h dosing

Self Assessment Question

DH is diagnosed with non-Hodgkin Lymphoma. On day 2 of chemotherapy, his labs were notable for WBC 42 x 10^9/L, BUN 36 mg/dL, serum creatinine 2.2mg/dL, potassium 5.7 mEq/L, phosphate 4.9 mg/dL, LDH 2810 IU/L and uric acid 8.6 mg/dL.

Along with allopurinol, which of the following is best to order first?

Self Assessment Question

A. 0.9% NS 1,000 mL x 1 infused wide open
B. Rasburicase 0.2 mg/kg IV x 1 dose
C. Sodium polystyrene sulfonate
D. Consult for emergent renal dialysis

Self Assessment Question

A. 0.9% NS 1,000 mL x 1 infused wide open
B. Rasburicase 0.2 mg/kg IV x 1 dose
C. Sodium polystyrene sulfonate
D. Consult for emergent renal dialysis

Key Takeaways

- Key Takeaway #1
  - CINV can be minimized best by prevention, rather than treatment, using the appropriate anti-emetic cocktail.
- Key Takeaway #2
  - The use of red cell and white cell growth factors must be timed appropriately, and only used according to current guidelines.
- Key Takeaway #3
  - TLS is best prevented and treated with aggressive IV hydration. Dosing of allopurinol for TLS is specific to that indication.