Intravenous Drugs

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Basics

- Sterility
- Final concentration
- Stability
- Administration
- Compatibility

Sterility

- Sterile IV admixture procedure in an isolated room
  - IV room
  - Sterile room
  - Clean room
- Inpatient Rx
- Home infusion Rx
- Satellite Rx in hospital

Sterile admixture

Sterility

- Clean room instructions for both pharmacists and technicians
- Laminar air flow hoods
  - Positive pressure room
- Horizontal for all IVs except for antineoplastic agents
  - Chemo-hood
  - Vertical hood
  - Negative pressure room

Total Parenteral Nutrition (TPN)

Candidates for receiving TPN

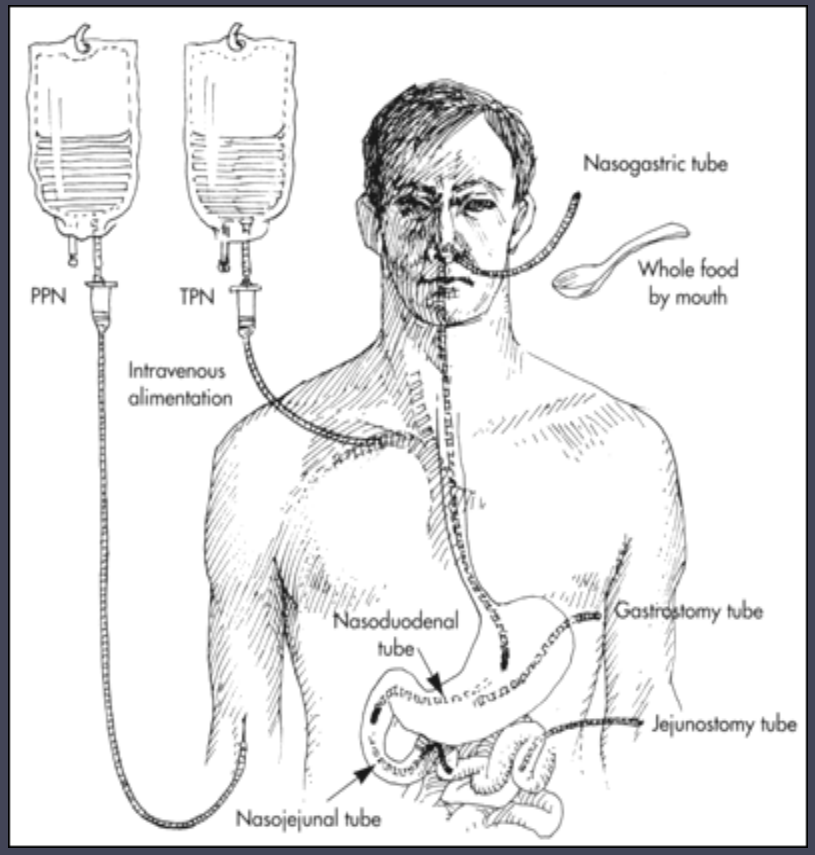
- Patient's with obstruction in a part of their GI tract
- Surgery, trauma
- Chemotherapy, radiation therapy
- GI cancers
- Inflammatory bowel diseases
- Oral and enteral feeding intolerance
- Any surgery or procedure requiring patient to be NPO

Types of TPN

- Central parenteral nutrition
  - Patient must have central line (through subclavian vein to SVC) or **PICC line** (peripherally inserted central catheterization)
  - High osmolarity (almost no limitation) due to high speed blood flow (2500 ml/min)
  - May be concentrated if volume limitation needed
  - Good for patients who need TPN for more than 7 days

Types of TPN

- Peripheral parenteral nutrition
  - Osmolarity limitations (< 900 mOsmol/litter)
  - Risk of phlebitis (due to lower blood flow rate: 25-50 ml/min)
  - Must be changed every 2-3 days to minimize inflammatory process and damages
  - Ok for TPNs of less than 7-14 days
  - Large volume needed to decrease osmolarity
  - Lower concentration of amino acids and dextrose must be prepared


PPN
TPN
Intravenous alimentation
Nasogastric tube
Whole food by mouth
Nasoduodenal tube
Gastrostomy tube
Jejunostomy tube
Nasojejunal tube

Types of TPN

- 3 in 1 (Total Nutritional Admixture) (TNA)
  - All macronutrients in one bag
  - Amino acids, dextrose, intralipids
  - Risk of missing visualization of possible precipitations (calcium phosphate)
  - Risk of fungal contaminations due to longer infusion time
  - Must use in-line filter 1.2 micron

Types of TPN

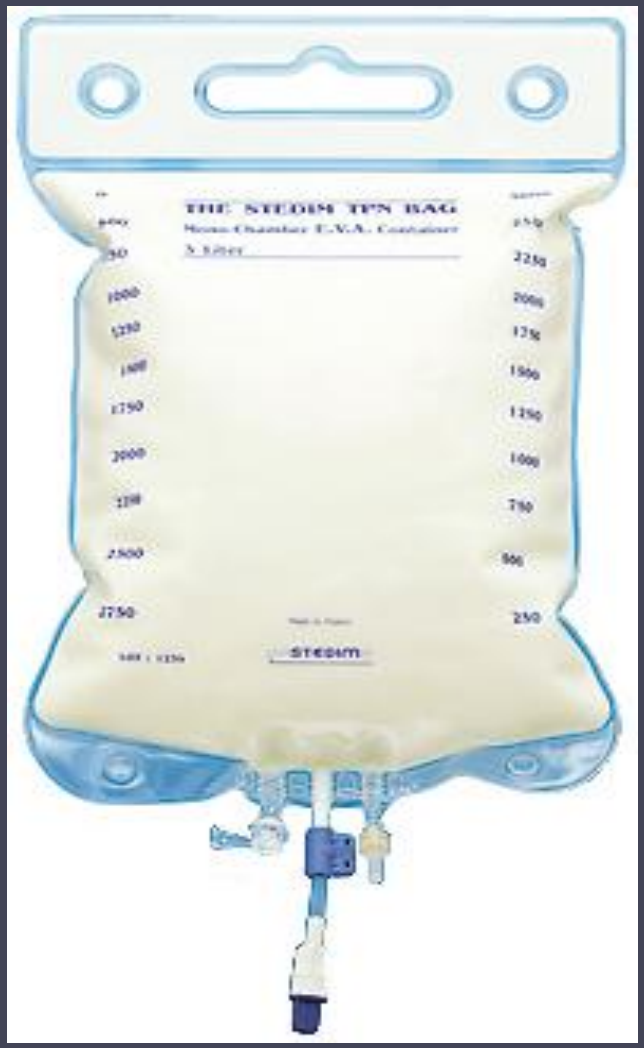
- 2 in 1
- Amino acids and dextrose in 1 bag
- Intralipid emulsion in separate bag
- No need to in-line filter for lipid emulsion
- Intralipid emulsion may be infused faster to minimize fungal growth
- Must use in-line 0.22 micron filter for AA and dextrose bag

Sterile admixture

- From 10 to over 40 injectable items to be mixed in a bag
- Prevention of CV or peripheral line infection and bacteremia
- Physical compatibility considerations
- Consistency
- Under pharmacist direct supervision

Sterile admixture

- Large volumes
  - –Amino acids
  - –Dextrose
  - –Sterile water
  - –Intralipids



Sterile admixture

- Electrolytes
  - Sodium chloride
  - Sodium phosphate
  - Sodium acetate
  - Potassium chloride
  - Potassium phosphate
  - Potassium acetate
  - Calcium gluconate
  - Magnesium sulfate

Sterile admixture

- Vitamins
  - –May be in one or more vials
- Trace elements
- Insulin

Administration

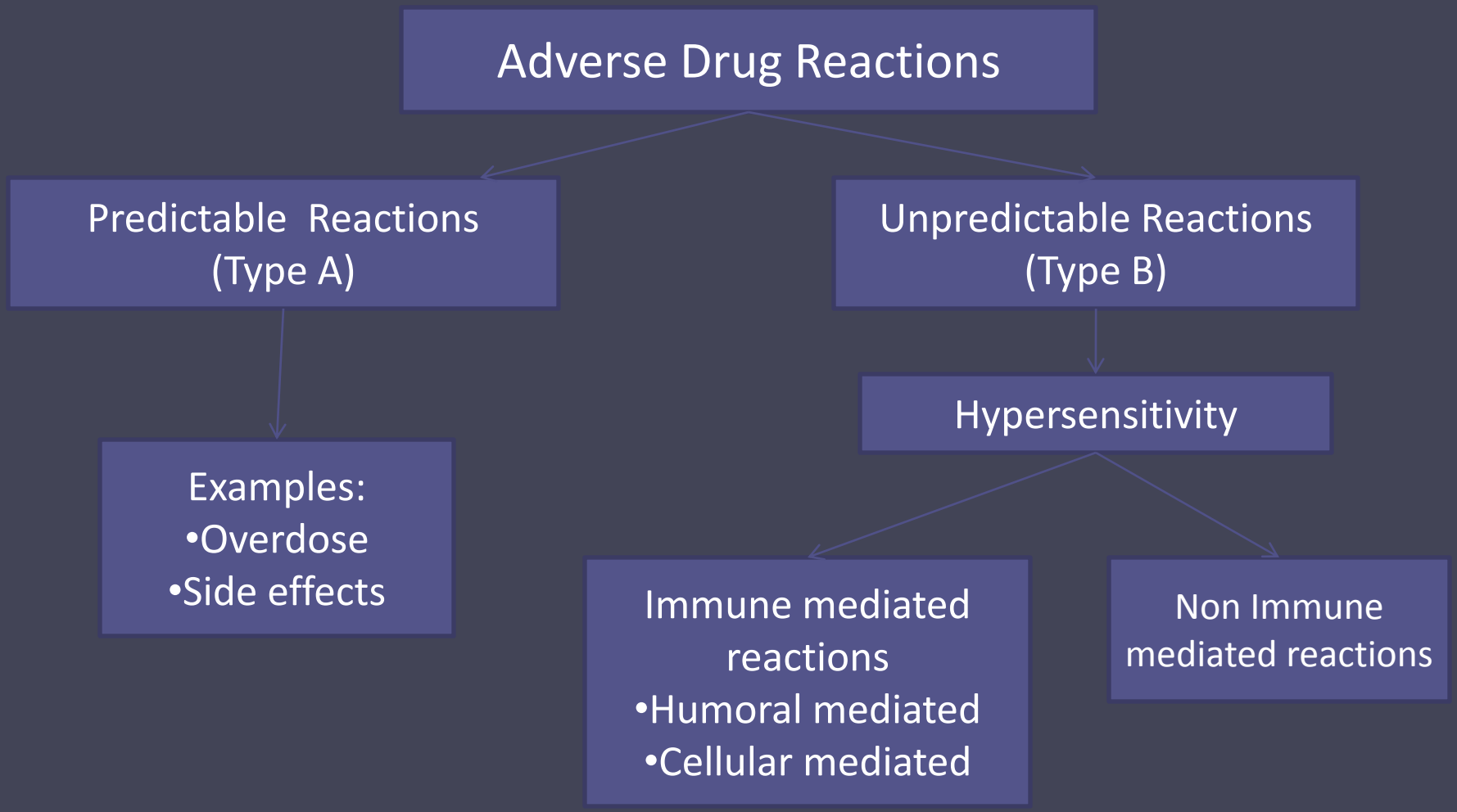
- Nurses to be trained
- Infusion time
- Y-site IV drug compatibilities to be checked with pharmacists
- Storage
- Intralipid infusion time
- Hanging time
- Following daily orders

Monitoring

- Daily lab values to be checked
  - Na, K, Cl, acetate, serum creatinine, FBS
- Twice weekly labs:
  - Mg, Phos, Ca, CBC
- Weekly labs:
  - Albumin, LFTs, TG, INR

Glucose to be checked every six hours and SSI

Classification of Adverse Drug Reactions



Drug Allergy

- Criteria for a drug reaction to be considered immunologically mediated
  - reaction occurs in small number of patients receiving the drug
  - Reaction does not resemble drug's pharmacologic effects
  - Reaction occurs even with small amount of drug
  - Reaction occurs by drug with similar structures
  - Presence of eosinophilia
  - Reaction resolves after discontinuation of the drug

Dipiro JT. Pharmacotherapy, A pathophysiologic approach, 5th edition. 2002;Chapter 89.1583-95

Hypersensitivity Reactions

Penicillin Hypersensitivity

- Adverse reactions to penicillin occurs in approximately 1% - 10% of treatment courses
- Fatal penicillin induced anaphylaxis occurs at the rate of 0.002% among general population
- Between 10%-20% of general population report PCN allergy, while about 90% of those reported cases are not truly hypersensitive to PCN
- Patients between the ages of 20-49 are at more risk of anaphylactic reactions
- Up to 80% of patients with a history of IgE mediated reactions to penicillin may have negative skin test in 10 years

Dipirro J T. Pharmacotherapy,A pathophysiologic approach; Allergic Drug Reactions. 5th edition.2002;chapter89: 1585- 96
Arroliga M E. Penicilin Allergy. Cleavland Clinic Publications;March 2005
Solensky R. Hypersensitivity reactions to beta-lactam antibiotics. Clin Rewiews in Allergy & Immune;2003(24):201-19

Cross-reactivities

- Less than 10% cross-reactivity between PCNs and Cephalosporins in general population
  - Less than 2% of general population without penicillin allergy are allergic to cephalosporins
  - Lower risk of cross-reactivity with later cephalosporin generations
- Up to 25.6% cross-reactivity between PCNs and carbapenems reported in general population
  - Minimal cross-reactivity with meropenem
  - Less than 3% of general population without penicillin allergy are allergic to carbapenems

Beta-lactam Antibiotics

- Penicillins
  - Penicillin
  - Nafcillin
  - Oxacillin
  - Piperacillin
  - Apmicillin
  - Amoxicillin

Beta-lactam Antibiotics

- Cephalosporins
  - Cefazolin
  - Cefuroxime
  - Ceftriaxone
  - Ceftazidime
  - Cefepime

Beta-lactam Antibiotics

- Carbapenems
  - –Ertapenem
  - –Imipenem
  - –Meropenem
  - –Doripenem

Imipenem

- Risk of seizures
  - 1-1.5%
- Drug-drug interaction
  - Decrease valproic acid serum levels
  - Monitor levels
  - Use alternative ABX if possible
  - Concurrent use with meperidine increases the risk of seizures
- Rate of administration
  - 20-30 minuts
  - Use lower rates if N/V occurs

Meropenem

- Risk of seizures
  - 0.7%
- Decreases valproic acid serum levels
  - Use higher doses of valproic acid
  - Monitor the levels
  - Use an alternative ABX if possible
- Intermittent infusion
  - 15-30 minutes

Vancomycin

- Infusion 10mg/minute
  - 1000mg at least over 60 minutes
- Concentration 5mg/ml
  - 1000mg in 200 ml of D5W or NS
- Faster infusion rates
  - Thrombophelebitis
    - IV site change q 2-3 days
  - Redman syndrome (usually upper torso, face and neck pruritis, chest pain, dizziness)
    - Use hydrocortisone, acetaminophen, antihistamine

Vancomycin

- Red man (red neck) syndrome:
  - Erythematous rash on face and upper body
  - To manage:
    - Administer antihistamines pre-infusion
    - Slow the infusion rate

Vancomycin

- Nephrotoxicity
  - Higher doses
  - Higher serum concentrations
  - Longer period of treatment
  - Reversible
- Drug-induces fever
  - Impurities
- Monitoring
  - Trough levels
    - Before the dose

Linezolid

- IV/PO
- Dug interactions
  - Serotonergic medications
    - Sertraline, citalopram, fluoxetine
  - Meperidine
  - Serotonergic syndrome
    - Hypertension, hyperthermia, mental status changes
  - Avoid concurrent use or monitor closely
- Myelosuppression if use longer than 2 weeks
  - Thrombocytopenia

Gentamicin

- Rate of 30-60 minutes
- Major toxicities
  - Nephrotoxicity
    - Usually reversible
    - Good hydration minimize the problem
    - Monitor drug serum levels
    - Monitor renal function
      - Serum Cr, BUN, Urine output
    - Avoid concurrent other nephrotoxic drugs if possible

Gentamicin

- Ototoxicity
  - Damages to the 8th cranial nerve
  - Sensory portions of the inner ear
  - Hearing loss may be irreversible
  - Once daily dosing: less toxic
  - Drug serum levels monitoring is strongly recommended
  - Peak level: 30-60 minutes after the dose
  - Trough level right before the dose

Amphotericin B

- Major adverse reactions
  - Hypotension, tachypnea, fever, chills, headache
  - Hypokalemia, hypomagnesemia
  - Nausea
  - Impair renal function (nephrotoxicity)
- Faster infusion rate: higher risk of adverse effects
  - Infuse over 4-6 hours to minimize ADRs
- Concentration
  - Up to 0.25mg/ml D5W

Amphotericin B

- Premedication 30-60 minutes prior to amphotericin
  - Ibuprofen
  - Acetaminophen
  - Diphenhydramine
  - Hydrocortisone
  - Meperidine (for patients who had rigors)
- Prehydration
  - Containing Mg, K

Amphotericin B

- Monitoring
  - Renal function
    - Serum Cr, BUN, Urine output
    - Electrolyte levels
      - Potassium
      - magnesium

Chemotherapy induced GI Toxicities

- Second to bone marrow in susceptibility to chemo agents
  - N/V
  - Mucositis
  - Esophagitis
  - Diarrhea
  - Constipation

CINV

- One of the most distressing and frightening adverse effects of chemotherapy
- Direct effect of chemotherapy agents on CTZ
- GI mucosal damage and inflammation
  - Enterochromaffin cells
  - 5HT3 realease
  - Vagal afferents
  - Stimulation of VC and NTS

CINV

- Major neurotransmitters involved in this process
  - **Serotonin (5HT3)**
  - **Dopamine**
  - **Neurokinin 1**
  - Others: muscarinic, histamine

CINV

- Types of CINV
  - Acute
    - Within the first 24 hours of the chemo Tx
    - Usually started in 1-2 hours post Tx and peaks at 5-6 hours post Tx
    - Better control with current antiemetic regimens
  - Delayed
    - After 24 hours of chemo TX
    - Peaks in 2-3 days post Tx
    - Subsides in next 2-3 days
    - Less control with current antiemetic regimens
    - **High dose cisplatin**
    - Also with Carboplatin, anthracyclies, cyclophosphamaide

Chemotherapy Agents

- Depends on the percentage of N/V induction
  - **>90% (high risk)**
    - Cisplatin, cyclophosphamide dose =>1500mg/m2, …
  - **30%-90% (moderate risk)**
    - Carboplatin, cycl;ophosphamide dose<1500mg/m2, doxorubicin, irenotecan, cytarabine>1g/m2, …
  - **10%-30% (low risk)**
    - Cytarabine =<1g/m2, docetaxel, paclitaxel,…
  - **<10% (minimal risk)**
    - Vincristine, rituximab, bleomycin

Mucositis

- Cells with rapid division affected by chemotherapy agents
- Concurrent radiation worsens
  - Xerostomia
  - Mucositis
  - Bleeding
  - Infection

GI Toxicities

- Prevention and treatment
  - Mucositis
    - Viscous lidocaine
    - Nystatin
    - Diphenhydramine
    - Magnesium hydroxide
    - Sucralfate
    - Benzocaine
    - Hydrocortisone plus nystatin plus diphenhydramine
    - Chlorhexidine 0.12%

GI Toxicities

- Topical anesthetics
- Antacids
- Antihistamines
- Antibacterial agents
- Antifungal agents
- Routine dental checks
- Avoid spicy and salty foods

GI Toxicities

- Avoid hot tea or coffee
- Avoid rough foods
- Attention to hydration
- Attention to supportive nutrition
- Liquid and soft diet
- TPN if needed

GI Toxicities

- Diarrhea
  - Irrinotecan induced diarrhea
    - Early
      - Within 24 hours
      - Cholinergic
      - Use atropine iv or sc 0.25 to 1 mg
    - Late
      - After 24 hours
      - Atropine not effective
      - Loperamide schedule, NOT PRN

GI Toxicities

- Irrinotecan induced diarrhea
  - 2mg q2h, 4 mg q4h, 4mg q2h
  - Until diarrhea free for 12 hours
  - For resistant cases
    - Sandostatin (octreotide)
    - 100-2000 mcg sc TID

Dermatologic Toxicities

- Alopecia
- Hypersensitivity reactions
- Extravasations
- hyperpigmentations

Dermatologic Toxicities

- Alopecia
  - 7 to 10 days after chemotherapy
  - Noticeable in 1 to 2 months of therapy
  - Regeneration after a couple months of regimen completion
  - Different look
- Prevention
  - Tourniquets
  - Ice caps

Dermatologic Toxicities

- Alopecia
  - Cyclophosphamide
  - Ifosfamide
  - Paclitaxel
  - Etoposide
  - Docetaxel

Dermatologic Toxicities

- Hyperpigmentation (diffused generalized)
  - 5-FU
  - Busulfan
  - Doxorubicin
- Nail changes
  - Paclitaxel
  - Docetaxel
  - cyclophosphamide

Dermatologic Toxicities

- Hand and foot syndrome
  - Tingling, burning sensation of the pals and soles
    - Cytarabine
    - 5-FU
    - Methotrexate
  - May need to D/C the medication until recovery
- Dry skin
  - Use emollient creams

Dermatologic Toxicities

- Other dermatologic toxicities
  - Radiation recall
    - Doxorubicin
  - Photosensitivity
    - 5-FU
    - MTX (sun burn recall)
  - Radiation enhanced reactions
    - Doxorubicin
    - hydroxyurea

Dermatologic Toxicities

- Extravasation
  - Generalized vascular disease
  - Elevated venous pressure
  - Injection site over joints
  - Recent venipuncture on the same vein

Dermatologic Toxicities

- How to manage
  - Stop injection
  - Do NOT pull needle
  - Aspirate medication then pull the needle
  - Site elevation
  - Surgical consult

Dermatologic Toxicities

- How to manage
  - Cold compress (for 1 day)
    - For most agents
  - Warm compress (for 1 day)
    - For vinca alkaloids
  - Topical DMSO (dimethylsulfoxide)
    - For doxorubucin extravasation
    - Free radical scavenger
    - Apply 1-2 ml on the site for 2 weeks
    - Do not cover and allow the air dry