Amphotericin B

**Indication:** progressive, potentially fatal fungal infection such as cryptococcal meningitis

**Action:** binding to sterols in fungal cell wall increasing cell wall permeability allowing leakage, may be static or cidal

**Metabolism:** not fully known, only 2-5% active drug excreted by kidneys

*Dose alteration not required in patients with pre-existing renal dysfunction.*

**Preparation:** reconstitute with non-bacteriostatic water (no preservatives) and dilute in D5W. Amphotericin precipitates in salt solutions.

**Contraindications:** hypersensitivity, anaphylaxis very rare--stop infusion, administer resuscitative efforts

**Common complications:**

1) **Acute reactions:**
   - Fever, chills, hypotension, nausea, vomiting, headache, tachypnea
   - Onset 1-3 hours after starting infusion
   - Pre-medication helps
   - Incidence and severity are highest with first few doses and diminish on subsequent days
   - *Rapid infusion is associated with hypotension, hypokalemia, shock, arrhythmias and should be avoided*

2) **Nephrotoxicity:**
   - The most important toxic effect:
   - GFR, renal blood flow, renal tubular dysfunction are prominent
   - Hydration and sodium loading may help prevent
   - Renal function improves with interruption of therapy, dose reduction, or increased dosing interval
   - Some permanent impairment does occur

3) **Electrolyte abnormalities:**
   - Especially hypokalemia, hypomagnesia, symptoms include severe muscle cramps, weakness, chest pain, palpitations, drowsiness, mental status changes.

4) **Adverse reactions:**
   - See separate table or PDR. (Note: We have seen thrombocytopenia, hypoglycemia more frequently than expected.)
**Amphotericin B protocol for Cryptococcal Meningitis**  
**SHCH, June 2002**

Daily procedure:

1) **Take history:**
   - Nausea, vomiting, diarrhea, anorexia, severe muscle cramping, weakness, chest pain, palpitations, CNS disturbance (lethargy, sleepiness), decreased urination, black stool or easy bruising/bleeding, pain at previous IV site.

2) **Draw labs if indicated:**
   - Routine monitoring: lytes, creat, Bun, CBC, glucose (day 1, 7, 14).
   - More frequently as indicated to evaluate symptoms elicited in the history. Example: muscle cramps check lytes, bleeding check CBC, lowered UOP check renal function.

3) **Pre-medication 30-60 minutes before infusion:**
   - Paracetamol 1 gm PO, Promethazine 25 mg PO.
   - (Hydrocortisone 50 mg IV if severe rigor/chills occurred on previous infusion).

4) **Record vital signs:**
   - T, P, R, BP initially and every 30 minutes during infusion.

5) **Hydrate N5 500 ml IV (over 2 hours)**

6) **Place on Cardiac Monitor**

7) **Infuse Amphotericin B over 4 hours**
   - Starting dose: Day 1: 0.3 mg/kg in 250 D5W.
   - Full dose: Day 2-14: 0.7 mg/kg in 250 D5W.
     1. Adjusted dose: if decline in renal function during therapy, or significant adverse reactions may cut full dose in half.
     2. The total cumulative should remain the same when dose is adjusted.
   - If chills/rigor develops give Pethidine 25 mg IV, hydrocortisone 50 mg IV.

8) **LP if patient has known or suspected increased intracerebral pressure – (>25 cm of H2O)**
   - Measure and record OP.
   - If > 25cm H2O drain 30cc of CSF.
   - Repeat daily until OP < 25 cm.

9) **Review instructions to patient:**
   - Drink 2-3 liters of fluids per day.
   - Small frequent meals, eat a meal before you come.
   - Report any new symptoms tomorrow.
   - After day 2, if pt tolerates infusion well, you may schedule follow up in early afternoon.
   - Replace with oral MgB, one tablet q day; KCL 600 mg q12h (*caution with K replacement if significant pre-existing renal failure).

10) **Record complications and outcome in Cryptococcus/ Ampho B log book**
    - By Manager.

11) **For seizures:**
    - Benzodiazepines then load with phenytoin. (may discontinue phenytoin at completion of 14 day Amphotericin regimen)

12) **Begin Fluconazole 400 mg per day for 8 weeks upon completion of the 14 day Amphotericin B regimen.**