UofL ACUTE LIVER FAILURE ORDERS

1. Admit to ICU under UofL GI/Hepatology
2. Diagnosis: Acute (Fulminant) Liver Failure
3. Condition & Prognosis: Grave
4. Allergies: Weight: Lbs or Kg (circle)
5. Diet: 2 gm sodium, 1500 mL/day total fluid restriction, 1-1.5 gm protein/kg, 30 kcal/kg/d, in 3 meals plus 4 snacks, while fully awake only. If patient is confused or lethargic, keep NPO and ask UofL GI to place endoscopic N-J tube.
6. Calorie count: if patient eats less than 70% of needs, or has endotracheal-intubation, ask UofL GI to place endoscopic Naso-jejunal or Oro-jejunal feeding tube.
7. IV access: ask Transplant Surgery to place an INTERNAL JUGULAR, 9 Fr or larger, "Cordis Port" under "SiteRight" or Ultrasound guidance. Before placement of central line, correct coagulopathy (if needed) according to "Coagulopathy Management Protocol" ("APPENDIX A: ALF COAGULOPATHY AND INVASIVE PROCEDURE PROTOCOL"). Monitor CVP closely. If a Swan-Ganz catheter is needed, place "SvO2 capable S-G catheter".
8. IV fluids: D10NS 1000 mL + 1 amp MVI + 1 amp trace elements + Thiamine 100 mg + Vit. C 500 mg: at 85 mL/h.; once patient is tolerating diet/ tube-feeds, change to "saline lock".
9. Consult:
-a) Dr. Martin Klapheke – Psychiatry: "Patient with Fulminant Liver Failure; please evaluate Psychological/ Psychiatric axis and risk".
-b) UofL Surgery (Drs Buell, Marvin, Ravindra, Eng) "Fulminant Liver Failure"; please evaluate for risk and assist with management"
-c) Transplant Social Worker: "Fulminant Liver Failure"; please evaluate social risk of patient and family, and assist with urgent need for insurance coverage.
10. Check for availability of consultant:

Please, call Neurosurgery ☐Dr. Thomas Becherer, or ☐Dr. Michael Doyle: inform him that a patient with Fulminant Hepatic Failure has arrived and ask him if he will be available if URGENT epidural ICP transducer placement is needed. Inform admitting team who will be available.
11. Continuous pulse oximetry; keep O2 sat >/= 90% giving O_2 as needed. Please, call us when O_2 sat drops below 90%.
12. Place intermittent pneumatic leg compression device.
13. All IV catheters should be locked only with Normal Saline; do not give heparin.
14. Cleanse skin before placement of any IV catheters and for all subsequent care with chlorhexidine gluconate (HIBICLENS).
15. Give Artificial Saliva, as needed for comfort, while patient is in "fluid restricted diet".
16. If an "Invasive Procedure" is needed, follow "APPENDIX A: ALF COAGULOPATHY AND INVASIVE PROCEDURE PROTOCOL"
17. Place Foley catheter to monitor urine output ONLY IF:
a) Urine output on previous 8 hours is < 400 mL, or
b) Previously normal creatinine raises to =/> 1.5 mg/dL, or
c) Patient is intubated.
18. Admission labs:
Blood type, Rh & antibody screen in 2 different blood draws.
Serum HCG pregnancy test (females). Acetaminophen level.
CBC with diff, PT/INR, PTT, fibrinogen, Factor-V quantitation.
CMP, Phosphorus, Mg, CK, Amylase, lipase, TSH.
Serum cortisol at admission and in a.m.(order also "free-cortisol" if albumin is </= 2.5 g/dL).
Arterial blood gas, arterial lactate, arterial phosphate.

RPR serology, rapid HIV serology, anti-HSV I&II IgG and IgM, anti-CMV IgG and IgM, anti-EBV complete serology, HBsAg, anti-HBc total, anti-HBs titer, anti-HCV, anti-VZV, HCV-RNA quantitation with Reflex to high-sensitivity, HBV-DNA quantitation.
Urine analysis with microscopic exam, urine eosinophiles, spot urine Na, Cl, K, and creatinine.
19. AFP on day 1 (today), day 3, and on day of 1st decrease of ALT.
20. Blood cultures (2 peripheral and all central or picc lines), urine culture, sputum culture
21. Unknown etiology special work-up (only marked tests):

☐**HAV:** anti-HAV IgM

☐**HBV:** anti-HBc IgM (others in #18)

☐**HCV:** HCV genotype (others in #18)

☐**HDV:** anti-HDV IgG and IgM

☐**HEV:** anti-HEV IgM and IgG

☐**CMV:** CMV digene (others in #18)

☐**HSV:** Buffy coat culture for HSV, serum Herpes Simplex PCR (others in #18)

☐**EBV:** EBV-PCR in blood (others in #18)

☐**VZV:** VZV-PCR in blood (others in #18)

☐**Wilson's:** 24h urine Cu, serum ceruloplasmin, uric acid, total & free serum Cu,
Consult UofL Ophthalmology for URGENT bed-side evaluation for Kayser-Fleischer rings: "Fulminant Hepatic Failure; evaluate for Wilson's disease"

☐**Autoimmune:** ANA, anti-LKM, anti-SLA, ASMA, ANCA, AMA, Rheumatoid factor, serum Quantitative IgG, IgA, and IgM.

☐**Alpha-1 antitrypsin:** alpha-1 antitrypsin phenotype and quantitation

☐**Iron overload:** Fe, TIBC, Transferrin saturation, Ferritin

☐**Drug/Toxin**: urine and serum toxicology drug screen.

☐**Paramyxovirus and Adenovirus**: serum PCR for adenovirus, anti-paramyxovirus antibody.

☐**Budd-Chiari, Ischemia, liver neoplasia**: ordered in #24 a & b

22. In case of recent foreign travel, ask UofL GI/Hepatology if "APPENDIX B: POTENTIAL HIGHLY INFECTIOUS EXOTIC VIRUS PROTOCOL" is applicable.
23. Daily CBC with diff, PT/INR, PTT, CMP, arterial ammonia, Mg, Phosphorus.
24. Tests for all patients:
-a) U/S of liver, biliary tree, pancreas & both kidneys + Doppler of liver vessels (portal vein, hepatic veins, splenic vein, and hepatic artery): "Fulminant liver failure: evaluate for liver tumor or liver ischemia": look for masses, steatosis, ascites, kidney/pancreas disease, and evaluate vascular flow".
-b) Echocardiogram with delayed/prolonged "bubble study" to be read by: ________________;
"Fulminant hepatic failure and portal hypertension: evaluate cardiac function, for evidence of hepatopulmonary syndrome, and for pulmonary hypertension"
25. EKG: "Fulminant liver failure - critically ill; assess for ischemia, arrhythmia and QTc interval"
26. Chest X-ray and Acute abdominal series X-ray: "fulminant hepatic failure; evaluate for pneumonia, ileus, or foreign body; in women evaluate if "intrauterine device" is present".

27. Inform UofL GI/Hepatology if radiologist reported presence of Intrauterine device or other foreign body**.** If an Intrauterine device is present, Consult UofL Gynecology to remove it: “Fulminant Liver Failure” with intrauterine device; please remove it due to infection risk”.
28. Check blood glucose at arrival to ICU and q 2h.
a) Keep glucose > 65 mg/dL: give 25-50 mL of D50 IV PRN for hypoglycemia =/< 65 mg/dL
b) If blood glucose level > 140 mg/dL: follow ICU Insulin Standing Orders (VF#7324545) (goal blood glucose 90-140 mg/dL).
29. Use ICU Electrolyte Replacement Protocol (VF#7325849) to correct K, and Mg. If Phosphorus is low, call for instructions to replace it.
30. Keep CVP between 10-15; If CVP is < 10, give boluses of 250 mL each, of 5% albumin up to 6 doses; then give boluses of 500 mL of 0.9% NaCl as needed until CVP is 10-15. Call for instructions to correct CVP above these parameters.
31. Strict In & Outs: call if urine output is equivalent to below 50 cc/h for 8 hours. Obtain BMP q 4 hours if urine output is < 50 cc/h.
32. Manage this patient as (physician should check one of each A & B):

A. ☐ Normotensive before ALF, _ ☐ Hypertensive before ALF.

B. ☐ Normal creatinine before ALF, ☐ Elevated creatinine before ALF.

Follow “ALF Hemodynamic Management Protocol” (see **Appendix C**), if:
a) Systolic BP </= 85 mmHg or MAP </= 60 mmHg (MAP </= 80 mmHg in patients who suffer from hypertension), or
b) Urine output is equivalent to below 50 cc/h for 8 hours, or
c) Previously normal creatinine rises to =/> 1.5 mg/dL.
33. Acetadote intravenously; <u>maximally concentrated in 0.45% NS</u> for up to 7 days:
-<u>day 1</u>: 150 mg/kg IV over 1 hour, then 50 mg/kg over 4h; then 100 mg/kg over 16 h;
-<u>days 2-7</u>: 150mg/kg/day until INR < 2, or 7 days of therapy.
34. Nexium 40 mg PO every day (IV if unable to take enterally)
35. Cytotec 200 mcg PO or by feeding tube every 8 hours (do not give to pregnant patients). Caution: pregnant NURSES must not handle tablets.
36. Vitamin K 10 mg PO or by FT every day, however limit to 3 doses a week in pregnancy. If can not take orally, give 5 mg IV in 50 mL of NS over 30 minutes daily.
37. Other vitamins: Multivitamins + Minerals PO/FTonce daily, + Thiamine 100 mg PO/FT daily, + Vitamin C 500 mg PO/FT daily.
38. Remove all body piercing decorations.
39. Do not give: sedatives/ benzodiazepines, or narcotics (except as in APPENDIX A); No NSAIDS (except as in Appendix E); No antiemetics other than Zofran or Kytril; No aminoglicosides, No heparin, and No vasopressin.
40. Keep serum Na between 140-150 mEq/L. If after correction of CVP as in order #30, the serum Na is:
-a) Na </= 137 mEq/L, give 3% NaCl for a total volume of:
Volume (mL) = [Patient “lean body weight” (in Kg) x 8 (mL/Kg)] = mL over 24 hours, intravenously,
-b) If serum Na is 138 or 139, give only half of the above volume (in 40a), over 24 hours,
-c) Do not start a new 3% NaCl infusion until a new serum Na has been measured after ending the current infusion.
41. Free-water restriction:
a) Give all Intravenous medications in Normal Saline; If not compatible with Normal Saline, then give medication maximally concentrated in 0.45% NaCl, or in D5W, in that order of choice.
b) Minimize amount of water in all oral medications, and all medications given by tube.
42. If temperature is > 37^0C, control temperature with cooling blanket to keep it at </= 36.5^0C.

43. If feeding tube is placed, Consult Dietitian for “Nutrition needs” using NutriHep + Beneprotein (1-1.5 g protein/kg, 30 kcal/kg/d). Start tube feeds at 30 mL/h for 4 hours, then increase to 60 mL/h for 4 hours, and then increase to goal rate. If tube is in stomach, do not hold unless “residuals” are > 300 mL. If tube is in small bowel, do not check “residuals”.
44. Neuro checks every hour.
45. If patient has petechiae or active bleeding, follow “APPENDIX A: ALF COAGULOPATHYAND INVASIVE PROCEDURE PROTOCOL”
46. Daily: blood, sputum, urine & line cultures. Daily: fungal blood culture.
47. Consult Infectious Diseases, Dr. , to give broad spectrum antibiotic and antifungal therapy if patient has two or more of the following criteria (“patient with Acute Liver Failure and SIRS: please give anti-bacterial and antifungal coverage”):
a) Temperature >38ºC or <35ºC,
b) Heart rate >90 beats/min,
c) Respiratory rate >20 breaths/min or PaCO2 <32 mmHg ,
d) WBC >12,000 cells/mm3, <4000 cells/mm3, or >10 percent immature (band) forms.
48. Monitoring for “Hepatic Encephalopathy” (discontinue after treatment of hepatic encephalopathy is started):
If patient develops ***any of 3 the following***:
a) Confusion, drowsiness, asterixis, incoherence, stupor, agitation, unresponsiveness, coma, decerebrate posturing, seizures, or areflexia,
b) Arterial ammonia > 100 mcM/L, or has
c) MELD > 32 (ask Hepatology to give you daily MELD score),
then start treatment for Hepatic Encephalopathy with:
- Lactulose 30 cc every hour until first BM, and then 15-60 cc every 4-8 hours to obtain 4 bowel movements a day or stool output of 600-700 mL/day,
- Rifaximin 400 mg PO/ by FT every 8 hours,
- Carnitor 1320 mg PO/ by FT every 8 hours
- Zinc sulfate 220 mg PO/ by FT once a day.
49. Monitoring for “Airway Penetration Risk” (discontinue after intubation):
If patient shows ***any of the following***: Incoherence, stupor, agitation, unresponsiveness, coma, decerebrate posturing, seizures, or areflexia, ***then***
a) Consult Pulmonary Dr ________________________ to endotracheal intubate “Patient with Fulminant Hepatic Failure and advanced encephalopathy; needs airway protection and management of ventilator”
b) After intubation, follow “APPENDIX D: ALF VENTILATOR MANAGEMENT PROTOCOL”
50. Monitoring for “Intracranial Hypertension High-Risk Status”:
A. Inform Hepatology that patient has reached “intracranial hypertension high-risk status” for ***any of the 3 following findings***:
- a) Arterial Ammonia > 150 mcM/L
- b) Arterial Ammonia > 100 but </= 150 mcM/L, not decreasing after 24 hours of treatment as in order #48,
- c) Grade IV Hepatic Encephalopathy demonstrated by ***any of the following***: unresponsiveness, coma, decerebrate posturing, seizures, or areflexia.
B. If patient reaches “intracranial hypertension high-risk status” (50.A), Consult Neurosurgery (physician found available in order #10) for URGENT placement of epidural Intra-Cranial Pressure (ICP) monitor, and correct coagulopathy before ICP monitor placement following “APPENDIX A: ALF COAGULOPATHY AND INVASIVE PROCEDURE PROTOCOL”
C. If patient reaches “intracranial hypertension high-risk status” (50.A), Consult Infectious Diseases, Dr. , to give broad spectrum antibiotic and antifungal therapy:

"Patient with highly probable intracranial hypertension during acute liver failure; likely infected with bacteria or fungus; please give antimicrobial coverage".

APPENDIX A: ALF COAGULOPATHY AND INVASIVE PROCEDURE PROTOCOL

1A. INVASIVE PROCEDURE:
a) For Invasive Procedures, inform the performing Physician that the preferred agents for sedation and analgesia in this patient are Propofol, or Midazolam with Fentanyl.
b) If platelets are less than 50000, or INR is higher than 1.5, or if Fibrinogen is less than 100 mg/dL, ask the performing physician if they want to prepare the patient following "Coagulopathy Management Protocol" as in 2A.
2A. COAGULOPATHY MANAGEMENT PROTOCOL: give blood products as per "Blood Product Transfusion Protocol" in the following situations.
- a) Prophylactic platelets: one unit of single donor platelets per transfusion episode: only if
    - Platelets =/< 10000, or
    - Platelets =/< 20000 with petechiae or mucosal bleed.
- b) Correct coagulopathy for invasive procedure, or for active bleeding if:
    - Platelets < 50000: give: one unit of single donor platelets per transfusion episode.
    - If INR > 1.5: give FFP (# units = weight in kg x 15/250, rounded-down) until INR close to 1.5;
    - If INR is still > 1.5 after FFP, then give: rVIIa 40 mcg/kg IV bolus immediately before invasive procedure (Do not give rVIIa in any of the following (ask physician if any applies): Budd-Chiari syndrome, active deep venous thrombosis, pregnancy related liver failure, or if in the last 2 weeks patient has had a myocardial infarction, unstable angina, or a cerebrovascular accident).
    - If Fibrinogen is < 150 mg/dL in patient bleeding: give cryoprecipitate 1-1.5 units per each 10 kg of weight
    - If Fibrinogen < 100 mg/dL in absence of bleeding but requiring invasive procedure: give cryoprecipitate 1-1.5 units per each 10 kg of weight

APPENDIX B: POTENTIAL HIGHLY INFECTIOUS EXOTIC VIRUS PROTOCOL

1B. Inform immediately the Infection Control Nurse that patient could have a highly infectious exotic virus infection and that advice for special isolation protocols is needed.
2B. Consult Infectious Diseases, Dr. Julio Melo, for urgent evaluation of the patient ("Acute Liver Failure after recent foreign travel; risk of exotic virus")
3B. Orders in 4B can be process only if Attending Gastroenterology/Hepatology Physician AND Attending Infectious Diseases Physician agree that are needed:

- GI/Liver Attending agrees with order 4B: ☐ Yes ☐ No
- Infectious Disease Attending agrees with order 4B: ☐ Yes ☐ No

4B. Order the selected serology below only if 3B has been satisfied (physician will choose according to history):

- ☐ **West Africa, or South America's Amazon region**: Yellow Fever capture enzyme immunoassay.
- ☐**Congo, Sudan, Uganda, Côte-d'Ivoire, Liberia**: anti-Ebola virus by ELISA,

- ☐**Uganda, Kenya, or Zimbabwe**: anti-Marburg fever IgM-capture by ELISA,
- ☐**Guinea (Conakry), Liberia, Sierra Leone, Nigeria, or other West African countries**: anti-Lassa fever antibodies,
- ☐**Senegal, Kenya, Saudi Arabia, Yemen, Egypt, Tanzania, Somalia, Jordan, and Mozambique**: Rift Valley fever antibody (ELISA)

<u>APPENDIX C</u>: ALF HEMODYNAMIC MANAGEMENT PROTOCOL

1C. LOW URINE OUTPUT OR RAISING CREATININE to =/> 1.5 mg/dL MANAGEMENT:

If mean urine output over last 8 hours is below 50 mL/hour or if previously normal serum creatinine raises to =/> 1.5 mg/dL (see order # 32), check CVP and if below 10, volume expand until CVP is 10-15 mmHg as in "order #30".
If correction of CVP does not increase urine output to >/=50 mL/h nor normalizes creatinine, and MAP is below 85, do the following:

a) Start Norepinephrine drip 0.1 mcg/kg/min and titrate (dose range = 0.01 - 3 mcg/kg/minute) to achieve and keep MAP of 85 mmHg.
b) Do not discontinue norepinephrine unless creatinine has fallen below 1.5 mg/dL <u>and</u> urine output is more than 50 mL/h.
c) If after maximal dose of Norepinephrine drip of 3 mcg/kg/min., the MAP has not achieved a value of >/= 85 mmHg change to LOW BLOOD PRESSURE MANAGEMENT protocol in **2C.b**.
d) If urine output dos not increase to =/> 50 mL/hour after 4 hours of reaching "goal MAP", then: Consult UofL Nephrology and ask to "start bicarbonate buffered SLED without heparin". Correct coagulopathy as in "APPENDIX A: ALF COAGULOPATHY AND INVASIVE PROCEDURE PROTOCOL" to place shiley. Coordinate with Nephrology for timing of shiley catheter placement.

2C. LOW BLOOD PRESSURE MANAGEMENT:

If Systolic BP </= 85 mmHg or MAP </= 60 mmHg (MAP </= 80 mmHg in patients who suffer from hypertension, as in "order #32"), check CVP and give 5% albumin or 0.9% NaCl as in "order #30", until CVP is 10-15. If correction of low CVP does not increase systolic BP to > 85 mmHg and MAP to > 65 mmHg (MAP >/= 85 mmHg in patients who suffer from hypertension, as in "order #32"), start:

a) Norepinephrine drip at 0.1 mcg/kg/min and titrate (dose range = 0.01 - 3 mcg/kg/minute) to achieve MAP of 70 mmHg (MAP >/= 85 mmHg in patients who suffer from hypertension, as in "order #32").
If after maximal dose of Norepinephrine drip of 3 mcg/kg/min., the MAP has not achieved a value of >/= 70 mmHg (MAP >/= 85 mmHg in patients who suffer from hypertension, as in "order #32"), then
b) Add Phenylephrine drip at 1.4 mcg/kg/min and titrate (dose range = 0.4 - 9.1 mcg/kg/minute) to achieve MAP of >/= 70 mmHg (MAP >/= 85 mmHg in patients who suffer from hypertension, as in "order #32", or who are being treated for creatinine =/> 1.5 mg/dL, or for low urine output below 50 mL/h), and place a "SvO2 capable Swan-Ganz catheter".
If maximal doses of Norepinephrine + Phenylephrine do not reach the MAP goal, or if Cardiac Index is < 3.5 L/min/m^2,
c) Add Dopamine drip starting at 5 mcg/kg/min and titrating as needed, not to exceed 20 mcg/kg/min, to achieve MAP >/= 70 mmHg (MAP >/= 85 mmHg in patients who suffer

hypertension as in "order #32", or who are being treated for creatinine >/= 1.5 mg/dL, or for urine output below 50 mL/h.).

d) If the patient is requiring 2 or more "pressors":

-Obtain a "basal" serum cortisol (and "free-cortisol" if albumin is </= 2.5 g/dL), and then give Cortrosyn 250 mcg bolus intravenous.

-Then, 30 minutes and 60 minutes after the Cortrosyn, obtain blood samples for "post stimulation" serum cortisol (and "free-cortisol" if albumin is </= 2.5 g/dL).

-If all 3 cortisol samples are </= 30 mcg/dL or if the post Cortrosyn increase-response is < 9 mcg/dL, then: I) Start Hydrocortisone 100 mg IV every 8 hours, and II) Ask laboratory to measure serum aldosterone in both, the "basal" and the "post stimulation" serum samples

3C. If, after previous steps, MAP can not be kept at 70 mmHg or higher (MAP 85 mmHg or higher in patients who were hypertensive), consult Infectious Diseases, Dr. , to give broad spectrum antibiotic and antifungal therapy: "Refractory hypotension in patient with acute liver failure; please give anti-bacterial and anti-fungal coverage".

4C. After achieving MAP >/= 65 mmHg (MAP >/= 80 mmHg in patients who suffer from hypertension, as in "order #32"), place an "SvO2 capable Swan-Ganz catheter". If the $ScvO_2$ or SvO_2 is < 70%:

a) Transfuse blood until hematocrit is >/= 30%, or

b) If hematocrit is already >/= 30%, start Dopamine drip starting at 5 mcg/kg/min and titrating as needed, not to exceed 20 mcg/kg/min, until SvO_2 is at least 70.

APPENDIX D: ALF VENTILATOR MANAGEMENT PROTOCOL

1D. If patient is endotracheally intubated, please sedate with IV Propofol, starting dose of 5 mcg/kg/min not to exceed 50 mcg/kg/min without a specific MD order which allows up to 80 mcg/kg/min.

2D. Please, ask Pulmonary consultant to manage ventilator but to:

- limit Tidal Volume to </= 6 mL/kg of "predicted body weight",
- limit Plateau Pressure to < 30 cm H_2O,
- increase respiratory rate to keep PCO_2 at 30-40 mmHg, and to
- avoid/minimize PEEP to minimize Intracranial Pressure.

3D. Once intubated, do the following:

- Keep head elevated 30 degrees at all times, unless CPP is below 50 mmHg,
- Avoid sudden head movement;
- Give endotracheal lidocaine for suction,
- Keep room quiet;
- Do only indispensable interventions.
- If Cerebral Perfusion Pressure (CPP) falls below 50 mmHg, flatten the bed to 0^0, until CPP is controlled and > 50 mmHg.

APPENDIX E: ALF INTRACRANIAL HYPERTENSION PROTOCOL

1E. Once patient has ICP Monitor, follow closely ICP pressure and "Cerebral Perfusion Pressure" (CPP); CPP = MAP-ICP in "mmHg".
2E. Goal is to keep ICP < 20 mmHg, and CPP > 50 mmHg.
3E. If patient is intubated:

- Keep head elevated 30 degrees at all times, unless CPP is below 50 mmHg,
- Give Propofol sedation, not to exceed 50 mcg/kg/h (unless specific MD order to give up to 80 mcg/kg/min),
- Avoid sudden head movements,
- Give endotracheal lidocaine for suction,
- Keep room quiet,
- Do only indispensable interventions,
- If Cerebral Perfusion Pressure (CPP) falls below 50 mmHg, flatten the bed to 0^0, until CPP is controlled and > 50 mmHg.

4E. Treat immediately for Intracranial hypertension, as in 5E, if **any of the following occurs**:
- a) Cushing Reflex = hypertension + bradycardia + irregular respiration;
- b) Pupillary abnormalities (asymmetry, or dilation with sluggish response to light), or decerebrate posturing, or epileptiform activity, or hypertonicity
- c) Intracranial pressure (ICP) >/= 20 mmHg,
- d) Cerebral perfusion pressure (CPP) [CPP = MAP-ICP] < /= 50 mm Hg after CVP is >/= 10.

5E. Intracranial Hypertension Treatment Protocol:
-a) Daily EEG. If seizure activity occurs, treat with Fos-Phenytoin 20 mg of Phenytion Equivalent (PE)/kg IV @ </= 150 mg PE/min (over 15 – 20 min) and consult Neurology, Dr_____________________, to assist with management.
-b) If urine output >/= 30 mL/hour, check plasma osmolarity stat and q 4 hours.
-c) If plasma osmolarity is 305 or below, give intravenous Mannitol 0.5 gm/kg over 60 minutes and repeat q4h PRN to keep plasma osmolarity between 310-320 mOsm/L;
-d) If Urine output is < 30 mL/h, consult UofL Nephrology to start "bicarbonate buffered SLED"; do not use heparin.
-e) Once patient is in hemofiltration, check plasma osmolarity q 4 hours.
-f) If plasma osmolarity is 305 or below, give intravenous Mannitol 0.5 gm/kg over 60 minutes and repeat q 4 hours PRN to keep plasma osmolarity between 310-320 mOsm/L.
-g) Ask Renal Team to remove by SLED 3 to 5 times the volume of the amount of Mannitol-volume given in each dose.
-h) If Mannitol can not control ICP & CPP: give Neupogen 300 mcg SQ, and place the patient in hypothermia following "APPENDIX F: ALF Therapeutic Hypothermia Protocol", until core temperature of 32-34 ^{0}C (best goal is 33 ^{0}C), and until ICP is kept at < 20 mmHg and CPP at > 50 mmHg; do not exceed 48 hours of hypothermia. After 48 hour, re-warm to 36.5 ^{0}C.
-i) If patient does not respond to Mannitol and Hypothermia: give Thiopental 5 mg/kg IV over 15 min, followed by 3 mg/kg/hour infusion; ask Neurology Dr. to monitor coma and regulate Thiopental dose by EEG & ICP/CPP response.
-j) If ICP & CCP are not controlled with previous interventions, give Indomethacin 25 mg PO/FT x 1 dose.

6E. Treat arterial hypertension only if CPP > 110 mmHg & ICP > 20 mmHg

APPENDIX F: ALF Therapeutic Hypothermia Protocol

1F. Inclusion criteria: ICP > 20 mmHg refractory to Mannitol or with contraindication to Mannitol.
2F. Strict NPO, discontinue tube feeds and any po/ngt/njt medications. Call MD for order changes to routes of po/ngt/njt medications. Restart IV fluids of D10NS + additives as in "ACUTE LIVER FAILURE ORDERS" order #8.
3F. Insert Foley catheter with temperature probe, to monitor hypothermia.
4F. Document temperature every 15 min during cooling initiation and during rewarming. Document temperature every hour during maintenance. Accurately document when the patient's temperature drops below 34 ^{0}C. Monitor for shivering with every vital sign check. Monitor with skin integrity checks every 2 hours, and wrap hands and feet in dry towel to prevent frostbite, while in hypothermia.
5F. 12-lead ECG (document QT-I) at baseline and every 8 hours while in hypothermia. Obtain baseline (pre-hypothermia): ABG analyzed at actual body temperature, troponin, CK-MB, CMP, lactate Magnesium, Ionized calcium, and Phosphorus.
6F. During initiation & rewarming of hypothermia: obtain every hour BMP, Magnesium, Ionized Calcium, Phosphorus.
7F. During maintenance of hypothermia: obtain every 4 hours BMP, Magnesium, Ionized Calcium, Phosphorus.
8F. 12 hours & 36 hours after initiation of cooling: obtain troponin, CK-MB, lactate, and CBC with diff.
9F. Hypothermia induction (see 11F, 12F, 13F, 14F, and 15F for necessary prophylactic management when hypothermia is given):
I) With "Arctic Sun" Device: follow machine's attached instructions to automatically cool to 33 ^{0}C (automatically over 6-8 hours). Select the correct "pad size" according to weight and height of the patient. Document "Arctic Sun" water temperature every hour during maintenance. Do not use ice packs nor cooling blanket.
II) With cooling blanket/ice packs/IV saline: Achieve goal temperature of 33 ^{0}C (range 32-34 ^{0}C) over 6-8 hours; place cooling blanket under the patient and on top of the patient (place a sheet between the patient's skin and cooling blankets to protect the skin); administer 20 mL/kg bolus of refrigerated "normal saline" over 30 minutes through a peripheral IV line; maintain the temperature for 36 - 48 hours.
10F. Rewarming: After 36 hours of maintenance cooling, begin "passive rewarming" at 0.25 to 0.33 ^{0}C per hour (no faster than 0.5 ^{0}C per hour) to achieve temperature of 36 ^{0}C ideally over 8-12 hours. Remove cooling blankets and ice packs. Maintain paralytics, sedation, and analgesics until temperature of 36 ^{0}C is achieved. Then remove paralytics and wait until complete recovery from neuromuscular block, and then wean fentanyl & propofol as appropriate. If temperature is not >/= 36 ^{0}C after 12 hours, initiate active rewarming with "warming blanket". After temperature is 36 ^{0}C, ask primary team if FosPhenytoin and Amiodarone are still needed.
11F. Dysrhytmia Prophylaxis: Amiodarone 150 mg IVPB over 10 minutes, then 1 mg/minute for 6 hours, then 0.5 mg/minute.
12F. Seizure Prophylaxis: FosPhenytoin 1000 mg IV loading dose, then 100 mg every 8 hours, if not already in therapy.
13F. Pain Prophylaxis: Fentanyl infusion IV (2500 mcg/250 mL NS): bolus of 50-200 mcg IV push, then continue with infusion at 1-2 mcg/kg/hour and titrate as needed.
14F. Continue Propofol as in order "APPENDIX D: ALF VENTILATOR MANAGEMENT PROTOCOL"
15F. Shivering Prophylaxis:
a) Initial dose: cisatracurium (Nimbex) bolus 0.15 mg/kg IV push over 10 seconds (5 mL of the 2 mg/mL cisatracurium injection-solution for an average 70 kg person), then give:

b) Maintenance infusion: watch first for early evidence of spontaneous recovery from the initial bolus and then give cisatracurium infusion (200 mg/500 mL 0.9%NaCl) starting at 3 mcg/kg/minute; titrate by 1 mcg/kg/min down or up to provide adequate neuromuscular block (usual range of 0.5 to 10 mcg/kg/minute) (for an average sized 70 kg patient, at this concentration of 0.4 mg/mL, the initial infusion rate would be about 30 mL/hour, and then titration will be done with decrements or increments of 10 mL/hour as needed).
Discard cisatracurium infusion-solution after 24 hours at room temperature, and replace with a fresh one.
Ensure adequate sedation and analgesia prior to cisatracurium initiation.
Initiate "Train of Four" (TOF) Monitoring: use peripheral nerve stimulant prior to neuromuscular blockade agent with the goal of 4 stimulations/ 4 twitches. After medication the goal is 4 stimulations/ 1-2 twitches.
16F. If Intracranial hypertension is not controlled with hypothermia, go to order # 5Ei in "APPENDIX E: ALF INTRACRANIAL HYPERTENSION PROTOCOL"