Guidelines for reversing coagulopathies in patients with symptomatic spontaneous intraparenchymal hemorrhage

Recommendations approved in 03/15/2010 by:

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Future updates are anticipated as new evidence accumulates. The most recent version of these guidelines will be posted on the Stroke web site (www.stroke.washington.edu). This document can be downloaded in its entirety as a PDF document from the Stroke web site by following the links to the Acute Stroke Algorithm and to intraparenchymal hemorrhage. For bleeding on tissue plasminogen activator (tPA), see online Stroke Algorithm* at the end of the document for IV tPA "inclusion/exclusion criteria". *Online Stroke Algorithm can be found under www.stroke.washington.edu, then click on the "Referrals and TeleStroke Service" link on the left bar and find the "Stroke Algorithm" link. Or go directly to http://uwmedicine.washington.edu/Patient-Care/Our-Services/Medical-Services/Stroke-Center/Documents/HMC_Rx_Algorithm.pdf

Any questions or comments about these guidelines can be addressed to any of the people indicated above or can be sent to Will Longstreth at wl@uw.edu.

For each patient, go through all 17 items below.

1. STAT bloods for:
    - Emergency Hemorrhage Panel (PT/INR, fibrinogen, platelets, hematocrit)
    - PTT, TT
    - Emergency Type and Screen. If crash craniotomy is considered, request 2 Units emergent uncrossmatched Group O (universal donor) packed red blood cells.

2. Obtain history about use of antithrombotic treatments (antiplatelet agents, warfarin, unfractionated heparin, low-molecular-weight heparin, and others).

3. **If on warfarin**:
    - Give vitamin K 10 mg slowly IV over one hour
    - If INR ≥1.5 order "2 units FFP STAT" and transfuse 2 units universal-donor (AB) thawed plasma (FFP). At Harborview, call Transfusion Support Services (4-3088) and request 2 units of thawed AB plasma stat from PSBC (30 minute turn-around time).
    - Depending on INR (see below) infuse Bebulin immediately upon arrival from Pharmacy, in the dose indicated below. Do not wait until the FFP is infused.

Bebulin is a prothrombin complex concentrate (PCC).
Relative contraindications to Bebulin use include:

1) *history of thrombotic or thromboembolic event in past 6 weeks such as DVT, pulmonary embolism, ischemic stroke, acute coronary syndrome, acute mesenteric ischemia or acute peripheral arterial ischemia*
2) *known prothrombotic condition such as major surgery within 6 weeks, malignancy, DIC, or polytrauma*
3) *hepatic disease*
4) *intraparenchymal hemorrhage thought not survivable*

IF ANY OF THESE CRITERIA IS MET, please discuss with stroke attending the possibility of giving bebulin nevertheless, or giving additional FFP (as outlined below) instead.

Bebulin-pathway

- If INR is 2-4, infuse 25U/kg (+/- 10%) body weight Bebulin over 10 minutes, not to exceed 200 IU/min
- If INR is >4, infuse 40U/kg (+/- 10%) Bebulin over 10 minutes, not to exceed 200 IU/min
- Repeat INR 15 minutes after completion of above Bebulin infusion and follow above algorithm for repeat Bebulin dosing as needed. Do not repeat more than twice (switch to "alternative pathway" if INR still elevated.)
- Once INR <1.5, repeat INR testing every 4 hours for 24 hours. If INR increases to > 1.5, give another 10mg vitamin K IV and consider 2 more units FFP. Consult hematology if needed.
- At 24 hours, repeat dose of Vitamin K 10 mg slowly IV over one hour

*** Obese patients, dose on a maximum weight of ideal body weight + 20% ***

Alternative (FFP) pathway

- Immediately give additional 2 Units (for total of 4 Units) universal-donor FFP and request 4 U of type-specific FFP to be sent as soon as possible. Begin transfusion of first 4 units of FFP as soon as possible. Use a diuretic such as furosemide if the patient has a history of congestive heart failure, because of the potential for volume overload.
- If INR is <1.5, stop infusion, if it has already been started, or do not initiate the infusion.
- If INR is >1.5, complete the infusion. Upon completion of the infusion, immediately repeat the STAT Emergency Hemorrhage Panel.
- If INR is still >1.5, give the 4 U of type- specific FFP. Upon completion of this infusion, immediately repeat the STAT Emergency Hemorrhage Panel.
- If INR is still >1.5, consult hematology through the paging operator.
- Once INR is 1.5 or less, repeat INR every four hours for 24 hours to make sure it does not drift up above 1.5.

At UWMC, the same protocol should be followed except that 4 U of

universal-donor FFP should be obtained from UWMC Transfusion Support Services (598-8700) and 4 U of type-specific FFP need to be requested from the Puget Sound Blood Center (206 522-2462).

4. **If on antiplatelet agents** (aspirin, clopidogrel, ticlopidine, prasugrel, NSAIDS, glycoprotein IIb/IIIa antagonists [abciximab, eptifibatide, or tirofiban]), request platelets before blood results return. At HMC, contact Transfusion Support Services (206 744-3088) and request 2 U universal-donor apheresis platelets to be sent to immediately from PSBC. Give platelets as soon as possible. At UWMC, the same protocol should be followed except that platelets need to be requested from the Puget Sound Blood Center (206 522-2462).

5. **If on full-dose unfractionated heparin**, stop it and give protamine 25 mg intravenously before blood results return. After infusion, repeat STAT PTT. If still abnormal, give protamine 10 mg intravenously. Repeat giving protamine 10 mg intravenously until PTT is 1.4 or less times the mean or until a maximum of 55 mg has been given. If platelets less than 100 THOU/µL, send for Heparin Induced Platelet Antibodies to screen for heparin induced thrombocytopenia (HIT). If positive, consult hematology through the paging operator.

6. **If on low-molecular-weight heparin**, such as enoxaparin, dalteparin, or tinzaparin within the last 8 hours, stop the agent and give protamine 50 mg intravenously before blood results return. If given within 8-24hrs (or not sure), give protamine 25 mg intravenously before blood results return. If bleeding continues, a second dose of protamine 25mg intravenously can be given.

7. **If having received IV tPA,** see online Stroke Algorithm at the end of the document for IV tPA "inclusion/exclusion criteria", under "Algorithm for Treatment of Suspected Intracranial Hemorrhage after tPA" or go directly to: https://depts.washington.edu/uwstroke/stroke_rx/IV_tPA_incl_excl.pdf.

8. **If on some other type of antithrombotic treatment**, stop the agent and STAT consult hematology through the paging operator. Such agents would include pentasaccharides such as fondaparinux and direct thrombin inhibitors (DTIs) such as lepirudin, bivalirudin, argatroban or dabigatran. There are no 'antidotes' for DTIs or fondaparinux. Lepirudin, bivalirudin, and argatroban have short-half lives. Repeat PTT at 30-60 minutes after stopping and if it is still prolonged consult hematology regarding potential use of rFVIIa (NovoSeven). Fondaparinux and dabigatran have very long half-lives - consult hematology regarding potential use of rFVIIa.

9. Notify Neurosurgery and Stroke attending (206 744 6789) about the patient. If surgery is considered, request 2 Units crossmatched PRBC (takes approx. 20-90 minutes). If crash craniotomy is considered, request 2 Units emergent **un**crossmatched Group O (universal donor) packed red blood cells (these are in house).

10. Review all blood results, which should be available within 30 minutes.

11. If prolonged PTT is the only abnormality identified on the STAT bloods, immediately consult hematology through the paging operator.

12. Request additional products, if not already requested as part of protocols above, based on the blood results and assuming an average-sized adult. At HMC, contact Transfusion Support Services (206-744-3088), and at UWMC, contact the Puget Sound Blood Center (206-522-2462). Emergency FFP and cryoprecipitate at UWMC can be obtained from Transfusion support Services (206-598-8700).

    - **If INR > 1.5, see above recommendations (#3) for use of FFP and/or Bebulin.**
    - **If fibrinogen < 125 mg/dL, request 2 pools of cryoprecipitate.**
    - **If platelets < 50 THOU/µL, request 2 U universal-donor apheresis platelets (see #4).**
    - **If platelets 50 to 100 THOU/µL, request 1 U of universal-donor apheresis platelets.**

13. As soon as requested products are available, give them. Use diuretic such as furosemide if patient has a history of congestive heart failure and is given FFP, because of the potential for volume overload.

14. Repeat STAT Emergency Hemorrhage Panel after products have been given. If coagulopathy persists, consult hematology through the paging operator.

15. Notify the family and neurology attending about patient's condition.

16. Repeat CT of head at 4 and 24 hours after initial scan or sooner if patient deteriorates.

17. Complete Hemorrhagic Stroke orders.

Abbreviations:
CT = Computer Tomography
DIC = disseminated intravascular coagulation
DTI = Direct thrombin inhibitor
DVT = deep vein thrombosis
FFP = fresh frozen plasma
HMC = Harborview Medical Center
INR = international normalized ratio (of PT)
IU = international units
IV = intravenous
NSAIDs= non-steroidal anti-inflammatory drugs
PCC = prothrombin complex concentrate, for example Bebulin
PSBC = Puget Sound Blood Center
PT = prothrombin time (extrinsic coagulation)
PTT = partial thromboplastin time (intrinsic coagulation)
TT = thrombin time
UWMC = University of Washington Medical Center