Message of the Editor:
In this volume of the Bulletin, a common clinical scenario of the management of anticoagulation in acute surgical patients on warfarin is presented. The dilemma of choosing between potential fluid overload with multiple fresh frozen plasma infusion and inadequate reversal of anticoagulation is a very difficult one. This is followed by the comments of Dr CW Lau, our specialist in hematology, on the proper clinical management in this scenario. Relatively new advances in this field will be discussed.

Drowning or bleeding?

Mr. A was a 75 years old man with history of tight mitral stenosis from chronic rheumatic heart disease and atrial fibrillation. Mitral valve replacement was refused by the patient. His exercise tolerance was fair with dyspnea on moderate exertion. He was on long term warfarin with fair compliance and the latest INR two weeks before this hospital admission was 2.5.

He attended the Accident and Emergency Department because of sudden onset of severe abdominal pain 2 hours ago. Examination showed diffuse tenderness and guarding. BP was 105/65 and pulse was 120/min. CXR erect was done and showed free gas under right hemi-diaphragm. He was therefore admitted to the surgical ward for management.

Dr. B was a first year resident and saw the patient 15 minutes after ward admission. Mr. A was confused and BP was 90/40. He gave 500ml of colloid and immediately called his senior for advice. Dr. B also arrange for cross matching as he anticipate that blood or fresh frozen plasma (FFP) may be needed. Dr. C was his senior and instructed Dr. B to book grade III emergency operation for pneumoperitoneum.

The urgent results showed that INR was 4.0 and platelet count was 110. Dr. B reckoned that it was necessary to reverse the anticoagulation in order to avoid severe bleeding intra-operatively. He ordered 4 units of fresh frozen plasma to be given full rate followed by checking of INR.

After 1 hour, the ordered FFP were given and Dr. B reassess the Mr. A. He noted the INR was 2.5, indicating incomplete reversal of anticoagulation. However, Dr. B also noted that Mr. A was very dyspneic and the SpO₂ dropped to 89% on 4L O₂. Chest examination showed diffuse fine crepitation, compatible with acute on chronic heart failure and pulmonary edema.

Dr. B was perplexed. If further FFP was given, the patient’s pulmonary edema would worsen and make posed a serious problem during operation. If he withheld further FFP infusion, there could be severe bleeding intra-operatively.
Comments of Dr. CW Lau, AC (M&G) TMH, specialist in Hematology

The effect of warfarin by inhibiting the vitamin K dependent coagulation factors II, VII, IX, X is well-known to all clinicians. In the past, fresh frozen plasma (FFP) is commonly used for warfarin reversal. However, FFP provides a dilute form of the clotting factors and it is not practical to infuse very large volumes of plasma (15–30 ml/kg) rapidly. In addition, FFP produces inferior (incomplete) correction.

On the other hand, factor concentrate Prothrombin Complex Concentrates (PCCs) produce complete and rapid correction of the coagulopathy. PCCs are able to completely reverse the warfarin-induced anticoagulation within 10 min. **PCCs is around 25 times more concentrated** in coagulation factors than FFP, thus the infused volume is much reduced. The drawback of PCCs is the risk of thrombogenicity. Irrespective to the use of FFP or PCCs, the accompanied use of 5mg intravenous Vitamin K is fundamental because of the **limited half-life of the infused clotting factors, the shortest of which is FVII at 6 hours**.

The latest BCSH Guideline on Warfarin (2011) recommended the use of 4-factors PCCs (Factor II, VII, IX, X) as the first line therapy for warfarin reversal. In NTW, the **only PCC available for warfarin reversal is however Prothrombinex-VF**, which has insignificant factor VII, the so-called 3-factors PCC. Thus, when using Prothrombinex-VF, we have to replenish factor VII by adding low dose FFP as well (recommended dose 150~300ml FFP, whereas 1 unit FFP ~220 ml).

There are some contraindications for PCCs, namely, hypersensitivity to the active substances or to any of the excipients including known allergy to heparin or history of heparin-induced thrombocytopenia (HIT); or in patients who have evidence of active thrombosis or disseminated intravascular coagulation (DIC).

In summary, we recommend the use of **Prothrombinex-VF 25~50 IU/kg, plus 5mg intravenous Vitamin K, plus 1 unit of FFP** for the first line therapy for warfarin reversal. If Prothrombinex-VF is unavailable or contraindicated, FFP (starting dose 10~ 15 ml/kg) is an acceptable alternative.

**Disclaimer:** All the cases that are included in this Bulletin have been adapted from sources including but not limited to: international Journal publications, MPS casebook, AIRS cases from NTWC and other clusters. All the details have been modified to preserve the anonymity of the persons involved. Please send all comments and enquiries to Dr KOO Chi Kwan (Email: koock@ha.org.hk)