Title: The CHORuS study – using a large animal model of acute traumatic coagulopathy to test the efficacy of cryopreserved red blood cells compared to aged and fresh refrigerated red blood cells.

Authors: Milford EM[1,2], van Zyl N[1], Diab S[1], Dunster K[1,3], Tung, JP[1,4], Reade MC[5,6], Fraser JF[1,7]

Presenter: CAPT Elissa Milford

Presenters Biography :

CAPT Milford is a fulltime Army medical officer and a part time Intensive Care Medicine trainee. She is currently posted to 2GHB. She is also undertaking a PhD on trauma resuscitation, with a focus on acute traumatic coagulopathy, the red cell storage lesion and the endothelial glycocalyx.

Abstract:

Haemorrhage is the primary reversible cause of death after trauma, estimated to cause 80% of preventable battlefield deaths[1], making the restoration of circulating blood volume and control of haemorrhage a clinical priority[2]. For the military, the threat of disruption to supply chains has driven the search for alternatives to refrigerated redblood cells (RBCs), which have a shelf life of only 42 days. Another, only recently recognised, problem with refrigerated RBCs is the development of a storage lesion over a period of time that is well within the current shelf life and is associated with poor clinical outcomes[3].

Cryopreservation of RBCs has emerged as the favoured alternative to address these problems[4]. Arresting metabolism by cryopreserving fresh blood should, in theory, deliver a storage lesion-free product that can be stored for up to 10 years. The logistic advantage of prolonged shelf-life has been utilised by the US and Dutch armed forces for over 15 years, and the ADF is acquiring this capability. From this limited use, we know that cryopreserved RBCs do not cause severe transfusion reactions, but there is no controlled, comparative evidence for their efficacy as a resuscitation fluid.

Coagulation, Haemorrhage and Oxygenation in Resuscitation of Severe trauma – Phase II (CHORuS-II) will use a large animal model of acute traumatic coagulopathy to study the effects of aged RBCs, fresh RBCs, cryopreserved RBCs, albumin and fresh frozen plasma transfusion at an organ and cellular level in the severe trauma setting. The study follows on from a successful pilot study (CHORuS-I) of twelve animals that demonstrated the development of acute traumatic coagulopathy from trauma and haemorrhage alone.

The study will test the hypothesis that cryopreserved RBCs are superior in efficacy to aged RBCs, and equal in efficacy to fresh RBCs, using the following endpoints:

- Organ level oxygenation – measured by tissue oxygen probes in liver, heart, kidney and brain.
- Microcirculation blood flow – measured by tissue Doppler probes and sidestream darkfield camera images in the same organs.
- Inflammation – measured by inflammatory biomarkers.
- Cardiac function – measured by echocardiography and cardiac biomarkers.
- Acute traumatic coagulopathy – measured by ROTEM and MULTIPLATE as well as coagulation factor levels.
- Endothelial glycocalyx damage – measured by electron microscopy imaging.

The study will also contribute to understanding the pathophysiology of acute traumatic coagulopathy, and provide mechanistic data to support growing clinical evidence suggesting aged red cells are harmful, particularly for the trauma patient.

The results of this study will be of considerable interest to Defence given its acquisition of a cryopreserved RBC capability. In addition, the nascent collaboration between the Critical Care Research Group based at The Prince Charles Hospital in Brisbane and Defence will provide an enduring opportunity for Defence members to pursue research in pre-clinical and clinical areas of critical care.

The study is planned to start in late June 2014, finish in late 2014, with results published early 2015.

The study is supported by grants from the Defence Health Foundation, the Queensland Emergency Medicine Foundation and the Intensive Care Foundation.