

WELCOME

Welcome to the Barts C4TS Summer newsletter. As we approach the end of our 3rd year, we reflect in this issue on our Centre's major achievements and where our focus is directed moving forward. A key aim of our research has always been to better understand the body's reaction to injury and our treatment practices, in order to improve patient survival and recovery after trauma. Our Research Spotlight shines on our knowledge of fibrinolysis (clot breakdown) in trauma haemorrhage and we round up our most recent outreach and dissemination activities. Finally we report on this year's MSc Summer School; our international gathering of future trauma leaders and researchers. Enjoy!



Professor Karim Brohi (Centre Lead)

C4TS - three years on

by Dr Simon Eaglestone (Head of Operations)

BACKGROUND

C4TS was established in October 2012 supported by a £3m Barts Charity award. Our underlying aim was to create a world-leading hub for local and global collaborative research that translates exceptional research into trauma practice, into global policy.

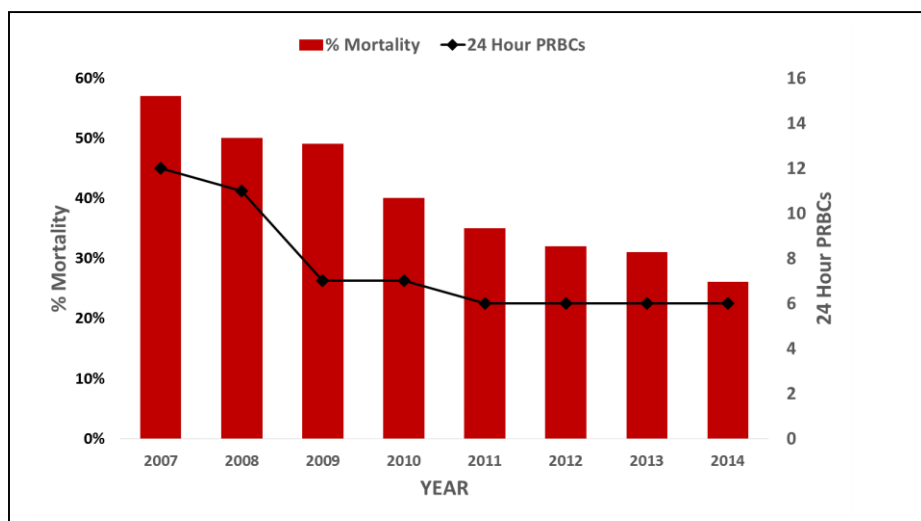


Major research projects

C4TS conducts fundamental and clinical research that spans the whole of the patient pathway, from injury through to rehabilitation & discharge from hospital.

Our ongoing research includes:

- Quantifying major trauma, health-care practices and costs in England
- Comparing strategies across the EC for managing trauma haemorrhage
- Defining the incidence and impact of multiple organ failure after trauma
- Testing novel agents for organ protection in bleeding haemorrhage
- Measuring the body's immediate response to injury & how this might be 'tuned' to improve patient outcome



The need for research

Barts C4TS ensures uptake of its research findings into practice by working as part of a multispecialty team of clinicians and transfusion specialists at The Royal London Hospital (RLH). Since 2007, RLH has halved the mortality and amount of blood required by critically bleeding trauma patients (Fig.1).

We appear close to the limit of what current clinical care can provide to the trauma victim. We need a step-change in our understanding of injury and new therapeutic strategies to significantly improve survival and longer-term outcomes for critically injured patients.

Figure 1 – Reduction of death and demand for blood in trauma. Annual % mortality and total number of packed red blood cells (PRBCs) transfused within 24hrs for 'Code Red' trauma patients admitted to the RLH (2007-2014).

You can find out more about our research streams and novel findings by visiting our [website](#). Our [video](#) also explains the global need for research into improved trauma treatments.



Research Project Spotlight

Unravelling the mysteries of fibrinolysis

By Lewis Gall (Clinical Research Fellow)

WHAT IS FIBRINOGEN?

Fibrinogen is an inactive, soluble protein which normally circulates in the blood and is essential to stemming bleeding from damaged tissues, a process known as haemostasis.

The first stage of haemostasis involves activation of tiny cells called platelets which form a plug at the site of injury. At the same time, a series of rapid enzymatic reactions occur which breaks fibrinogen into insoluble strands of fibrin. These fibres aggregate and wind around one another to form a meshwork which acts as a platform for a strong clot to form at the site of injury and prevent further blood loss. In healthy people, there is normally 2.5g of fibrinogen in every litre of blood circulating. However, these levels can become rapidly depleted in times of major bleeding, such as severe injury, as the body fights to keep blood within the arteries and veins.

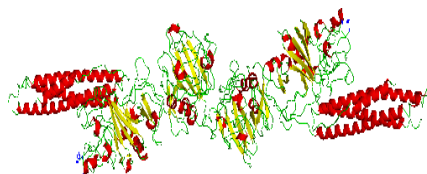


Figure 2- Crystallographic structure of a human fibrin

THE FIBRINOLYSIS PROBLEM

Our research (including the [Activation of Coagulopathy and Inflammation in Trauma](#) study) has demonstrated that an early reduction in levels of substrate for clot formation and an increase in clot breakdown (i.e. fibrinolysis) are common in trauma patients and likely to play a significant role in Acute Traumatic Coagulopathy (ATC) pathophysiology.

ATC can occur within minutes of injury and results in uncontrolled bleeding, but the underlying mechanism remains ill-defined.

We demonstrated that increased fibrinolysis is common in trauma patients. 1 in 8 trauma patients presenting to the Emergency Department experience severe fibrinolysis. This represents a previously unrecognised cohort of trauma patients with higher transfusion requirements, morbidity and mortality.

IMPLICATIONS AND NEXT STEPS

These novel findings imply that transfusion therapy for coagulopathic bleeding and patient outcomes can be enhanced by a greater focus on early fibrinogen supplementation and anti-fibrinolytic administration.

The C4TS is currently in the final planning stages of a large multinational Randomised Control Trial (RCT) involving trauma centres across the UK, Europe and North America to evaluate whether



Figure 3 - Lewis Gall

fibrinogen replacement therapies will save more lives in cases of major trauma haemorrhage. A C4TS pilot study (CRYOSTAT) showed early administration of high dose cryoprecipitate maintained acceptable blood fibrinogen levels during active bleeding. CRYOSTAT 2 aims to answer the question: does early fibrinogen reduce mortality in adult patients with trauma haemorrhage?

More information about fibrinogen in trauma can be found in [this article](#).

A detailed article about the CRYOSTAT study can be found [here](#).

STUDY HIGHLIGHTS

A large observational study conducted at C4TS that involved over 500 trauma patients showed that low levels of fibrinogen levels on admission to the Emergency Department are an independent predictor of mortality. This important finding provided the impetus to develop and carry out a randomised controlled trial to test safety and efficacy of fibrinogen supplementation.

In a pilot study we were able to evaluate the feasibility and potential effectiveness of early fibrinogen replacement with cryoprecipitate a blood transfusion product rich in fibrinogen. This study constituted the UK's first co-developed civilian-military RCT which was conducted in parallel at the Royal London Hospital, John Radcliffe Hospital (Oxford) and Camp Bastion, Afghanistan

Results reported in 2015 suggested that early use of cryoprecipitate improved survival from major bleeding in trauma but that a larger definitive study was required to fully answer the question. This will be CRYOSTAT 2 (2016-2019).

MSc Trauma Sciences- Summer School

By Susan Brundage, Professor of Trauma Education

In August of 2015, 42 students from around the world journeyed to London for the 4th Annual Trauma Sciences Summer School. For 2 weeks at the end of the first of their two year course, our MSc students get to connect with each other and with international leaders in the trauma sciences field in an immersive educational experience. The 40+ local and international TraumaMasters Faculty contributed 1000% for the 2 weeks, achieving a 1:1 Faculty:Student ratio.

Visiting faculty included: Dr. Teri Reynolds – The Lead for Trauma, Emergencies and Acute Care at The World Health Organization (WHO), Professor Sherry Wren – Director of Global Surgery at Stanford University, Professor Richard Gosselin – Director of the Orthopaedic Trauma Institute (OTI) at the University of California San Francisco and Mr. Christos Giannou – former Lead Surgeon for the International Committee of the Red Cross/Red Crescent (ICRC) and primary author of the “War Surgery” Textbooks.

MSc students completed many practical skills sessions, including Surgical Workshops and Difficult Case Discussions at the Royal College of Surgeons, and critical care training at the London’s Air Ambulance Institute of Pre-hospital Education. Students also work together and present a major project – this year’s challenging topic was “Create a Paediatric Trauma System for London for 2025”



Figure 4 - The Class of 2015 – trauma and ortho MSc summer school students

Students’ reactions:

“The most inspirational and educational experience ever! Thanks to the faculty for making it real!” – Francesca Colombo

“Completely jealous of everyone @TraumaMasters Summer School. It’s an incredible 2-week Master Class.” – Richard Carden

“What a fantastic 2 weeks and a great way to finish. My head is spinning with everything I’ve learnt. Roll on year 2!” – James Crichton

Find out more about our trauma MScs [here](#).

Local outreach

In May, Professor Brohi participated in the popular [Pint of Science festival](#). In the relaxed atmosphere of a London East End pub, Karim spoke to locals about what it takes to bring ‘science from bench to bedside’!



Figure 5- Professor Karim Brohi at the Pint of Science Festival

STEM education and outreach

By Scarlett Gillespie, Research Assistant and Outreach Lead

“Monday 29th June saw the trauma team pack up the car with our ‘science of the bleeding obvious’ stand to make our way down to the South of England show ground for the Big Bang South East 2015. The trauma mannequin gives youngsters the chance to practice saving a life through ‘damage control surgery’, with some children playing the role of anaesthetist and feeding the ‘obs’ such as heart rate and blood pressure back to the rest of the budding surgeons! Clot plunk gives us the opportunity to talk through the formation of blood clots including the roles of platelets and the protein fibrin, and how an alteration in this process can be devastating. We also introduced our new trauma team game where children can discover the wide range of professions supporting a trauma patients’ journey through the hospital from the ED consultant in A&E to the researchers carrying out new studies in our team. Over 20 school groups passed through our exhibition and the positive feedback from teachers was fantastic!”



Figure 6- The Trauma Outreach team at Big Bang South East 2015. From left: Hew Torrence, Lewis Gall, Tim Jones, Emma Jane Mallas, Scarlett Gillespie

You can contact C4TS through [our website](#), or tweet [@CommsC4TS](#). We’d love to hear from you!