### 1. Platelet Dysfunction in a Model of Complex Military Trauma

Herbert Chitambira*, Mark Bates, Sara Watts, Emrys Kirkman. CBR Division DSTL. Porton Down, JHG (SE)

**Background**

Haemorrhage is a principal contributory factor in trauma-related deaths in military (battlefield) and civilian settings. A significant proportion of severely injured casualties develop an early trauma-induced coagulopathy (TIC), which is an independent predictor of death. One aspect of TIC is an alteration in platelet function. In vivo trauma models are often essential to develop new treatments. The aim of this study was to evaluate whether an established model of trauma incorporates platelet dysfunction.

**Method**

The study was conducted in accordance with the Animals (Scientific Procedures) Act, 1986. Blood was collected from terminally anaesthetised pigs before (Baseline) and 30 minutes after the induction of trauma/haemorrhagic shock (S30), and again after 90 minutes of hypotensive resuscitation (R90) with either 0.9% saline, 1:1 packed red cells and plasma (PRBC:FFP) or whole blood (WB). Platelet function was assessed by aggregometry in response to ADP and TRAP (Multiplate®). Platelet count was obtained using a haematology analyser, and shock was quantified by measuring Actual Base Excess (ABE) of arterial blood.

**Results**

ABE fell significantly from Baseline to S30 and remained negative (-7 ± 1 mEq/L) until R90 in all groups (P<0.001), without significant difference between groups (P=0.4747). Injury, shock and resuscitation were associated with a significant fall in platelet aggregation in response to ADP (P<0.0001) and TRAP (P=0.0006), but no difference between treatment groups (P=0.9388 ADP; P=0.06385 TRAP). The response to TRAP was markedly less than that to ADP. Platelet count fell significantly (P<0.0001) again without significant difference between treatment groups (P=0.8574). After 90 minutes of resuscitation, the response to ADP had fallen to 62% of the baseline response while platelet numbers had only fallen to 85% of baseline over the same period.

**Conclusions**

Our model of trauma results in an attenuation of platelet function that, in the early phase, is independent of resuscitation strategy.

### 2. Developing a Militarily Relevant Ex-Vivo Model of Traumatic Injury and Haemorrhagic Shock

1Laura Cotthey*, 2Alex Stoll, 3John P Stone, 4Timothy R Entwistle, 5Kavith Amin, 3Jas Kerr, 3William R Cowey, 2Corban JT Bowers, 6Jason E Smith, 2Sarah Watts, 5James E Filides.

1Academic Department of Military Emergency Medicine, Royal Centre for Defence Medicine, Birmingham, UK; 2CBR Division, Dstl Porton Down, Salisbury, UK; 3TheEx-VivoResearchCentre, 3F66Building3, AlderleyPark, NetherAlderley, Macclesfield, UK; 4University Hospitals Plymouth NHS Trust, Plymouth, UK; 5School of Chemical Engineering, College of Physical Sciences, University of Birmingham, UK

**Background**

Traumatic injury is a leading cause of death worldwide. There is a crucial need to develop therapies that improve critically injured patient outcomes. Current trauma research models are ethically and financially challenging, with poor translation. However, traumatic injury and haemorrhagic shock can be modelled using ex-vivo normothermic perfusion (EVNP), a methodology adapted from transplantation. The aim of this study was to develop a 24hr EVNP duel porcine limb and kidney model.

**Method**

Eight porcine forelimbs, bilateral kidneys and blood were retrieved via standard protocols. Following <4hrs cold storage, the kidneys were connected to a bespoke Ex-Vivo Research Centre circuit via the renal artery, and a mean arterial pressure (MAP) of 80mmHg was maintained. The perfusate consisted of leucocyte-deplete blood and Ringer’s solution. Once the kidney was haemodynamically stable, the limb was connected via the brachial and radial collateral arteries. Haemodynamic parameters were continuously monitored, biochemical perfusate assessment performed hourly and histopathology baseline and end timepoints samples taken.

**Results**

Perfusion was maintained for 24hrs in all limbs, with blood flows of 345.03mls/min (±54.78 SD) and MAP of 77.57mmHg (±3.82 SD). Three kidneys achieved 24hr perfusion, with flows of 214.53mls/min (±41.6 SD) and MAP of 80.58mmHg (±0.51 SD). Biochemical analysis showed a statistically significant potassium elevation at 24hrs compared to baseline, p=0.0078. A further three kidneys were disconnected from the circuit at 7, 11 and 12hrs, and two kidneys showed decline in flow >15 hrs due to declining haemodynamics. Compared to baseline, evidence of cell death was observed in 24hr muscle samples. In the end-point kidney samples, tubular degeneration, protein loss and necrosis extended along the nephron.

**Conclusions**

Limb EVNP can be successfully achieved for 24hrs, but further protocol improvements are required to sustain renal perfusion for 24hrs alongside adjustments to reduce the ischaemic insult and cell death.

### 3. Cardiopulmonary, Functional, Cognitive and Mental Health Outcomes Post Covid, Across the Range of Severity of Acute Illness, in a Physically Active Working Age Population: Baseline Findings from the MCOVID Study

1Oliver O’Sullivan*, 2David A Holdsworth, 3Peter Ladow, 4Robert M Barker-Davies, 5Rebecca Chalmer, 5Andrew Houston, 1Samantha May, 5Dominic Dawson, 5Daniel Mills, 5Kayleigh Pierce, 5James Mitchell, 3Cheng Xie, 6Edward Sellon, 3Jon Naylor, 7Joseph Mulae, 1Mark Cranley, 6Nick P Talbot, 8Oliver J Rider, 6Edward D Nicol, 1Alexander N Bennett.

1Academic Department of Military Rehabilitation (ADMIR) Defence Medical Rehabilitation Centre (DMRC) Stanford Hall, Loughborough, UK; 2,3Academic Department of Military Medicine; 4University Hospitals Oxford University Hospitals (OUH) NHS Foundation Trust, Oxford; 5Academic Department of Military Medicine

**Abstract**

The medium-long impact of coronavirus disease 2019 (COVID-19) on active populations is yet to be fully understood, with potential individual and operational impact on military personnel (SP). The M-COVID study was established to investigate cardiopulmonary, functional, cognitive, and mental health post-COVID-19 SP outcomes, across the spectrum of acute COVID-19 severity.

**Method**

Observational four-cohort study: hospitalised, community-based illness with on-going symptoms (community-symptomatic), community-based illness now recovered (community-recovered) and age, sex, job-role matched control. Participants underwent extensive clinical assessment involving...
cardiopulmonary imaging, submaximal and maximal exercise testing, pulmonary function, cognitive assessment, blood tests, electrocardiogram and questionnaires on mental health and physical function.

**Results** 113 participants (aged 39±9, 86% male) were recruited; Hospitalised (n=35), community-symptomatic (n=34), community-recovered (n=18) and control (n=26), 159±72 days following acute illness. Hospitalised and community-symptomatic groups were older (p=0.003), with a higher body mass index (p<0.001), and worse mental health (anxiety, p=0.011; depression, p<0.001; post-traumatic stress, p<0.001), fatigue (p<0.001), and quality of life scores (p=0.001), with a mean of 2±2 and 2±1 symptoms, respectively. Hospitalised and community-symptomatic participants also performed less well on sub-maximal (p<0.001) and maximal exercise testing, with hospitalised individuals displaying impaired ventilatory efficiency (p<0.001), less work at the anaerobic threshold and at peak (both p<0.001), and significantly reduced forced vital capacity (p=0.004). Clinically significant abnormal cardiopulmonary imaging findings were present in 6% of hospitalised participants, lower than those seen in other studies. Those who recovered from community-based, mild-moderate COVID-19 had no significant differences from controls on any parameter.

**Conclusions** Recovered SP who suffered mild-moderate COVID-19 do not differ from an age, sex and job-role matched controls. This is reassuring for the vast majority of COVID-19 do not differ from an age, sex and job-role matched controls. This is reassuring for the vast majority of COVID-19. Those who recovered from community-based, mild-moderate COVID-19 had no significant differences from controls on any parameter.