

2018 European Conference on Donor Health and Management

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SUMMARY

The third European Conference on Donor Health and Management (ECDHM) was held in Copenhagen from 5th to 7th September 2018 and was co-organised by the ECDHM committees and European Blood Alliance. This is an international conference with a focus on 'donor health', including donors of blood, organs and other substances of human origin, and remains the only conference focusing exclusively on donor medicine.

This overview presents a selection of research topics in relation to iron, the keynote speeches and plenary talks. The keynote speeches cover the epidemiology of donors and recipients, whole-blood donor recruitment and retention and the safety of donors and recipients of plasma and plasma products. Talks from the plenary speakers reviewed modern multi-omic approaches to study red cell quality and the central, perennial question of what motivates a donor to give blood and how can this be encouraged.

Key words: blood donation, donor health and management, haemoglobin levels.

This conference on donor health occurs biennially, and this year, it has maintained its popularity with approximately 250 delegates. The areas covered in posters and oral presentations were diverse, and a selection is reported here.

IRON

The long-term effects of blood donation on iron stores are a concern for blood services not only because of the increased chance of failure to pass the haemoglobin threshold but also the potential impact on donor health.

Muriel Lobier (Finnish Red Cross Blood Service) presented information from the FinDonor 10 000 cohort on influencing blood donation frequency and how lifestyle factors, blood donation frequency and iron supplementation may modulate donor iron levels by gender and menopausal status. There was some, but not complete, consistency of the factors that significantly modulate serum ferritin levels, and this may reflect the power of the study to examine effects in all sub-groups. The factors that predicted ferritin levels in the three groups examined were:

- Pre-menopausal women – age, body mass index (BMI), smoking and time since last donation
- Post-menopausal women – BMI and time since last donation
- Men – age, BMI, number of donations in the last 2 years, time since last donation and iron intake

Interestingly, iron supplementation was not associated with higher iron stores in blood donors. This may reflect continued blood donation.

Two oral presentations on zinc protoporphyrin (ZPP) were given by Saurabh Zalpuri (Donor Studies, Division Research, Sanquin, The Netherlands). ZPP is formed when iron levels are low and protoporphyrin binds with zinc instead. Raised levels of ZPP have long been investigated as an early marker of iron deficiency (Schotten *et al.*, 2018).

The first presentation looked at whether ZPP levels could predict future haemoglobin levels in blood donors. Data were used from the Netherlands Cohort study, which consisted of about 9000 whole-blood donors. ZPP showed statistically significant associations with subsequent haemoglobin levels in both men and women, but the size of the prediction estimate was small (for women, the regression coefficient was -0.17 , and for men, it was -0.09). The predictive value of ZPP for haemoglobin is perhaps not surprising for two reasons: the existing standard practice in blood services is based on testing of blood donors for haemoglobin rather than iron levels, and iron-deficient erythropoiesis occurs well before iron deficiency anaemia is evident.

The second presentation looked at the predictive value of haemoglobin, ferritin and ZPP (individually and in combination) for subsequent deferral of blood donors due to low haemoglobin. The study population was derived from repeat donors of the observational cohort study Donor InSight III

The next European Conference on Donor Health and Management will be held in Hamburg, Germany in 2020.

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(DIS-III). Haemoglobin and ferritin had a higher predictive value for subsequent low haemoglobin deferral than ZPP. The predictive model was improved by using previous donation history and age.

The topic of iron and donor health was further explored in a panel debate chaired by Dr Nick Watkins (Assistant Director – Research and Development, National Health Service (NHS) Blood and Transplant, UK). A series of presentations by experts in the field was given to provide the context for further discussion.

Following the INTERVAL blood donor study, where there was some evidence that the haemoglobin screening tests used by National Health Service Blood and Transplant (NHSBT) had a significant false acceptance rate, NHS Blood and Transplant have explored different haemoglobin screening strategies to reduce error rates in haemoglobin testing (Di Angelantonio *et al.*, 2017). Prof. Emanuele di Angelantonio (UK) gave an update on the COMPARE Study, which looked at the use of a simple ‘post-donation strategy’ (where the Hb result from the last blood donation is used to decide if a donor can be accepted for a subsequent donation), capillary HemoCue pre-donation and two non-invasive medical devices for measuring Hb pre-donation. The non-invasive methods were associated with high inappropriate acceptances and inappropriate deferrals. The ‘post-donation strategy’ was just slightly worse than pre-donation capillary HemoCue [based the Receiver Operator Characteristics (ROC) curve].

The Danish Blood Donor Study has provided much original longitudinal data on donors, and Prof. Henrik Ullum (Denmark) presented an update on donor haemoglobin and ferritin in the study. Previous work from this group has shown that a high proportion of donors are iron deficient. Among high-frequency donors (with more than nine donations in the past 3 years), they found iron deficiency (ferritin below 15 ng mL^{-1}) in 9, 39 and 22% of men, pre-menopausal women and post-menopausal women, respectively (Rigas *et al.*, 2014). Iron deficiency can have clinical significance beyond anaemia, for example, in the study, it is associated with depression, Restless Legs Syndrome and low birth weight (Rigas *et al.*, 2018). The use of the Copenhagen algorithm, using ferritin measurements to advice on iron supplementation, was explained. In general, the high proportion of iron-deficient donors can be alleviated either by extending the inter-donation intervals or by guided iron supplementation, and they have concluded that routine ferritin measurements and iron supplementation are feasible and effective ways of reducing the proportion of donors with low haemoglobin levels (Rigas *et al.*, 2017).

Sanquin, based in Amsterdam, has a long history of donor studies and has recently examined the healthy donor effect (van den Hurk *et al.*, 2017). At this conference, Dr Katja van den Hurk (Sanquin, the Netherlands) updated the meeting on Donor InSight and FIND’EM studies, which look at donor haemoglobin and iron. Sanquin has introduced pre-donation screening of ferritin every fifth donation. Low ferritin levels lead to a change in the deferral period, and no iron supplementation is given. The

impact of this change on donor outcomes and well-being is being assessed using a stepped-wedge study design.

There was active discussion between the audience and the panel members, but no consensus was reached on the definitive role of the testing of iron in blood donors. Panel members did support a post-donation strategy for haemoglobin testing, but there are different protocols for implementing this across blood services, and there is a need to understand current practice.

KEYNOTE SPEAKERS

There were three keynote speakers who gave interesting and informative overviews of key areas in donor medicine.

Epidemiology lies at the heart of our understanding of disease and risk. Gustaf Edgren (Associate Professor of Epidemiology, Karolinska Institute, Sweden) has led a series of major studies on donor health and recipient outcomes (Edgren & Hjalgrim, 2017). He described the SCANDAT database that is a collaboration between Sweden and Denmark, which allows tracking of blood donations to recipients and their health outcomes. Currently, there are data on about 1.7 million donors and 2 million patients. He gave examples of the use of SCANDAT studies. One study has shown that there is no evidence of the transmission of neurodegenerative diseases, such as Alzheimer’s disease or Parkinson’s disease, by blood products, and another survey undertook a nation-wide hepatitis lookback (Edgren & Hjalgrim, 2017).

Wim de Kort (Professor of Donor Medicine, Sanquin, the Netherlands) discussed current dilemmas in donor protection and selection. Analysis of donor motivation must start with whether donation is a voluntary, non-remunerated act. Pure altruism means that someone is doing something for others without gaining anything. This may in fact be a rare motivation. Wim questioned whether it really is unsafe if donors were to receive remuneration, although it could be hard to evaluate the effects of paying for donation because some products are already very safe. Furthermore, remuneration might take different forms and be called by different names. A direct payment to a donor might be seen differently from compensation for a donor’s travel expenses.

Plasma donation and fractionation has provided many efficacious blood products. Paul Strengers (International Plasma and Fractionation Association) spoke about plasmapheresis and donor health. The global demand for intravenous immunoglobulin has been consistently rising in the last 10 years and is projected to rise further. The effects of frequent plasma donation on donors are unclear because studies tend to be associated with high dropout rates, with only a minority completing the studies. Furthermore, there are international variations in what volumes and frequencies plasma can be collected from donors. The United States is responsible for 72% of the world’s plasma supply, and there are potential risks for Europe through over-reliance on the importation of plasma. It is argued that Europe should move towards ‘strategic independence’ by increasing production locally.

PLENARY SPEAKERS FROM UNITED STATES AND AUSTRALIA

There was some novel work arising from blood services outside Europe. Variation in the quality of blood products from donor to donor can now be investigated using high-throughput proteomics, metabolomics and genotyping. Dr Mike Busch (USA) spoke about the REDS-III RBC-Omics Study and future international collaborations (Stone *et al.*, 2019). He described how red cells are metabolically active, and deterioration of red blood cells in storage may lead to adverse events in transfusion. Blood from donors underwent testing for osmotic fragility, storage haemolysis and oxidative haemolysis. This information was combined with donor genotypes in Genome Wide Association Studies of red cell phenotypes. It appears that osmotic fragility and oxidative haemolysis are reproducible across blood donation episodes, suggesting heritability, whereas storage haemolysis varied from donation to donation. Storage haemolysis was lower in females, potentially because of greater red cell turnover due to menstruation.

Direct clinical application of such haemolysis studies was investigated with Dr Mark Gladwin (Chief of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh School of Medicine) who has studied the outcome of transfusion in sickle cell patients and demonstrated that some single nucleotide polymorphism were associated with increased osmotic haemolysis.

Nareg Roubinian (University of California San Francisco (UCSF), USA) presented an alternative approach to study the influence of donor, component and recipient factors on the efficacy of erythrocyte transfusions. A linkage analysis was conducted of blood donor and component data with electronic health records of hospitalised patients who received a single-unit RBC transfusion (21 701 recipients). Recipients of donations from male donor RBC units had larger post-transfusion increments in Hb compared to those of female RBC units (11 vs 10 g L⁻¹, $P = <0.01$). Female recipients had a larger rise in Hb per RBC unit compared to male recipients (12 vs 10 g L⁻¹, $P < 0.01$). RBC storage age and blood donor age did not have a significant effect on Hb increment in recipients in multivariate analysis ($P = 0.55$ and 0.94 , respectively).

Finally, Prof. Barbara Masser (Brisbane, Australia) has published widely on the problems of retaining first time donors (Bagot *et al.*, 2016), on vaso-vagal reactions (Thijssen & Masser,

2018) and the theoretical underpinnings of donor behaviour (Williams *et al.*, 2018). Here, she spoke about the time course of emotion in donors on the pathway through donation. The aim of the study was to boost retention of blood donors by using emotion-focused interventions. In an initial work, 414 participants were given iPads throughout the donation journey to measure immediate emotion at certain points. 'Joy', 'Calm' and 'Stress' were considered key aspects of emotion. These parameters changed during the donation journey and provided a trajectory over time. A trajectory of medium-high joy and calmness, increasing after venepuncture and low stress and decreasing after venepuncture, was associated with the highest odds of return for a second donation within 6 months. Her group went on to use immersive, virtual reality technology that showed 360° footage filmed in a donor centre. Donors undertook emotion regulation tasks in the waiting and refreshment areas of the virtual donation centre. This led to significantly higher levels of joy and calmness. Further work is planned to try to induce favourable emotional trajectories in blood donors with the hope of improving return rates.

CONCLUSION

It is of real value to have a conference devoted to donor health and management, and the talks, posters and discussions covered a wide selection of research, including iron, the epidemiology of donors and recipients, wholeblood donor recruitment and retention and the safety of donors and recipients for plasma and plasma products. Talks from the plenary speakers reviewed modern multi-omic approaches to study red cell quality and the central, perennial question of what motivates donors to give blood and how can this be encouraged.

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CONFLICT OF INTEREST

The author has no competing interests.

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