HAEMATOLOGY ASSOCIATION OF IRELAND

HAEMATOLOGY ASSOCIATION OF IRELAND ANNUAL MEETING 2023

Galway Bay Hotel, Galway
Friday 13 October 2023

LABORATORY SESSION: FRIDAY 13 OCTOBER 2023

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HAEMATOLOGY ASSOCIATION OF IRELAND

LABORATORY SESSION PROGRAMME
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17.00	*Close of Session* *Awards will be announced at Conference Dinner*	*Dr Claire Wynne*

This is a CPD Event

This meeting will also be available as a Hybrid Event and details of how to access this will follow in due course. Please contact Sinead on sinead@sineadcassidy.com for further details.

Paul Fitzsimons, Quality Manager

I studied medical science in university college cork from 2008 to 2012. I went on to do my clinical placement in Waterford University Hospital in 2012 to 2013. I began my career in Blood Transfusion science in the IBTS in Cork and then in the National Blood Centre in Dublin between 2013 and 2016. I then moved to St James' Hospital blood bank where I began my master's degree. In 2017 I moved to University Hospital Limerick blood transfusion laboratory where I completed my master's degree and carried out a project in patient blood management. In 2019 I started my first senior role in the Galway Clinic blood transfusion laboratory and studied leadership & management in UCD. I went on to work as laboratory manager through the pandemic in the Bon Secours Hospital Limerick in 2020. Finally I moved back to University Hospital Limerick in 2022 where I am now working as quality manager in the blood transfusion laboratory.

Julie Long is a distinguished medical scientist currently employed at the Irish Blood Transfusion Service. In 2016, she successfully obtained her Bachelor's degree from the Technological University Dublin having conducted her undergraduate research project evaluating anti-CD38 mitigation methods within the Red Cell Immunohematology Laboratory. She is now on the cusp of completing her Master's degree from Ulster University, where her current research project focused on 'Mitigating the interference caused by anti-CD47 in pre-transfusion serological testing'. Julie Long's dedication and expertise continue to contribute significantly to serological advancement specialising in the area on monoclonal antibodies.

Fiona Murray, Specialist Medical Scientist

I am a Specialist Medical Laboratory Scientist, recently retired April 2023. I spent the majority of my career working in the Haematology Laboratory in University Hospital Galway. After I qualified I spend 6 months working in the transfusion laboratory in St James Hospital, Dublin. I spent 2 years working in Haematology/Blood transfusion in the Royal Prince Alfred Hospital in Sydney, returning to work for a year in Ennis Hospital. I took a career break in 1994 from Galway to work for 1 year in the Blood transfusion dept. of the King Fahad National Guard Hospital in Riyadh, Kingdom of Saudi Arabia. The latter part of my career I spent working and developing the flowcytometry laboratory to ISO 15189 standard. I extended the service to include extensive panels to diagnose Leukaemia/ Lymphomas, analysis of CSF, PNH and stem cell analysis for the Blood and Tissue department. I introduced RCD 11 (Refractory Coeliac Disease type 11) testing by flow cytometry in 2013, which has become an invaluable service to the hospital. I set up MRD for CLL monitoring and before I retired, I introduced MRD monitoring for myeloma to the service which was ISO 15189 accredited. Throughout my career as a Medical Laboratory Scientist, I was a very active member of the MLSA (Medical Laboratory Scientist Association) having served as an agent until I retired. Currently I am promoting the profession in schools.

MANUAL TITRE SCORES DETERMINED BY COLUMN AGGLUTINATION TECHNOLOGY FOR ANTENATAL MONITORING OF ANTI-D ANTIBODIES IN THE NATIONAL MATERNITY HOSPITAL

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Introduction: Haemolytic disease of the fetus and newborn (HDFN) ranges from mild to severe cases (1). It is caused by maternal sensitisation due to either transfusion of an incompatible red cell unit or a feto-maternal haemorrhage during a past or current pregnancy. The most common antibody implicated is Anti-D (2). Anti-D Immunoglobulin Prophylaxis (IP) prevents maternal alloimmunisation by clearing fetal red blood cells that have entered maternal circulation. Passive Anti-D may be detected in the plasma of RhD negative women up to 16 weeks following administration of Anti-D IP. The British Society of Haematology (BSH) guidelines (4), advise that any Anti-D detected in pregnancy, be measured by Continuous Flow Analysis (CFA). Misinterpreting immune Anti-D for prophylactic Anti-D and vice versa can cause HDFN due to insufficient monitoring of immune Anti-D or the absence of Anti-D IP when required (4,5). Titre scores (TSs) are a more accurate reflection of the strength of an antibody than a titre end point result alone. The objective of this study was to validate manual TSs using antibody titre (ATs) by column agglutination technology (CAT) as an alternative method to Anti-D Quantitation (ADQ) for the monitoring of prophylactic Anti-D detected antenatally in RhD negative pregnant women.

Materials and Methods: Sample selection was based on exclusion and inclusion criteria along with an algorithm currently in use in the blood transfusion lab to determine if referral of samples for ADQ is required. A total of 63 samples with varying strengths of Anti-D were referred for ADQ to the Irish Blood Transfusion Service (IBTS) and also tested in house using manual TSs determined by CAT. Sample reproducibility testing to estimate uncertainty of measurement and sample stability testing were also carried out. A cost analysis was performed to compare the cost of referring samples to the IBTS for ADQ with the cost of analysing these samples in the blood transfusion laboratory using manual TSs.

Results: ROC curve analysis indicated that a TS of <30 accurately predicted an ADQ of <0.4IU/ml and a TS of >30 accurately predicted an ADQ of >0.4IU/ml. Therefore, these results show that a TS of <30 accurately predicted the presence of prophylactic Anti-D and a TS of ≥30 accurately predicted the presence of immune Anti-D. The results of the cost analysis showed a potential average saving of 91% or €8000 per year with the introduction of manual TSs for passive Anti-D detected antenatally as an alternative method to referring samples to the IBTS for ADQ.

Conclusion: This study found that manual TSs obtained by CAT were comparable with ADQ by CFA for prophylactic Anti-D. The implementation of this study in the blood transfusion laboratory of the National Maternity Hospital will result in huge cost savings in terms of reduction in cost of referrals and courier transport. There will also be a decreased ADQ workload for the IBTS and improved turn around times for these results.

1. de Haas M, Thurik FF, Koelewijn JM, van der Schoot CE. Haemolytic disease of the fetus and newborn. Vox Sang, 2015 Aug; 109 (2): 99-113. 2. Bruce DG, Tinegate HN, Williams M, Babb R, Wells AW. Antenatal monitoring of anti-D and anti-c: Could titre scores determined by column agglutination technology replace continuous flow analyser quantification? Transfus Med, 2013 Feb; 23: 36–41. 3. Fasano RM. Hemolytic disease of the fetus and newborn in the molecular era. Semin. Fetal Neonatal Med, 2016 Feb; 21: 28-34 4. White J, Qureshi H, Massey E, Needs M, Byrne G, Daniels, G, Allard S. Guideline for blood grouping and red cell antibody testing in pregnancy. Transfus Med 2016 Aug; 26: 246–263. 5. Bolton-Maggs PHB, Poles D, Watt A, Thomas D, Cohen H. The 2012 Annual SHOT Report. Serious Hazards of Transfusion 2012

OPTIMISATION OF AN ASSAY TO DETECT CAR T-CELLS AND T-CELL EXHAUSTION MARKERS POST CAR T-CELL THERAPY

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Introduction: Chimeric Antigen Receptor (CAR) T-cell therapy has emerged as a promising therapy in the treatment of haematological malignancies, however, not all patients experience durable remission. The proliferation and persistence of CAR T-cells *in vivo,* has a direct impact on the therapeutic success of this novel therapy. Currently, in the clinical setting, there is no universal flow cytometric method available for the detection of $CD19^+$ CAR T-cells. CAR T-cell exhaustion, due to prolonged exposure to antigenic stimulation, results in the CAR T-cells losing their response capabilities. There is a requirement to develop a robust and reproducible CAR T detection method for routine monitoring of CAR T-cell quantity and CAR T quality and function post infusion.

Methods: A total of nine samples were obtained from patients at day 30 ±7 days, post CAR T-cell infusion. Peripheral blood mononuclear cells (PBMCs) were isolated from these samples, cryopreserved and subsequently thawed for analysis. Healthy donor buffy pack products (n=3) were used in this study for the optimisation of T-cell activation methods. In addition, antibody titrations and stain index calculations were performed to obtain the optimal antibody concentration.

The samples were analysed by flow cytometry for $CD19^+$ CAR T-cells, using a specific CD19 CAR antibody reagent (Miltenyi Biotec). The samples were also analysed for $CD19^+$ CAR T-cell exhaustion markers. The five exhaustion markers analysed in this study were T-cell Immunoglobulin and Mucin-Domain-Containing Protein-3 (TIM-3), Programmed-Cell-Death-Protein-1 (PD-1), B and T Lymphocyte Attenuator (BTLA), Cytotoxic-T-Lymphocyte-Antigen-4 (CTLA-4) and Lymphocyte-Activation-Gene-3 (LAG3). Healthy donor buffy packs (n=5) were used as controls.

Results: This preliminary study optimised the $CD19^+$ CAR T antigen-specific reagent and demonstrated that it was effective in detecting $CD19^+$ CAR T-cells in patients post CAR T-cell therapy. Absolute $CD19^+$ CAR T-cells counts ranged from 0.37 to 22.7 PBMC/µL and $CD19^+$ cell percentages ranged from 0.69% to 13.6%. At day 30 ±7 days, post infusion, it was demonstrated that patients who had responded to the therapy had an increased expression of exhaustion markers, TIM-3 and BTLA, compared to partial and non-responders. Other markers (PD-1, CTLA-4 and LAG3), were inconclusive at this timepoint.

Conclusions: The success observed with antigen-specific detection of $CD19^+$ CAR T-cells highlights the potential for this method to be utilised in the clinical setting. All patients (n=9) had $CD19^+$ CAR T-cells detected at day 30 ±7 days, post infusion, at levels similar to the limited literature available. The significance of the CAR T PBMC/µL and T-cell exhaustion marker expression, at any given time point will require further planned longitudinal assessment to establish a predictive biomarker for CAR T-cell therapy response. Patients who are currently responding to treatment (n=5 at most recent clinical review), showed increased expression of $CD19^+$ CAR T-cell exhaustion. It can be hypothesised that $CD19^+$ CAR T-cells are expressing exhaustion markers due to significant efforts of the CAR T-cells to eliminate disease. Further evaluation with subsequent patients and additional time points are required to understand the significance of CAR T-cell enumeration and the presence of exhaustion markers for long term patient outcome.

REMOVING INTERFERENCE FROM DIRECT ORAL ANTICOAGULANTS IN ROUTINE AND SPECIALISED COAGULATION ASSAYS USING ACTIVATED CHARCOAL

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Introduction:

Direct oral anticoagulants (DOACs) are increasingly used for the prevention of arterial and venous thromboembolic events. DOACs directly inhibit factors of the coagulation cascade and, as such, can interfere with both routine and specialised coagulation assays[1]. Therefore, the *ex vivo* removal of DOACs from coagulation samples is emerging as an important pre-analytical factor to minimize or eliminate the impact of DOAC-associated interference [2].

Herein, we report a cost-effective, in-house methodology for the removal of DOACs with acid-washed activated charcoal (AC), to minimise potential interferences in routine and specialised coagulation assays on CS-series analysers (Sysmex, Kobe, Japan).

Materials and Methods:

Standard human plasma and commercial material were treated with 20 mg/mL of AC to assess AC-induced interference in routine and specialised coagulation assays in the absence of anticoagulation. Commercial material containing clinically relevant concentrations of rivaroxaban and apixaban were subsequently assayed to determine the ability of AC to remove DOAC-associated interference.

Results:

Treatment of non-anticoagulated samples with 20 mg/mL of AC caused a statistically significant change in the activated partial thromboplastin time, Clauss' fibrinogen and D-dimer concentrations. However, only changes in the activated partial thromboplastin time were considered clinically significant. All other assays remained largely unaffected by treatment with AC. In DOAC-containing plasma samples, therapeutic and supratherapeutic concentrations of apixaban and rivaroxaban were efficiently adsorbed below the limit of quantitation of quantitative testing. DOAC removal by AC corrected clinically relevant prolongations of the prothrombin time and activated partial thromboplastin time, as well as prevented false positives in lupus anticoagulant and false negatives in activated protein C resistance testing.

Conclusion:

Collectively, we report on a cost-effective method of adsorbing rivaroxaban and apixaban *ex vivo* with acid-washed AC prior to routine and specialised coagulation assays.

1. Moser KA, Smock KJ. Direct oral anticoagulant (DOAC) interference in hemostasis assays. Hematology Am Soc Hematol Educ Program. 2021;2021(1):129-133. 2. Siriez R, Dogné JM, Gosselin R, Laloy J, Mullier F, Douxfils J. Comprehensive review of the impact of direct oral anticoagulants on thrombophilia diagnostic tests: Practical recommendations for the laboratory. Int J Lab Hematol. 2021;43(1):7-20.

EVALUATION OF THE SYSMEX XN AUTOMATED HAEMATOPOIETIC PROGENITOR CELL COUNT AS A SURROGATE MARKER FOR FLOW CYTOMETRIC CD34+ CELL COUNT IN AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTS

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Background: Enumeration of peripheral blood stem cells (PBSCs) is essential for determining the optimal timing to initiate the apheresis harvesting process in order to successfully harvest a sufficient harvest yield (≥2 x 10^6 CD34+ cells/kg) for autologous peripheral blood stem cell transplantations (PBSCT).[1] Currently, PBSC enumeration relies on a flow cytometric CD34+ cell count, which requires technical expertise and can be time-consuming. A pre-apheresis PBSC CD34+ count of ≥20 cells/µL is commonly used as the threshold to initiate apheresis. An alternative, fully automated method of counting haematopoietic progenitor cells (HPC) by the Sysmex Corporation utilises the difference in cell membrane lipid composition between early progenitor cells and more mature cells.[2] This study aims to evaluate the performance of the XN-HPC parameter and its value in optimising the current PBSCT apheresis workflow.

Materials and Methods: Within- and between-run precision, repeatability, sample stability and selectivity of the Sysmex XN-HPC parameter were evaluated using XN-CHECK™ IQC and selected patient samples. Pre-apheresis peripheral blood samples (n=28) from 12 autologous PBSCT patients were analysed simultaneously by flow cytometric CD34+ counts and the Sysmex XN-HPC parameter. The statistical analysis of the paired measurements included Wilcoxon's signed-rank test, Spearman's correlation test, Passing-Bablok regression and Bland-Altman difference plots. The diagnostic accuracy of XN-HPC for predicting CD34+ cell counts of ≥20 cells/µL was assessed using receiver operating characteristic (ROC) analysis.

Results: The XN-HPC parameter showed high precision (Coefficient of variation, CV=7%), acceptable repeatability (CV=20.7%), high selectivity and good stability for at least 24 hours. The paired measurements between XN-HPC and CD34+ did not show statistically significant differences. The correlation between the paired measurements was good (rho=0.719; slope=1.32). The mean Bland-Altman difference was 10.8 cells/µL, with a wide 95% limit of agreement (-54.8 to 76.3 cells/µL). An XN-HPC positive cut-off of >78/µL demonstrated excellent specificity (100%) and positive predictive value (100%) for identifying target CD34+ cell count of ≥20/µL, thus serving as a reliable marker for initiating the apheresis harvest process. Conversely, the XN-HPC negative cut-off was ≤9/µL, showing 100% sensitivity and negative predictive value for CD34+ cell counts of <20/µL, indicating its potential to identify cases where apheresis should be delayed, and additional mobilisation may be required.

Conclusions: The study establishes XN-HPC as a viable surrogate for CD34+ cell counts in pre-apheresis peripheral blood samples. Integrating XN-HPC cut-off values into routine PBSCT protocols could significantly improve workflow efficiency. Further validation with larger patient cohorts is necessary to validate its applicability.

1. Bender JG, To LB, Williams S, Schwartzberg LS. Defining a therapeutic dose of peripheral blood stem cells. Journal of Hematotherapy. 1992; 1:(4)329–341. 2. Tanosaki R. Kumazawa T, Yoshida A, Oguni S, Nakano A, Yamagata S, et al. Novel and rapid enumeration method of peripheral blood stem cells using automated haematology analyzer. International Journal of Laboratory Hematology. 2014; 36:(5)521–530.

The Inappropriate Use of the Coagulation Screen in the A&E Department in UHL

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Background: University Hospital Limerick (UHL) Haematology Laboratory has encountered a 26% increase in coagulation profile requests from across UHL Group users over the past 5 years from 85,482 requests in 2017 to 107,706 tests in 2022. Coagulation screens assess haemostatic function and are regularly requested when triaging patients. In UHL, the Coagulation Screen includes Prothrombin Time/International Normalised Ratio (PT/INR) to assess the Extrinsic Coagulation Pathway, and Activated Partial Thromboplastin Time (APTT) to assess the Intrinsic Pathway Factors. Literature advises against the routine use of A&E coagulation studies in the absence of haemorrhage/suspected coagulopathy. Criteria has previously been suggested to indicate the appropriateness of coagulation testing in ED. This criteria includes: evaluation of unexplained bleeding, diagnosing DIC, prior to anti-coagulation, monitoring anti-coagulation and in the presence of severe disease (sepsis/liver disease). Liver disease is associated with hemostatic impairment as the liver is responsible for synthesis of coagulation and anti-coagulation factors as well as fibrinolytic proteins. Fibrinogen Assays, which quantify the amount of fibrinogen in the blood are often reflex ordered by Medical Scientists based on abnormal or unexplained coagulation results to out rule coagulopathy and liver disease. The aim of the study was to assess the incidence of coagulation profile requesting in the A&E department, total proportion of abnormal coagulation screens from A&E and the cost associated with further laboratory testing (e.g. fibrinogen levels) when anti-coagulation and relevant clinical details were not provided.

Materials & Methods: Non-patient level data relating to 2022 A&E attendances was requested from the UHL Planning, Performance & Business Information Department, eHealth Division. The laboratory information and COGNOS software were interrogated for the volume of A&E coagulation profile requests. Prolonged A&E adult coagulation screens from 6th-12th March 2023 were assessed. Abnormal parameters for PT, APTT and Fibrinogen were defined as PT >17s, APTT ≥44s and fibrinogen as <2.0 g/L as per UHL laboratory reference ranges. Request forms from abnormal PT (*n*=86) and APTT (*n*=45) results were screened to determine if anti-coagulation, and relevant clinical details (bleeding/bruising/fall) were provided with the request. Fibrinogen assays (*n*=59) from the A&E department during the same time period were assessed for abnormality. Normal and abnormal Liver Function Tests (ALP,ALT,GGT) in parallel with coagulation screens were documented.

Results: In 2022, UHL A&E department recorded 61,517 adult attendances. It was estimated that 53% of adult patients attending A&E were phlebotomised for coagulation profile tests. The laboratory received 711 PT/INR requests, and 706 APTT requests from A&E over a seven-day period in 2023. A proportion (12.1%) of PT/INR (*n*=86) requests during this period were prolonged with 89.5% of requests failing to provide anti-coagulation details, 97.7% without relevant clinical details and 58.1% of PT/INR requests with normal LFTs. Of the 6.4% prolonged APTT requests (*n*=45), 93.3% failed to provide anti-coagulation details, 95.5% of requests were without relevant clinical details and 47.4% of requests had normal LFTs. A total of 59 Fibrinogen assays were reflex tested based on abnormal PT/APTT findings with only 1.7% (*n*=1) abnormal low Fibrinogen detected.

Conclusion: For PT, APTT and fibrinogen results, ≥88%, ≥94%, and ≥98% of findings respectively were within the laboratory reference range. Approximately 50% of abnormal coagulation screens had normal LFTs, indicating liver dysfunction was absent and the cause of the prolonged screen was unclear. This study recommends the introduction of clear testing criteria to minimise the incidence of overutilization of the coagulation test profile in A&E. Providing the laboratory with anti-coagulation details at the point of test requesting could also help reduce unnecessary reflex fibrinogen assays and in-turn reduce laboratory-associated costings.

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The Validation of a Laboratory Method for Reticulocyte Haemoglobin (Ret-He) on the Sysmex XN Platform and an Evaluation of its Relationship to Established Biochemical Markers of Iron Metabolism.

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Introduction: Iron deficiency (ID) is prevalent worldwide (Steinbicker Muckenthaler, 2013) and may progress to iron deficiency anaemia (IDA) if untreated. Conventional indices of iron status e.g. Haemoglobin (Hb), serum ferritin (SF) and transferrin saturation (TSAT), do not always accurately reflect current iron stores. In addition, underlying clinical disorders may cause anaemia of inflammation (AI), which can also adversely impact the key markers used to assess iron (Fe) metabolism.

It is increasingly recognised that Ret-He is a useful index of the current erythropoietic state in bone marrow and therefore can act as a rapid and more effective test of ID (Auerbach et al., 2021). In particular, Ret-He reflects current availability of Fe for erythropoiesis (Flately, 2019).

This project initially describes the validation of a Ret-He method, with the subsequent assessment of its relationship with laboratory indices of Fe metabolism and its potential to differentiate ID, IDA and AI clinical states.

Materials and methods: Following ethical approval, samples from 504 patients aged 40-70 years were randomly selected and analysed for, Ret-He, C-reactive protein (CRP), Hb, SF and TSAT. Ret-He was measured by fluorescence flow cytometry on the Sysmex XN 20, with TSAT and CRP analysed using Roche Cobas 701 and SF using Siemens ADVIA Centaur XPT. Based on the above results, four clinical groups were established for further study representing normal iron status (n= 450), ID (n=16), IDA (n=43) and AI (n=22).

Results: The validation procedure for Ret-He demonstrated that the Ret-He is precise, reproducible, and has stability of up to 3 days.

Within the clinical groups, the median Hb for the normal and ID cohort was 14g/dL and13g/dL respectively. The median Hb for both the IDA and the AI groups was 11g/dL.

The median Ret-He value for IDA was 25pg which is lower than the normal reference range (29.7-35.4 pg.) as expected. Of note, the median Ret-He in ID (31 pg) and AI (31 pg) was within the normal range.

There was a strong correlation between the Ret-He and the IDA cohort (R=0.67). Also, the Ret-He correlated strongly with SF in ID (R= 0.66) and IDA (R = 0.5) cohorts. In contrast, there is only poor correlation between the Ret-He and the other cohorts studied.

In reference to the iron studies, there was a only a weak positive correlation between Hb and SF in ID (R=0.23), IDA, (R=0.24) and normal cohorts (R= 0.24) and there no correlation for the Al cohort (0.09). A moderate correlation was observed between Hb and TSAT in the IDA (R=0.51) and in the AI (R=0.43) cohorts and a weaker correlation observed in the normal cohort (R=0.21) and the ID (R = 0.06) group.

Conclusion: The findings indicate that the Ret-He has the potential to act as an adjunctive predictive marker of IDA. A larger cohort study would further elucidate a putative role for Ret-He in IDA and validate the results found in this pilot study.

Auerbach, M., Staffa, S. J., and Brugnara, C. (2021) Using reticulocyte haemoglobin equivalent as a marker for iron deficiency and responsiveness to iron therapy. Mayo Clinic Proceedings, 96 (6), pp. 1510-1519 DOI: 10.1016/j.mayocp.2020.10.042 (accessed 10 March 2022) Flatley, E. (2019) Advanced haematology parameters: Reticulocyte haemoglobin equivalent (RETHe). LabWire Laboratory News and Analysis for Clinicians. Available at https://d2xk4h2me8pjt2.cloudfront.net/webjc/attachments/55/f5adecd-012219-labwirefinal.pdf (accessed 14 December 2021) Steinbicker, A.U., and Muckenthaler, M.U. (2013) Out of balance-systemic iron homeostasis in iron-related disorders. Nutrients, 5(8), pp. 3034-306. doi:10.3390/nu5083034. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3775241/ (accessed 28 February 2022)

The Challenges and Impact associated with providing a National Adult Haemoglobinopathy Service in a Large Tertiary Hospital

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INTRODUCTION

Sickle Cell Disease (SCD) and Thalassaemia are both genetically inherited haemoglobin disorders commonly referred to as haemoglobinopathies. SCD is one of the most prominent inherited genetic disorders worldwide. Patients with severe manifestations of these disorders may require lifelong red cell transfusions to prevent and treat complications such as stroke, acute chest syndrome and anaemia. The number of patients with a haemoglobinopathy in Ireland has increased rapidly over the last number of years with over 700 paediatric and adult patients now nationwide.

St. James's Hospital (SJH) has provided the National Adult Haemoglobinopathy Service since 2016.

MATERIALS AND METHODS

A retrospective audit of red cell usage in SJH over an eight-year period (January 2015 – December 2022) was performed. The data for this audit was collected from monthly blood component usage reports routinely prepared by the Haemovigilance officers. Patients with a haemoglobinopathy diagnosis (SCD or Thalassaemia) who had received ≥1 transfusion in the hospital during the audit period were identified and additional data was collected for this patient cohort. The additional data included: age, gender, red cell antigen phenotype/genotype, antibody production and reported transfusion reactions. The additional data gathered on the haemoglobinopathy patients was obtained through the laboratory information system (LIS) and electronic patient record (EPR).

RESULTS

The mean number of red cell units transfused annually in SJH during the audit period was 11,546. In 2015, there were 11,002 red cell units transfused in SJH compared to 12,497 units transfused in 2022. There was a 13.6% increase in the number of red cell units transfused in SJH between 2015 and 2022.

The total number of patients attending the haemoglobinopathy service increased from 112 in 2015 to 256 in 2022.The number of patients that were transfused by the haemoglobinopathy service increased from 15 in 2015 to 78 in 2022. Inherent differences in red cell antigen expression between the haemoglobinopathy patients and the mainly Caucasian Irish donor population were observed. The majority (60%) of haemoglobinopathy patients expressed the R0r genotype. The R0r genotype occurs in 1.25% of the Irish donor population[1].

CONCLUSION

The number of haemoglobinopathy patients receiving transfusions in SJH has caused the level of annual red cell usage in SJH to be maintained at over 11,000 units despite optimal patient blood management. In order to ensure the future provision of red cells for the growing haemoglobinopathy patient cohort in Ireland, the diversity of the Irish donor population must be improved to reduce the disparity in red cell antigen expression between donors and haemoglobinopathy patients. Also, improving the ethnic diversity of the donor pool will provide a supply of blood of similar genotype to the haemoglobinopathy patients thus reducing the number of group O RhD negative red cells transfused to haemoglobinopathy patients and conserving the limited national supply of group O RhD negative units.

1. Browne A, Kinsella A, Keogh M, Morris K, Field S. A Snapshot Of ABO , RH, And JK Blood Group Systems in Modern Ireland. Health Science Reports. 2021 Jun;4(2).

DRIED BLOOD SPOT GLYCATED HAEMOGLOBIN; AN ALTERNATIVE METHOD FOR MONITORING GLYCAEMIC CONTROL IN PAEDIATRIC PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Background: Glycated haemoglobin (HbA1c) levels correspond to long-term glycaemic control in Diabetes Mellitus. Elevated HbA1c levels are linked to the adverse effects of Diabetes. HbA1c levels in paediatrics are measured using point of care or whole blood samples. Dried Blood Spots (DBS) are less invasive blood collection devices and were assessed as an alternative method for monitoring HbA1c levels in paediatric patients with Type I Diabetes.

Material and Methods: Paediatric patients having POC HbA1c measured at diabetic appointments in University Hospital of Limerick were recruited. DBS HbA1c samples were collected and stored at 4°C (n =33), RT (n =27) or under both temperature conditions (n=25) for four days, before HbA1c extraction and measurement on the Tosoh HLC-723®G11 analyser. Statistical analysis included: linear regression, Bland-Altman plots and Pearson's correlation coefficient, precision, bias using external quality control material, and stability of DBS HbA1c in days.

Results: POC and DBS HbA1c concentrations at 4°C and RT were strongly correlated with r =0.695 and r =0.845 respectively, and had a linear relationship ($p<0.05$). Under different temperature conditions, T1DM DBS HbA1c samples were stable ≤6 days, had precision ≤7.5%, and had a positive increase over time (≤+12.5%). Bias ranged from -3.3%-4.8%. In contrast, non-diabetic DBS HbA1c samples were unstable, HbA1c concentrations changed from non-diabetic to diabetic levels by day four storage.

Conclusion: DBS HbA1c samples stored at 4°C and analysed by day four post sample collection were stable and more suitable (than DBS stored at RT) for the monitoring of glycaemic control in paediatric diabetic patients. DBS HbA1c require temperature storage (4°C) during transportation to the laboratory and during storage prior to analysis. DBS HbA1c samples in non-diabetic patients were unstable and imprecise and therefore should not be used to monitor glycaemic control in non-diabetic paediatric patients

COLD HANDS; WARM HEART? COLD- AGGLUTININS IN CARDIO-PULMONARY BYPASS. A REVIEW OF PRE-SURGICAL LABORATORY SCREENING OVER A 10 YEAR PERIOD

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Introduction: Cold Agglutinins (CAs) are red cell specific antibodies that can cause complement activation and red cell agglutination at low temperatures. The majority of CAs are not clinically significant and are found incidentally in healthy individuals.

Patients who undergo cardiothoracic surgery may require hypothermic Cardiopulmonary Bypass (CPB) intra-operatively. Due to the rare possibility of red cell agglutination in hypothermic conditions; some centres, including Cork University Hospital (CUH), perform pre-operative CA screening on all patients undergoing CPB. However, there is limited evidence that this approach detects clinically significant CAs that are not otherwise detectable via clinical history and other laboratory indicators of haemolysis.

Published data show positive CA screening rates as low as 0.2% and argue that additional cardiac pre-operative screening is neither necessary nor justified[1]. We examined the CUH CA screening tests and associated serological and haemolytic parameters over a 10 year period to assess this hypothesis for our patient cohort.

Materials and Methods: At the CUH Blood Transfusion Laboratory the CA screen is performed by incubating patient plasma with group O red cells at room temperature for thirty minutes and then macroscopically examining for agglutination. All CA test requests are logged on the Dedalus APEX Laboratory Information System (L.I.S.) with the code 'CAGG'.

Using Cognos Impromptu Software, we searched all of the 'CAGG' screens performed in CUH for the ten year period from 01/01/2013 to 31/12/2022. We further assessed the data using a location- specific filter in order to exclude non pre-operative cardiac patients. We then used the local electronic patient record (EPR) system to search the associated patient diagnosis and surgery performed. We used the APEX L.I.S. to collect information on serological testing, haemolysis markers and transfusion requirements.

Results: Over the 10 year period, 5369 CA screens were performed in total and 59 (1.1%) were positive. However, 4570 tests were performed on cardiac patients with 19 (0.4%) positive screens, for a total of 17 patients. Of those 17 patients, 4 had Cold Agglutinin Syndrome and required all of their laboratory assays to be performed at 37 degrees. 2 others had a positive antibody screen due to weak cold non-specific antibodies. A further 2 had a raised MCHC most likely due to cold agglutinins. The other 9 patients showed no other laboratory indications of Haemolysis. Of the 17 patients only 4 had EPR operative notes available. 3 underwent cold cardioplegia with no adverse outcomes while the other patients surgery was modified to warm cardioplegia.

Discussion and Conclusion: Our results for the CA screen at CUH show a low positivity rate of 0.4%. Of the 4,570 Cardiac patients who were screened for CAs 17 were found to be positive. 8 of these 17 had other strong Laboratory results indicative of CAs. Our data furthermore shows that even with a positive CA screen, the CPB protocol is not always modified.

Based on the low positivity rate and the lack of CA result impact on perioperative management, the burden this additional testing places on the Transfusion Laboratory and hospital resources does not seem to outweigh the benefit of CA screening.

1.Sapatnekar, S., & Figueroa, P. I. (2016). Cold Antibodies in Cardiovascular Surgery: Is Preoperative Screening Necessary?. American journal of clinical pathology, 145(6), 789–795.

IMPROVED STANDARDS IN RED BLOOD CELL ANTIBODY TESTING DURING PREGNANCY IN THE COOMBE HOSPITAL

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Introduction: Establishment of a woman's red cell antibody status during pregnancy is essential to identify the presence of clinically significant antibodies. Clinically significant antibodies are antibodies that are implicated in Haemolytic Disease of the Foetus and Newborn (HDFN) and/or Haemolytic Transfusion Reactions (HTR). Common antibodies implicated in both HDFN and HTR include anti-D, anti-c and anti-K amongst others. Clinically significant antibodies must be monitored during pregnancy to stratify the risk of HDFN to the infant and to ensure the provision of suitable blood for the mother and/or infant at delivery. The British Society of Haematology (BSH), the Royal College of Obstetricians and Gynaecologists (RCOG), the National Institute for Health and Care Excellence (NICE) and The National Women and Infants Health Programme (NWIHP) have guidelines recommending the blood group and antibody status of a pregnant woman be established at both booking and at 28-weeks' gestation, regardless of RhD status. Considering these guidelines, a review of current practice within the Coombe Hospital was performed.

Materials and Methods: A retrospective audit was conducted using the Laboratory Information Management System, LabCentre, to identify women who had a clinically significant antibody detected for the first time at delivery between the 1st of November 2021 and the 31st of October 2022. Assessment of the potential clinical implications for both these women and their neonates was then performed.

Results: Despite current BSH, RCOG, NICE and NWIHP guidelines, 87% of women attending the Coombe do not routinely have the recommended 28-week Group & Screen (G&S). Most of these women are RhD Positive. 7,026 women delivered between the studied period. Of the women who delivered during this period, a total of 59 (59/7,026) had a red cell antibody identified during their pregnancy. Forty-three women (43/59) had antibodies detected at booking, two RhD Negative women (2/59) had novel antibodies detected at 28-weeks' and one woman (1/59) had a new antibody incidentally detected. 22% (13/59) of women's red cell antibodies were first detected at delivery with only approximately 30% of women having a delivery (G&S) sample taken. Clinically significant antibodies were detected in twelve (12/13) of these women. Eleven women (11/12) had an antibody of a single specificity detected (anti-c=3, anti-E=2, anti-Jka= 2, anti-Fya=1, anti-C=1, anti-M=1 and anti-Cw=1). One woman (1/12) had antibodies of multiple specificities detected (anti-c and anti-E). All women with antibodies first detected at delivery were RhD Positive. None of these women had received the recommended 28-week sample. A wide variation in the clinical outcome and laboratory parameters were observed in the neonates of women who had a clinically significant antibody first detected at delivery. Most neonates were unaffected. Of greater significance, suitable blood for these women may not have been available at the time of delivery had they urgently required it.

Conclusion: These findings highlight the need to introduce the recommended 28-week G&S. Implementation of this sample would enable appropriate risk stratification and management of HDFN and, ensure the provision of suitable blood for these women should the need to urgently transfuse at delivery arise.

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EVALUATION OF ANTIBODY TITRATION TESTING PROCEDURES ON THE GRIFOLS IMMUNOHAEMATOLOGY SYSTEMS

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Introduction: Establishing an accurate and precise titre of an identified antibody is crucial for the management of foetuses at risk of potential Haemolytic Disease of the Foetus and Newborn (HDFN). Antibodies of the Rh, Duffy, Kidd and Kell blood group systems have all been linked with HDFN of varying severities. While Anti-D and Anti-c are quantified in pregnancy owing to the availability of a national standard, all other antibodies are titrated. An Antibody Titre (AT) of 32 or greater is considered the threshold for HDFN risk (excluding Anti-K) resulting in referral to a specialist in foetal maternal medicine for vigilant foetal monitoring and possible treatment intervention. Given the essential role of the AT in guiding treatment regimens, it is paramount that Blood Transfusion laboratories adopt a robust, verified, and standardised AT method. Automation can offer standardised protocols, walk-away capabilities, elimination of most human error and clearly defined AT endpoints. An evaluation of the antibody titration testing procedures on the Grifols immunohaematology systems, including two fully automated Erytra Eflexis systems and one manual method, against the pre-existing manual Bio-Rad method was performed.

Materials and Methods: An analytical verification and method verification of the Grifols immunohaeamatology systems, against the current manual Bio-Rad AT method for AT establishment was performed. Accuracy, precision, and the analytical ranges of each Grifols immunohaemotology system were defined. A method verification of 30 plasma samples containing non-ABO clinically significant IgG antibodies of various known specificities was then performed. Each sample was analysed on each Grifols and Bio-Rad platform to obtain an AT. Bland Bland-Altman plot analyses were used to examine method bias while a Box-and-Whisker plot, with accompanying Wilcoxon signed-rank tests and a Freidman test were performed to analyse statistically significant differences between the methodologies. Finally, a Spearman's rank correlation was then performed to evaluate agreement between the Grifols and Bio-Rad methodology.

Results: The analytical validation perceived the manual Grifols AT method as the superior Grifols method for establishing the AT of a patient. However, the differences were slight, and the statistical analyses conducted for the method verification demonstrated that there were no statistically differences between any of the Grifols AT methodologies and the pre-existing Bio-Rad methodology. Concordance existed across all methodologies for establishing the AT of a patient. It appears that neither automated nor manual method is entirely superior at establishing the AT of a patient.

Conclusion: The Grifols automated Erytra Eflexis platforms and the Grifols manual AT methodologies demonstrated a high level of agreement and concordance to the Bio-Rad AT method. All AT methods are suitable to determine the AT of a patient. However, the Grifols automated AT method can offer the advantages of speed, time, and ease of use. Most importantly, it can improve patient care through improved turn-around-times for AT reporting enabling timely appropriate referrals to foetal-medicine units for further foetal monitoring and possible treatment intervention. Therefore, the Grifols platforms appear to be an excellent alternative to the Bio-Rad manual AT method and may serve to improve laboratory operations in the future.

White, J., Qureshi, H., Massey, E., Needs, M., Byrne, G., Daniels, G. and Allard, S. (2016) Guideline for blood grouping and red cell antibody testing in pregnancy. Transfusion Medicine, 26(4), 237-314.

DOAC-Remove: A pre-analytical strategy to overcome direct oral anticoagulant interference in lupus anticoagulant testing.

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Anti-phospholipid syndrome (APS) is an acquired systemic autoimmune disease characterised by the presence of the antiphospholipid antibodies (APL) that target the phospholipid-binding proteins such as β2-glycoprotein 1 and prothrombin (Arreola-Diaz *et al*., 2022). APS diagnosis is based on a clinical and laboratory criterion where one of each must be met (Noureldine *et al*., 2019). A clinical presentation of one or more episodes of an arterial, venous, or small vessel thrombosis, within any tissue or organ and pregnancy morbidity must have occurred. Along with this, the laboratory criteria of being persistently positive for one of the APL; lupus anticoagulant (LA), anticardiolipin or anti-β2-glycoprotein 1 must be present (Miyakis *et al*., 2006) (Mezhov *et al*., 2019). To demonstrate the persistence of the positive APL testing should be carried out on more than two occasions with at least 12 weeks apart from the clinical event (Tektonidou *et al*., 2019).

LA testing is an essential as part of the diagnosis of APS, however from a laboratory prospective it can be problematic when conducting LA testing on patients taking direct oral anticoagulants (DOACs) such as apixaban, rivaroxaban and dabigatran. The LA assay is a clot-based haemostasis assay which is sensitive to DOACs which can result in erroneous results. Because of this, it is not recommended to perform LA testing when a patient is actively prescribed a DOAC as per the guidelines set out by the International Society on Thrombosis and Haemostasis (ISTH) (Devreese *et al*., 2020). To overcome the interference DOACs have on LA testing a commercially available product, DOAC-Remove has been manufactured whereby this study aims to assess effectiveness of DOAC-Remove in the absorption of DOACs from patient plasma.

Within this study, 39 DOAC treated plasma samples (23 on apixaban, 14 on rivaroxaban and 2 on dabigatran) and 98 control patients plasma samples from those not on a DOAC were treated with and without DOAC-Remove while also carrying out DOAC quantification and LA testing. Results determined that DOAC-Remove should only be used on DOAC treated patients. DOAC-Remove effectively reduced the DOAC levels in the plasma from 100.51 to 2.38 ng/mL for apixaban (p=<0.001), 134.36 to 1.76 ng/mL for rivaroxaban (p=0.001) and 54.16 to 7.35 ng/mL for dabigatran. To conclude, this study successfully investigated the ability DOAC-Remove has on absorbing the DOAC within the plasma and describes that rivaroxaban is the most effective DOAC in overcoming the interference with LA testing to allow for the accurate reporting of LA detection. Through the promising results gathered, future direction to this study would involve continuing to gather more samples for analysis for each DOAC and to eventually implement DOAC-Remove into the laboratory practise. This in turn would improve patient care and management by allowing for LA testing to be carried out on patients on DOACs and without the need to temporarily hold off the dose which may led to the increased the risk of thrombosis.

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