

Sunday 18 October
HSANZ Symposium: MPD incl CML

0900-1030
Hall C
0900

The Pathogenesis of Myeloproliferative Syndromes

Radek Skoda

University Hospital Basel, Experimental Hematology, Department of Biomedicine, Basel, Switzerland

An acquired somatic mutation in the JAK2 gene resulting in a valine to phenylalanine substitution at position 617 (JAK2-V617F) is present in the majority of patients with myeloproliferative disorders (MPD). The JAK2-V617F mutation is located in the "pseudo-kinase" domain of JAK2, which physiologically exerts an inhibitory effect on the kinase domain. The mutation is thought to de-repress the kinase activity by an allosteric mechanism. Expression of the mutated JAK2 cDNA in mouse models resulted in increased white blood cell numbers and red cell mass, recapitulating the MPD polycythemia vera phenotype. Mutations in exon 12 of the JAK2 gene have been identified in a subset of MPD patients negative for JAK2-V617F and mutations in exon 16 were found in 18% of patients with B cell ALL and Down syndrome. A number of observations suggest that JAK2-V617F in patients with MPD may be acting in concert with mutations in as yet unknown gene(s). Recently, mutations in the TET2 gene have been found in about 15% of patients with MPD and up to 30% of patients with myelodysplastic syndromes (MDS). The presentation will focus on the biology of the disease and the relation between the known mutations and the phenotype. In particular, the following questions will be addressed:

1. Why does JAK2-V617F cause 3 different clinical phenotypes?
2. Is JAK2-V617F the primary cause of MPD?
3. What is the role of JAK2 mutations in leukemic transformation?
4. How do mutations TET2 relate to the mutations in JAK2?

The currently available data suggest that JAK2 mutations may be sufficient to cause MPD. However, evidence has accumulated indicating that a considerable proportion of MPD patients carry additional mutations. Predisposition to acquiring JAK2 mutations can be increased in cases of familial MPD and the hereditary component is more frequent than is generally assumed.

Sunday 18 October
HSANZ Symposium: MPD incl CML

0900-1030
Hall C
0945

Optimising Response in CML

Tim Hughes

Department of Haematology at SA Pathology, RAH, Adelaide, South Australia

(1) Is there really any important difference between the patient who achieves CCR but not MMR by 18 months and the patient who achieve MMR? We know that patients who achieve CCR by 18 months have a good prognosis and that patients who achieve MMR by 18 months do even better. The risk of disease transformation over the next 5 years is 4% compared to 1% in patients achieving MMR. Perhaps a more significant consideration is the risk of loss of CCR which is 24% in patients with CCR but not MMR by 18 months compared to 4% in patients with MMR ($p=0.001$). This data is based on the IRIS trial. A single centre study from the Hammersmith supports these findings.

(2) Does this failure to achieve MMR in a patient who has achieved CCR justify any change in management? We don't have enough data to answer this question but the following considerations may help.

(3) With a further 6-12 months of standard dose imatinib, what are the chances these patients will achieve MMR. Patients in the IRIS study who maintained the 400 mg dose of imatinib had a probability of MMR of 40% at 12 months and 56% at 24 months. An estimated 55% of patients who had achieved CCR but not MMR at 12 months went on to achieve MMR by 24 months. In the TIDEL trial where higher doses of imatinib were used 62% of patients in CCR without MMR at 12 months achieved MMR by 24 months. Patients in the TIDEL study had a dose increase from 600 to 800 mg /day (or maximally tolerated dose if they couldn't tolerate 800 mg) at 12 months.

(4) Is achieving MMR between 12 and 24 months just as favourable as achieving this response by 12 months?

The MD Anderson studies would support the notion that earlier molecular response is more favourable (ASH 2006) in terms of progression free survival. Our recent studies from the IRIS trial suggest that MMR achieved early or late are equally reassuring in terms of the risk of progression.

(5) If a higher dose of imatinib is used and is actually successful at reducing BCR-ABL to a lower level over the next 12 months has this really improved the prognosis? There is now emerging evidence from the MD Anderson studies suggesting that inducing an earlier and deeper molecular response using higher doses of imatinib leads to better progression free survival.

(6) Can we identify patients who are more likely to benefit from higher dose imatinib. We have recently demonstrated that an in-vitro assay to measure OCT-1 mediated influx of imatinib into blood cells taken from CML patients pre-therapy is predictive of molecular response to imatinib therapy. Patients who have low OCT-1 activity are more likely to have suboptimal response, especially if they receive dose modifications in the first 12 months of therapy. Patients with high OCT-1 activity generally do very well on imatinib, and dose intensity does not seem to be so important. Thus a patient who has not achieved MMR at 12 months and has low OCT-1 activity is quite likely to have a substantial improvement in molecular response if the dose is increased, whereas patients with high OCT-1 activity do equally well whether or not the dose is increased.

(6) Are plasma imatinib measurements helpful for optimising response? Studies from the French group and the IRIS study suggest that patients with higher trough plasma imatinib levels are more likely to achieve CCR and MMR. These studies suggest a role for measuring imatinib blood levels in patients who are not responding optimally, have compliance issues or are taking drugs that may affect imatinib metabolism.

In the future we may be able to use predictive assays like OCT-1 activity and ongoing monitoring with RQ-PCR for BCR-ABL as well as imatinib blood levels to determine where a dose increase will probably be beneficial and where it may not be worthwhile.

Sunday 18 October
ANZSBT Symposium: Transfusion Practice

0900-1030
Hall B
0900

Artificial Oxygen Carriers and Erythropoietin Use in Trauma Patients

Lena Napolitano

Abstract not received at time of going to print

Sunday 18 October
ANZSBT Symposium: Transfusion Practice

0900-1030
Hall B
0945

Intra-operative Blood Salvage

Dafydd Thomas

Abertawe Bro Morgannwg University NHS Trust, Swansea, Wales, UK

The role of intra-operative blood salvage in blood conservation is now firmly established. Of all the autologous transfusion methods, intra-operative salvage has stood the test of time and is proving that an operative method of blood conservation can easily be incorporated into the vast array of techniques that are implemented to ensure an improved surgical outcome. Other methods of autologous transfusion have not been as successful for a variety of reasons, but salvaging autologous red cells at the time of surgical haemorrhage seems to be a very sensible option.

However there is a need to ensure that quality and safety issues are addressed and that standard operating procedures are followed to maintain the highest standard of care. Whilst decreasing exposure to allogeneic blood and preservation of existing blood supplies are both laudable aims, it is not good practice to replace a treatment that currently has such high quality assurance with an alternative, albeit an autologous option, that is not equally quality assured.

The UK has been obliged to look at alternatives to allogeneic transfusion mainly due to the vCJD problems, and although donor supplies remain healthy, demographic change and the impact of the precautionary approach to deal with prion disease may yet lead to a significant shortfall in allogeneic supplies. Anticipating this problem a significant amount of expertise and resource has been invested in developing educational and technical support for hospitals wishing to develop and promote intra-operative cell salvage programs. The UK Cell Salvage Action Group (UKCSAG) has developed educational material, technical factsheets and competency assessment literature to enable a standardized UK approach to teaching and training. The positive spin-off is that this work and supporting educational literature is available free of charge from the website – www.transfusionguidelines.org.uk.

Sunday 18 October
ASTH Symposium

0900-1030
Hall D
0900

Tissue Factor – In Health and Disease

Nigel S Key

University of North Carolina, Chapel Hill, NC, USA

Tissue factor (TF) is a 47kDa trans-membrane glycoprotein that when bound to FVII(a), initiates coagulation. The presence of extravascular TF has been recognized for well over a century, but a specific role in coagulation initiation was first proposed in 1905, when ‘thrombokinas’ was proposed as one of the essential 4 factors needed for coagulation by Morawitz. Until the 1990s, it was not appreciated that very low levels of intravascular TF can be detected in the circulation. Subsequently, in both human studies as well as in mouse models of thrombosis, much attention has focused on the measurement of TF procoagulant activity, particularly in circulating microparticles (MPs). MPs are sub-micron sized fragments of membrane and cytoplasm released by most cells that are undergoing activation or apoptosis. Detection of MPs in cell-free plasma by flow cytometry is a considerable technological challenge that has only recently been subjected to standardization efforts. However it is easier to measure TF procoagulant activity on MPs, and we, and others, have developed assays to address this issue. The data indicate that MP-TF activity is detectable in normal individuals, and is elevated in certain pathologic states. Perhaps the disorder in which the potential importance of circulating MP-TF is gaining increased acceptance is in the pathogenesis of cancer-associated thrombosis. Several groups have demonstrated elevated levels of MP-TF activity, particularly in patients with certain forms of malignancy such as pancreatic or non-small cell lung cancer. While these data are intriguing, there is as yet no good evidence from appropriately designed prospective studies that circulating MP-TF can be considered a true biomarker of thrombotic risk. Finally, although not as well studied in disease states, it should not be forgotten that cell-associated TF – particularly on monocytes, and probably also on activated platelets – may be equally or even more important than the pool of TF which is present on derived MPs.

Sunday 18 October
ASTH Symposium

0900-1030
Hall D
0945

Stratifying Risk of Recurrent Venous Thrombosis

Paul Kyrle

Medical University of Vienna, Austria

Over the last years several clinical and laboratory risk factors of recurrent venous thrombosis have been identified. These include male sex, proximal deep-vein thrombosis or pulmonary embolism, recurrent venous thromboembolism, residual vein thrombosis, elevated levels of coagulation factors, natural coagulation inhibitor deficiencies, antiphospholipid antibodies or hyperhomocysteinemia. The impact of many of these risk factors on the recurrence risk is however moderate or is even regarded controversial. Determination of some laboratory markers of thrombophilia either lacks standardization or is too elaborate for routine purposes. Many patients with venous thromboembolism carry more than one risk factor and their combined risk of recurrence is unknown. Most importantly, clinical studies that would show a benefit of extended anticoagulation in patients with one of the aforementioned risk factors are lacking. Thus, routine thrombophilia screening is no longer warranted and predicting recurrence in an individual patient remains a major challenge.

Use of global coagulation markers that encompass the effects of clotting and/or fibrinolytic defects may improve risk assessment. There is now strong evidence that patients with a low d-dimer level after withdrawal of anticoagulation have a low risk of recurrence and may not benefit from long-term anticoagulation. Similarly, low in vitro thrombin generation is associated with a moderate recurrence risk. In a future step, global coagulation markers need to be integrated with clinical risk factors of recurrence. Validated and simple scoring systems may improve stratification of patients into low and high-risk categories regarding their recurrence risk and may optimize duration of anticoagulation.

Sunday 18 October
Nurses Symposium

0900-1030
Hall A
0900

Patient Blood Management

Sherri Ozawa

Englewood Hospital and Medical Center, Englewood, New Jersey, USA

The transfusion of allogeneic blood is an issue of vital importance to healthcare systems, consumers, and providers the world over. Constant and ever present concerns about existing and emerging pathogens, skyrocketing costs, and the struggle for adequate supply place increased focus on the pressing issues that surround this common procedure. Recent years have seen the publication of hundreds of studies and analysis that link the transfusion of blood products to poor patient outcomes, including longer length of hospitalization, increased morbidities, increased mortality, and many other serious negative complications. This information compels physicians, nurses, and other providers to dramatically change their use of transfusion from a default procedure to manage anemia to a relatively rare intervention when evidence of potential benefit outweighs risk. Statistics from throughout the world give evidence to the fact that clinicians use blood transfusions based on individual and institutional habit, instead of true clinical need. Such lack of an evidence based approach to this serious procedure repeatedly puts both patients and providers at risk.

Vital to this end is the concept of Patient Blood Management, an organized approach aimed at conserving a patient's own blood and minimizing or avoiding the need for the transfusion of allogeneic blood components. Patient Blood Management also proactively addresses the needs of patients for whom blood is not an option. This can be accomplished through the combined use of new and existing pharmaceuticals, devices, management strategies, and medical and surgical techniques which can obviate the need for transfusion, or at the very least ensure that benefit outweighs risk in a given transfusion related clinical situation.

Sunday 18 October
Nurses Symposium

0900-1030
Hall A
0915

Patient Blood Management in Australia: Where are We Up to?

Barbara Parker

BloodSafe Program South Australia

Increased patients' exposure to allogeneic blood products has been associated with increased incidence of transfusion related complication and significant financial implications. Allogeneic blood remains a freely given but inherently limited resource.

Blood management is a philosophy to improve patient outcomes through the appropriate provision and use blood, its components and derivatives by integrating all available techniques to reduce or avoid the need for blood transfusion. It is a patient centred, multidisciplinary, multimodal, planned approach to patient care.

There is clear scope to optimise the management of transfusion practice using the Three Pillars of Patient Blood Management:

- Optimising pre-operative Hb through detection, diagnosis and treating reversible anaemia (eg iron deficiency)
- Minimising blood loss
- Optimising physiological tolerance of anaemia

Patient blood management programs are evolving in a number of states. This presentation explores some of the barriers and potential solutions, possible nursing models and outlines examples of blood management practices across Australia.

Sunday 18 October

0900-1030

BMTSAA Symposium: Regulation - Implementation and Impact

Meeting Rooms 1/ 2

0900

Regulation from the Auditor's Perspective

Wendy Harris

National Association of Testing Authorities (NATA), Silverwater, NSW

The presentation will discuss NATA requirements for accreditation of Apheresis units and where the accreditation of apheresis units is at present. It will also explain the process and what has been found in the first few assessments.

Sunday 18 October

0900-1030

BMTSAA Symposium: Regulation - Implementation and Impact

Meeting Rooms 1/2

0920

The Impact of Quality Management on a Collection Service

Bev Wake, Ann Canty, Rebekah Lamb and Peter Casey

Haematology Day Centre, Royal Adelaide Hospital, Adelaide, South Australia, Australia

The Haematology Day Centre (HDC) of the Royal Adelaide Hospital has a contract to collect haemopoietic progenitor cells and other blood components as required by apheresis for autologous or allogeneic transplantation with the Therapeutic Products Facility (TPF) of the Institute of Medical and Veterinary Science.

As part of the process of attainment of a Therapeutic Goods Administration (TGA) licence in 2003 by the TPF to manufacture therapeutic goods from human blood and blood components, the HDC implemented a quality system in accordance with the "Australian Code of Good Manufacturing Practice -Human Blood and Tissues 2000". The National Pathology Accreditation Advisory Council's (NPAAC) decision to include the collection process in apheresis units in a national standard as outlined in "Requirements for Procedures related to the Collection, Processing, Storage and Issue of Human Haemopoietic Progenitor Cells 2007" will impact on management of collection services and has resulted in review of documentation and practices in the apheresis setting.

No conflict of interest to disclose

Sunday 18 October

0900-1030

BMTSAA Symposium: Regulation - Implementation and Impact

Meeting Rooms 1/ 2

0935

NPAAC Guidelines and Requirements – Current Issues

Nancy Messino¹ & Annette Trickett²

¹Royal Children's Hospital, Melbourne, VIC, Australia; ²BMT Network NSW, Sydney, NSW, Australia

The National Pathology Accreditation Advisory Council (NPAAC) has recently released the third edition of the Requirements for Procedures Related to the Collection, Processing, Storage and Issue of Human Haemopoietic Progenitor Cells. In an effort to attain global harmonisation, this edition is based on the FACT-JACIE international standards, but formatted to NPAAC style.

The second edition NPAAC document was only a guideline and inspection / accreditation via NATA was voluntary. The third edition document contains standards, and compliance is mandatory.

The major differences between the second and third edition NPAAC documents are the inclusion of requirements for collection facilities and more stringent requirements for processing laboratories. This session will focus on detailing the new requirements and give suggestions on how the more challenging areas can be met.

Sunday 18 October
HSANZ Symposium: BM Failure

1100-1200
Hall C
1100

Pathogenesis and Treatment of Bone Marrow Failure

Neal S Young

Hematology Branch, National Heart, Lung, and Blood Institute and Center for Human Immunology, National Institutes of Health, Bethesda MD, USA

The human bone marrow failure syndromes include acquired aplastic anaemia, myelodysplasia (MDS), paroxysmal nocturnal haemoglobinuria (PNH), and constitutional Fanconi anaemia and dyskeratosis congenita (DKC). These diseases share pathophysiologic features and effective treatments, and clinical observations and basic laboratory studies have been mutually informative. In all the syndromes, deficient stem and progenitor cells characterize the haematopoietic failure and lead to pancytopenia and death from infection, bleeding, anaemia and the complications of chronic transfusion. In acquired aplastic anaemia, immunosuppressive therapy with antithymocyte globulin (ATG) and cyclosporine is effective in most cases, implicating an immune mechanism of marrow destruction. T cells producing type I cytokines induce apoptosis in hematopoietic target cells; this process is interrupted by ATG but the exact mechanism of action of effective therapies is not clear. Some MDS also responds to ATG, and target antigens resulting from chromosome aberrations have been identified. Mutations in genes of the telomere repair complex and related protective proteins are the aetiology of DKC, and these genes also are mutated in some adults with apparently acquired aplastic anaemia. In the laboratory, short telomeres lead directly to genomic instability and aneuploidy, and in the clinic they are the major risk factors for late clonal evolution to monosomy 7 MDS from aplastic anaemia; constitutional mutations in *TERT*, the telomerase gene, also occur in *de novo* acute myeloid leukaemia. Androgens, historic therapy for marrow failure, positively regulate *TERT*. Mutations in telomerase complex genes also affect regeneration and repair beyond the bone marrow, of lung (pulmonary fibrosis) and liver (cirrhosis). Aplastic anaemia thus is a model of genetic factors interacting with environment, resulting in organ failure and malignant transformation. Current and future treatments can target specific molecular pathways, in immune effector cells and hematopoietic target cells, and appropriate patient populations.

Sunday 18 October
ANZSBT Symposium: Transfusion Safety

1100-1200
Hall B
1100

Patient Safety and Blood Transfusion

Paul Ness

Transfusion Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

The only positive benefit of the AIDS epidemic and its associated publicity has been the increased utilization of alternatives to blood transfusion. Based upon the increased perception of the infectious risks, reduction of homologous blood transfusions has been recommended and the increased utilization of alternatives to transfusion such as autologous blood has taken place. Physicians are now encouraged to use drugs without biohazardous risks in favor of blood components. Patients with von Willebrand's disease are given DDAVP rather than cryoprecipitate to improve hemostasis, aprotinin and other fibrinolytic inhibitors have been used in high blood loss surgeries, many patients are receiving hematopoietic growth factors to prevent or treat perioperative anemia, and new agents such as recombinant VIIa have been used off-label for a growing list of hemorrhagic conditions. Older agents such as vitamin K and fibrin sealants are increasingly being used as adjunctive therapy for bleeding and hemorrhagic prophylaxis. This review will focus upon a number of pharmacologic agents that have the potential to reduce bleeding complications in patients undergoing surgery and thereby limit the quantities of allogeneic blood components they require.

In addition to autologous options including perioperative hemodilution and blood salvage the quest to provide transfusion safety may include the use of blood substitutes in the future or modifications of current blood components (leukocyte reduction, pathogen inactivation) that may reduce the risk of transfusion complications. A number of these approaches are under development and appear to be efficacious for some clinical indications. In other studies, drugs and growth factors that may reduce the need for transfusions may cause safety concerns such as tumor recurrence, renal dysfunction, and thrombotic complications. Although reducing the quantity of blood components that are transfused to a perioperative patient is an important goal, the ultimate goal of any transfusion alternative should be to permit the patient to undergo surgery with the lowest possible risk of morbidity or mortality. Reduction of blood transfusion should not be regarded as a primary endpoint or the ultimate goal; if reducing transfusion involves increased risks from adverse effects of drugs or other manipulations, the benefit to the patient may be minimized or in some cases eliminated.

Sunday 18 October
ANZSBT Symposium: Transfusion Safety

1100-1200
Hall B
1130

Pathogen Reduction by Inactivation Technologies – The New Frontier for Safeguarding Cellular Blood Products?

Ken Davis

Transfusion Medicine, SA Pathology – Royal Adelaide Hospital, Adelaide, Australia

Although the infectious risks of blood transfusion are remarkably small, the current multi-layered approach of donor screening, testing and deferral is unlikely to have as much impact in the future as it has in the past.

Pathogen inactivation [PI] technologies have all but eliminated the infectious risks of plasma-derived protein fractions and will potentially provide additional protection against both known and as-yet-unidentified agents.

The treatment of blood components using PI technologies continues to evolve and the impact of PI on product quality and recipient safety remains paramount and is yet to be fully determined.

The presentation will focus on the issues surrounding pathogen inactivation of blood components and how they contrast with those involved in plasma fraction manufacturing.

References

Prowse C: Properties of Pathogen-Inactivated Plasma Components. Transfus Med Rev. 2009 April 23 (2):124-133.

Proceedings of a Consensus Conference: pathogen inactivation – making decisions about new technologies. Transfus Med Rev. 2008 Jan;22 (1):1-34.

Barbara J. Bryant, MD; Harvey G. Klein, MD: Pathogen Inactivation The Definitive Safeguard for the Blood Supply. Arch Pathol Lab Med. 2007;131:719–733.

Sunday 18 October
ASTH Symposium: Current Controversies

1100-1200
Hall D
1100

Thrombophilia and Pregnancy Complications – To Test or Not to Test

Claire McLintock

National Women's Health, Auckland City Hospital, New Zealand

Until the mid 1990s, the connection between haematology, obstetrics and the thrombophilias was confined to the antiphospholipid syndrome - pregnancy complications such as recurrent miscarriage, fetal death and preeclampsia, in women with lupus anticoagulant, anticardiolipin and beta2 glycoprotein 1 antibodies. Thromboses and infarcts frequently found in the placenta of women with these pregnancy complications prompted studies to examine a potential and biologically plausible relationship between the inherited thrombophilias and placental mediated obstetric complications. As with inherited thrombophilias and venous thromboembolism, the promise of a simple blood test to identify women at risk from these serious pregnancy complications was just too alluring. The floodgates opened to release a deluge of case control and cohort studies investigating the association of various combinations of placental mediated pregnancy complications with inherited thrombophilias. Odds ratios and 95% confidence intervals emerged with widely ranging results. Extrapolation of odds ratios led many clinicians to believe that having one of the inherited thrombophilias increased the risk of women developing one a pregnancy complication de novo or having a recurrence of such a complication in a subsequent pregnancy. Moreover, in the absence any data from randomised clinical trials, many women were given thromboprophylaxis with low molecular weight heparins to prevent such pregnancy complications.

However, recently, the backlash has begun. Some authors¹ have challenged the importance of the inherited thrombophilias in the placental mediated pregnancy complications and called for an end to thrombophilia testing outside the setting of clinical trials. Two prospective studies have failed to confirm an increased risk of preeclampsia in women with thrombophilias. A nested case-control study from Canada⁴ showed no increase in the prevalence of FVL, PT20210 and the MTHFR polymorphism in women with preeclampsia (n=113) compared to women (n=443) with uncomplicated pregnancies, [OR 1.2 (95%CI 0.3-4.1); OR 1.1 (95%CI 0.1-8.8); OR 0.2 (95%CI 0.2 (0.1-1.0), respectively. A large prospective cohort study⁵ revealed similar rates of preeclampsia in women (n=134) who were heterozygous for FVL (n=5, 3.7%) compared to women (n=4751) without the mutation (n=141, 3%), [OR 1.3 (95% 0.4-2.8)]. Similarly, studies have failed to demonstrate that women with FVL or PT20210 are at increased risk of fetal loss.⁶ Entering the second decade of the new millennium what should clinicians do? To paraphrase the immortal bard, "To test, or not to test: that is the question."

1. Rodger MA, Paidas M, McLintock C, et al. Inherited thrombophilia and pregnancy complications revisited. *Obstet Gynecol* 2008; 112(2 Pt 1):320-4
2. Kahn SR, Platt R, McNamara H, et al. Inherited thrombophilia and preeclampsia within a multicenter cohort: the Montreal Preeclampsia Study. *Am J Obstet Gynecol* 2009; 200: 151.e1-9.
3. Dizon-Townson D, Miller C, Sibai B, et al. The relationship of the factor V Leiden mutation and pregrna
4. Coppens M, Folkeringa N, Teune MJ, et al. Outcome of the subsequent pregnancy after a first loss in women with the factor V Leiden or prothrombin 20210A mutations. *J Thromb Haemostat* 2007 Jul;5(7):1444-8

Sunday 18 October
ASTH Symposium: Current Controversies

1100-1200
Hall D
1130

To Bridge or Not To Bridge? – Managing Perioperative Anticoagulation

Christopher M Ward

*Northern Blood Research Centre, University of Sydney;
Department of Haematology and Transfusion Medicine, Royal North Shore Hospital,
St Leonards, NSW*

Longterm use of warfarin is increasing in the community, particularly for atrial fibrillation. Managing anticoagulation around major surgery or an invasive procedure can be challenging, with risks of both thromboembolism and bleeding. “Bridging” implies perioperative switching of patients from warfarin to (low molecular weight) heparin. There are little trial data to guide this practice, and a wide range of clinical opinion. It is important to consider the risks for each individual patient and their procedure. With most bridging protocols, there will be a short period of subtherapeutic anticoagulation during which the patient is at risk of thromboembolism (TE). We can calculate a daily risk of TE recurrence, but this may be significantly increased by surgery itself and postoperative immobilisation. Patients with low-risk atrial fibrillation (AF) may not require bridging anticoagulation and warfarin can simply be ceased 5 days prior to surgery. Similarly, patients with venous TE more than 3 months prior may only require prophylactic LMWH for bridging. The most problematic groups are patients with high-risk AF or mechanical heart valves; here, standard bridging protocols appear sufficient to prevent venous events but not stroke. More aggressive anticoagulation, such as a monitored unfractionated heparin infusion, may be needed to avoid arterial TE.

Bridging protocols can increase the rates of clinically relevant bleeding, particularly if heparins are restarted too soon after surgery. Bleeding events can trigger prolonged delays in anticoagulation and put the patient at risk of TE. For high-risk surgery, LMWH should be restarted at a prophylactic dose, or withheld for more than 24 hours. Successful bridging strategies require the cooperation of the surgical and anaesthetic teams. Prospective trials of bridging protocols are currently underway; these trials are clearly needed to guide clinical practice.

Sunday 18 October

1100-1200

Nurses Symposium: Extreme Haematology Nursing Out of the Metropolitan Area

Hall A
1100

Transfusion in the Top End

Julie Domanski

Royal Darwin Hospital, Darwin, Northern Territory, Australia

The role of the Northern Territory Transfusion Nurse is a unique and challenging one. Although the Northern Territory is one-sixth of the Australian landmass it has less than one percent of the population. It has the smallest population (220 000) and population density of all of the Australian states and territories.

The five Northern Territory public hospitals are located in Darwin, Alice Springs, Katherine, Nhulunbuy and Tennant Creek. These hospitals are not only isolated from the rest of Australia, they are also isolated by great distances from one another. The distance between Darwin and Alice Springs is 1500kms. Each hospital provides a transfusion service; however the three smaller hospitals hold only a small stock of blood products and provide a limited transfusion service.

The NT hospitals do not have a central managing body; each functions as an independent institution. At present there is limited or no co-ordination of nursing and medical education, pathology services and quality activities between the sites. This has proved to be quite a challenge for introducing standardised transfusion practice, performing transfusion quality activities, and co-ordinating transfusion education. The workforce in the NT, particularly in health, is very transient with many staff on short contracts from one to six months. Also many positions remain vacant for long periods of time as it is difficult to attract suitably qualified staff to work in remote areas. This can affect the level of transfusion service provided by each individual hospital.

The Transfusion Nurse currently reports to two senior staff members at the Royal Darwin Hospital. There is no direct reporting line that covers all five hospitals. The establishment of a territory-wide Transfusion Committee in March 2009 was a major milestone.

Sunday 18 October

1100-1200

Nurses Symposium: Extreme Haematology Nursing Out of the Metropolitan Area

Hall A

1130

Assisting the Development of Outpatient Day Centre in India

Lisa Elliot

Abstract not received at time of going to print

Sunday 18 October

1100-1200

BMTSAA Symposium: Post Transplantation Chimerism Analysis

Meeting Rooms 1/2
1100

Chimerism Analysis and Methodology – The RAH Experience

Judy Stevens, Michael Vo, Monika Kutyna, Pamela Dyson, Ian Lewis
SA Pathology- RAH, Adelaide, South Australia, Australia

In transplantation medicine, chimerism refers to the co-existence of cells from two individuals in the one body. In patients who have undergone allogeneic transplantation, donor cells should be present in the blood or bone marrow. Chimerism testing quantitates the percentage of donor cells in the recipient and is used initially to monitor engraftment and later for possible relapse.

Quantitation of donor chimerism utilises differences in donor and recipient polymorphic genetic markers. We use a PCR-based method utilising polymorphisms known as short tandem repeat (STR) units -multiple copies of an identical DNA sequence, 2 to 5 base pairs long. A commercially available STR identity kit, called Identifiler is used, with probes for 16 different STR loci. STR units are highly polymorphic, and differences between the donor and recipient in at least some of the 16 loci are expected. Using this kit, all 16 loci may be tested with the aim of finding at least three informative markers.

Suitable informative markers are found by testing donor and recipient material collected prior to transplant and these markers are subsequently used for all testing. Generally, the first sample for chimerism testing is taken one month after the transplant and at regular intervals thereafter. Testing is done using either peripheral blood or bone marrow.

Chimerism analysis is a multi-step procedure comprising density gradient separation of mononuclear cells, sorting of cells into three subsets, subsequent extraction and amplification of the DNA followed by separation by genescan (capillary electrophoresis) technology.

Genescan results are analysed using Identifiler software. For pre-transplant material all sixteen markers are analysed, while post-transplant three markers are usually analysed.

We have utilised this procedure to follow engraftment in 19 patients with MM, 26 CML, 33 lymphoma and 77 AML. We have also performed testing on patients following double cord transplant.

No conflict of interest to disclose

Sunday 18 October

1100-1200

BMTSAA Symposium: Post Transplantation Chimerism Analysis

Meeting Rooms 1/2

1120

Chimerism and MRD post-SCT in children. A guide to immunotherapy in ALL?

Tamas Revesz, Heather Tapp, Colin Story, Judith Stevens & Pam Dyson
SA Pathology at Women's & Children's Hospital and IMVS, Adelaide

Stem cell transplantation is used to improve results in high-risk and in relapsed acute lymphoblastic leukaemia (ALL). Monitoring the level of minimal residual disease (MRD) and chimerism post transplant usually shows rapid reduction of MRD and establishment of full donor chimerism. If MRD remains detectable and/or chimerism shows increasing patient signal, it usually signals resistant disease and the prognosis is poor.

Recent advances in MRD and chimerism monitoring enable us to intervene in some cases of mixed chimerism. In the first instance this takes the form of rapid tapering of immunosuppression. If this approach doesn't work or the patient is already off immunosuppressive therapy, the next step is to introduce immunotherapy – preferably at a time when there is still relatively small leukaemia burden. This can be achieved through the use of donor lymphocyte infusions. The ultimate aim is to provoke grade 2 graft-versus host disease (GVHD) which in turn is treated promptly to prevent rapid deterioration due to progressive GVHD.

There is some evidence that early-stage GVHD is associated with increased leukaemia-free survival without long-term toxicity. Whilst this approach works in some of the patients, the majority who relapse post SCT seem to present with such rapidly expanding leukaemia that there simply isn't the time for immunotherapy to work.

Sunday 18 October

1100-1200

BMTSAA Symposium: Post Transplantation Chimerism Analysis

Meeting Rooms 1/2

1140

Chimerism Analysis and GvHD

Cheryl Hutchins

Abstract not received at time of going to print

Sunday 18 October
ASTH: Barry Firkin Oration

1200-1300
Hall C
1200

Guidelines for Venous Thromboembolism Prophylaxis –Complexity, Confusion, Controversy

John Fletcher

University of Sydney and Westmead Hospital, Sydney, New South Wales, Australia

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are major health problems with deaths from venous thromboembolism (VTE) greater in number than deaths from bowel cancer, prostate cancer, breast cancer and road traffic accidents. VTE is responsible for 0.2% of hospital admissions and 7% of hospital deaths and can lead to long term complications of pulmonary hypertension and post thrombotic chronic venous insufficiency. Mechanical and pharmacological prophylactic modalities have been shown to be effective in randomised control trials, with hip and knee joint replacement surgery providing a useful model for testing of efficacy of pharmacological agents for VTE prophylaxis. Anticoagulants are associated with bleeding risk which may compromise surgical outcomes in the short and long term. Bleeding is a much more readily apparent complication for the surgeon whose experience of fatal PE will be limited due to the overall low incidence of clinical VTE and with the majority of VTE events occurring after hospital discharge. There are abundant guidelines on VTE prophylaxis such as those from the American College of Chest Physicians (ACCP), the International Union of Angiology (IUA), the UK National Institute of Clinical Excellence (NICE) and the American Academy of Orthopaedic Surgeons (AAOS), with each guideline interpreting extensive data and assigning grades of recommendations according to level of evidence. Patients entered into randomised control trials do not necessarily reflect everyday clinical practice and newer interventional techniques are increasingly being used where there is limited or no information on VTE risk. Nevertheless, rational guidelines are needed for clinicians who have to make judgements for individual patients, weighing up the risk of development of VTE against the risks of available prophylactic modalities. Prevention of VTE remains one of the most important safety interventions in the management of surgical and medical patients.

Sunday 18 October

1400-1530

HSANZ BMTSAA Nurses Combined Symposium: Transplantation 1. Which alternative donor to use?

**Hall C
1400**

Choosing The Optimal Donor - Going Beyond Siblings

Sergio Giralt

Department of Stem Cell Transplantation and Cellular Therapies of the University of Texas M.D. Anderson Cancer Center, USA

Over the last 5 years the field of allogeneic stem cell transplantation has undergone major changes. The availability of reduced intensity conditioning regimens have expanded the pool of potential patients, while the advent of molecular typing and increases in the size of the volunteer unrelated donor banks, increases in cord blood transplantation and the use of post transplant cyclophosphamide as GVHD prevention post haploidentical allograft has vastly increased the pool of potential donors. This means that for patients without an identical sibling donor various alternatives exist: 1) Matched volunteer donor; 2) cord blood transplantation; 3) mismatched related transplant. The optimal source of stem cell will depend on patient age, urgency of stem cell transplant and donor availability. No prospective studies comparing different sources of stem cell have been performed, however, registry studies suggest a benefit for cord blood transplantation in paediatric patients when compared to unrelated donor marrow or peripheral blood stem cells. Prospective trials are urgently needed to provide guidance to patients and physicians.

Sunday 18 October

1400-1530

HSANZ BMTSAA Nurses Combined Symposium: Transplantation 1. Which alternative donor to use?

**Hall C
1445**

Cord Blood

Jeff Szer

*Department of Clinical Haematology & BMT Service, The Royal Melbourne Hospital
VIC 3050, Australia*

Umbilical cord blood (CB) was shown in to contain sufficient haemopoietic progenitor cells (HPC) to engraft in an appropriately conditioned individual more than a decade ago. First applied clinically in the paediatric population, the increasing availability of donor units, understanding of histocompatibility requirements for reliable engraftment and the use of multiple simultaneous CB units has led to increasing use in the adult population. In 2007, 59 patients received CB transplants 19 of whom were over the age of 15 years. Intriguingly, the total nucleated cell numbers required for engraftment are approximately one log lower for CB when compared with bone marrow and this observation, combined with differences in the immunological characteristics of CB have resulted in a different portfolio of conditioning and immunosuppressive regimens than those usually used in bone marrow or peripheral blood stem cell transplantation. Nevertheless, there are many common factors common to all three stem cell sources of prognostic importance: most importantly, cell dose and histocompatibility. Cell dose is of particular importance in larger adult recipients and the observation that ultimate engraftment is derived from only one of the multiple CB units infused and the biological characteristics of the “dominant” unit may help to further improve selection of donors. A major barrier to more widespread adoption of CB transplantation in the adult population of Australia and New Zealand is delayed engraftment and the downstream clinical and resource implications of this. CB is rapidly becoming a mainstream alternative cell product for transplantation which will result in almost all patients requiring a donor being able to find one. Current studies with ex-vivo expansion will, if ultimately successful, help to abrogate the engraftment issue and further increase the clinical use of CB transplantation.

Sunday 18 October

1400-1530

HSANZ BMTSAA Nurses Combined Symposium: Transplantation 1. Which alternative donor to use?

**Hall C
1505**

Haploidentical

Ken Bradstock

Abstract not received at time of going to print

Sunday 18 October
ANZSBT Symposium: The Universal Blood Cell

1400-1530
Hall B
1400

Towards a Universal Blood Supply – Fact or Fiction?

Martin L Olsson

Dept. of Clinical Immunology and Transfusion Medicine, University and Regional Laboratories, Skåne, Sweden

Dept. of Laboratory Medicine, Lund University, Lund, Sweden

Eliminating the risk for blood-group-incompatible transfusion errors and simplifying blood logistics by creating a universal blood inventory is a challenging idea but not a new one.

This lecture will summarize current concepts that have been proposed and tested to generate universally transfusable red blood cells (RBCs) for administration to patients. Several principally different lines of thinking have been applied to achieve this goal, for instance antigen masking, antigen stripping, humanised animal RBCs, siRNA-silenced blood group genes and *ex vivo* RBC production. These efforts will be described and their *pros* and *cons* mentioned briefly.

One of the projects will be discussed in more detail: An international team of collaborators explored the possibility to use a newly discovered family of bacterially-derived exoglycosidases to cleave off the A- and B-defining sugars in a specific manner on RBCs to convert them enzymatically into cells that type as group O. These RBCs were characterized extensively by immunohaematological and biochemical methods. In addition, storage parameters were measured and toxicological tests performed with the most promising enzyme candidates. Finally, clinical trials involving healthy volunteers have been started for the first time with group A RBCs converted to type as group O. The presentation will review the current status of this technology and its potential for introduction in the clinical component preparation laboratory.

Of all the strategies envisioned to make universal blood, only the enzyme-converted RBCs have yet been tested in humans. The other principles have shown promising initial results and some were tested in animal models. However, each methodology faces major challenges including difficulties to scale up production, regulatory issues, high costs for clinical trials and production. Thus, it will be several years before any of these products can become available to patients in need for blood. In the meantime, matching efforts and group O shortages will continue.

Sunday 18 October

ANZSBT Symposium: The Universal Blood Cell

1400-1530

Hall B

1445

Kodecytes – Designer Red Cells Created with KODE™ Biosurface Engineering Technology

Stephen Henry

AUT University & KODE Biotech Ltd, Auckland, New Zealand

KODE™ Biosurface Engineering Technology comprises the use of specifically designed constructs to introduce functional moieties (including antigens) into the surface of living cells without affecting their vitality or innate functionality. Previously this attachment technology has been used to create ABO sensitivity controls, by adding carbohydrate A and B antigens onto group O red cells and creating A_{weak} and/or B_{weak} kodecytes (a generic term used to describe cells modified by KODE™ cell surface engineering). Additionally kodecytes bearing Lewis, Galili, fluorophores and biotin have also been created.

Recently the repertoire of constructs able to be attached to cells has been expanded to include blood group peptides and other diagnostic markers. This has allowed for the creation of specialised red cells for antibody identification and expansion of the antigenic profiles of antibody screening and identification panels. The ability to also use this technology *in vivo* has opened up new possibilities for the study of incompatible transfusion reactions and the tracing and targeting of circulating cells.

Sunday 18 October
ANZSBT Symposium: The Universal Blood Cell

1400-1530
Hall B
1505

Use of Modified Red Cells as Diagnostic Tools

Damien Heathcote

CSL Bioplasma Immunohaematology, Melbourne, Australia.

Human red blood cells have been in routine use for diagnostic purposes ever since Landsteiner bled his colleagues in 1900 and discovered the ABO blood group system. During this time they have remained essentially unchanged although their use has been extended into newer platforms such as Column Agglutination Technology and solid phase. Donor units destined for reagent manufacture have traditionally been washed and resuspended into diluents without any alteration to their antigenic makeup.

In 2005 CSL produced the first example of a diagnostic human red cell reagent that had blood group antigens added to it *in vitro* in the form of blood group A and B antigens. These cells have enabled a closer control of the ABO blood grouping process as well as allowing the user to routinely experience weak ABO reactions. The design and manufacture of the samples prevents predictive result interpretation which also makes them ideal for staff competency assessment and monitoring.

In late 2008 CSL released into international markets the first example of a human red cell reagent for antibody screening that has the *in vitro* addition of peptide-based antigens. These cells are capable of detecting IgG examples of antibodies directed against the MNS antigens MUT and Mur. These antibodies are more commonly seen in Asian populations and have been shown to be a common cause of haemolytic disease. Donors with glycophorin variants exhibiting these antigens do exist in Asian populations but these cells will also detect non-clinically relevant IgM examples of these antibodies which are more common than the IgG examples, and thus create unwanted testing. The successful addition of both carbohydrate and peptide-based antigens heralds a new age for the use of red cells in the diagnostic arena and opens up numerous possibilities for the creation of cell phenotypes not seen in nature.

Sunday 18 October

ASTH Symposium: Anti-platelet Therapy and Arterial Thrombosis

1400-1530

Hall D

1400

Overview of Anti-platelet Therapy

Huyen Tran

Abstract not received at time of going to print

Sunday 18 October

ASTH Symposium: Anti-platelet Therapy and Arterial Thrombosis

1400-1530

Hall D

1445

Measuring Resistance to Anti-Platelet Drugs – Methods and Clinical Utility

Marco Cattaneo

Clinica Medica, Ospedale San Paolo, Università degli Studi di Milano. Milano. Italy

The definition “resistance to anti-platelet drugs” should be limited to situations in which failure of the drug to hit its pharmacological target has been documented by specific laboratory tests. Aspirin resistance, as determined by specific tests (e.g., serum thromboxane B₂), appears to be rare (1-2%) and, in most instances, is caused by poor compliance. In contrast to aspirin, studies that used specific tests to measure the pharmacological effect of thienopyridines (e.g., VASP phosphorylation) showed a wide variability of responses to these drugs, with significant proportions of subjects (about 30%) who are very poor responders. Inter-individual differences in the extent of metabolism of thienopyridines to their active metabolites is the most plausible mechanism for the observed inter-individual variability in platelet inhibition. The demonstration that some patients may be “resistant” or “poor responders” to the pharmacological effect of anti-platelet drugs, has prompted the need of laboratory monitoring of anti-platelet therapy. However, many published studies have been performed using unspecific tests of platelet function, which identify patients on anti-platelet treatment with high residual platelet reactivity, which is not necessarily due to resistance to anti-platelet drugs. Despite this drawback, identification of patients with high residual platelet reactivity may be useful to predict their risk of atherothrombotic events. However, many studies still need to be done to identify the ideal laboratory test and to answer basic questions on its clinical utility and cost-effectiveness, before monitoring anti-platelet therapy can be recommended in the clinical practice. Until then, monitoring of anti-platelet therapy should be considered for investigational purposes only.

Sunday 18 October
HSANZ Symposium: Multiple Myeloma

1600-1730
Hall C
1600

A Guide for Clinicians on the New Therapies and How They Line Up Against Autologous Transplant

Thierry Facon
CHU Lille, France

The treatment of multiple myeloma (MM) has undergone significant developments in the recent past. The availability of the novel agents, thalidomide, bortezomib and lenalidomide, has expanded treatment options and has improved outcomes for patients. Following the introduction of these agents in the relapsed/refractory setting, they are also undergoing investigation in the initial treatment of MM. A number of phase 3 trials have demonstrated the efficacy of novel agent combinations in the transplant and non-transplant settings and based on these results, standard induction regimens are being challenged and replaced.

In patients not eligible for transplantation, MP-thalidomide (MPT) and MP-Bortezomid (MPV) have been found superior to the traditional MP regimen. Several studies investigating MP-Lenalidomide (MPR) or Lenalidomide-Dexamethasone (Rd) are ongoing (or have been recently completed). Of note MPT and MPV have resulted in median PFS/TTP and OS times around 2 and 4 years respectively, and these results are similar to those achieved in the early 1990s using conventional chemotherapy followed by a single transplant (IFM90)

In the transplant setting, a number of newer induction regimens are now available that have been shown to be superior to VAD (Bortezomib-Dexamethasone, VTD, PAD) For the last 15 years, high-dose therapy(HDC/ASCT) has been a standard therapy for MM in younger patients. The superiority of HDC/ASCT compared to conventional dose therapy is due to a higher very good partial response rate or better (\geq VGPR), which is correlated with prolonged survival (both progression-free and overall survival).Over the past 4 to 5 years, the arrival of novel agents (specifically, thalidomide, bortezomib and lenalidomide) has radically changed treatment regimens, as the use of these new drugs has improved the results of HDC/ASCT to such a degree that the timing and need for HDC/ASCT as first-line treatment of younger patients is currently a key question. This is the rationale of the question raised by the upcoming IFM/DFCI 2010 protocol (VRD + HDC/ASCT vs VRD alone). Additionally, the important issue of maintenance treatment is being investigated.

Sunday 18 October
HSANZ Symposium: Multiple Myeloma

1600-1730
Hall C
1600

Australian Studies in Myeloma

Andrew Spencer

Malignant Haematology & Stem Cell Transplantation Service, Alfred Health, Melbourne, Victoria, Australia 3004

Over the past 20 years a number of multicentre investigator-initiated clinical trials evaluating new therapies for multiple myeloma (MM) have been undertaken in Australasia. The Australian Leukaemia Study Group (ALSG) MM2 trial (1990-1992, n=113) evaluated the impact of Interferon-alpha (IFN) as both a co-induction agent and maintenance strategy. Consistent with other data from this era the positive effect of IFN was marginal and had to be weighed against IFN-induced toxicities. The single arm study of oral induction therapy with cyclophosphamide, idarubicin and dexamethasone (CID) (1997-2000, n=36) suggested equivalent efficacy to VAD and the approach has now been widely adopted in routine clinical practice. A randomised trial of amifostine cytoprotection (1999-2000, n=90) in patients undergoing HDT demonstrated a significant reduction in severe mucositis (33% versus 12%, p=0.02) with the use of amifostine and informed a pilot study (ALLG MM5) (2000-2001, n=10) of very high dose melphalan (220mg/m²) in combination with amifostine that again confirmed the ability of the agent to abrogate melphalan-induced mucositis. Two early multicentre Phase II trials of thalidomide (1999-2003, n=141) undertaken by the group at the Peter MacCallum Cancer Centre demonstrated the lack of feasibility in combining thalidomide with either IFN or celecoxib but did confirm the efficacy of thalidomide in the setting of relapsed MM (ORR 30-40%). Subsequently the Phase III ALLG MM6 trial (2002-2005, n=269) demonstrated that post-HDT consolidation with thalidomide and corticosteroids significantly prolonged both progression free (p<0.001) and overall survival (p<0.004) compared to corticosteroids alone. The results of the study generated significant interest thus stimulating further research activities including the ongoing collaboration between the ALLG (ALLG MM11) and GIMEMA exploring the efficacy of delaying HDT in favour with lenalidomide and alkylating agents and the ALLG MM12 study designed to explore the utility of a variety of measures of post-HDT tumour burden.

Sunday 18 October
HSANZ Symposium: Multiple Myeloma

1600-1730
Hall C
1710

Pathophysiology of Bone Disease in Multiple Myeloma

Andrew Zannettino

SA Pathology-RAH, University of Adelaide, South Australia, Australia

Multiple Myeloma (MM) is an incurable haematological malignancy characterised by the clonal proliferation of malignant plasma cells (PC) within the bone marrow (BM). MM accounts for approximately 1% of all cancers and is the second most common haematological malignancy after non-Hodgkin's Lymphoma (NHL). Each year in Australia, approximately 1,100 people are diagnosed with MM, almost 80% of whom are over the age of 60. Alarming, in the period between 1993 and 2003, there was a 44% increase in the number of Australians diagnosed with MM. The main clinical manifestations of MM are the development of devastating osteolytic bone lesions, bone pain, hypercalcaemia of malignancy, renal insufficiency and increased BM angiogenesis. MM is the most common cancer to metastasize to bone, with up to 90% of patients developing bone lesions. The bone lesions in MM are purely osteolytic in nature, and up to 60% of patients develop a pathologic fracture over the course of their disease. The MM-induced bone lesions are a result of increased osteoclast (OC) activity in areas adjacent to MM PC. This increase in OC activity is also accompanied by a MM PC-mediated suppression of osteoblast (OB) differentiation and activity, resulting in severely impaired bone formation. This presentation will cover our current understanding of the pathophysiology underlying bone disease in MM and will review emerging therapies designed to target MM bone disease.

No conflict of interests to disclose

Sunday 18 October
ANZSBT ASTH Combined Symposium: Critical Bleeding

1600-1730
Hall B
1600

Transfusion Medicine in Acute Bleeding

Dafydd Thomas

Abertawe Bro Morgannwg University NHS Trust, Swansea, Wales, UK

As with many other emergency medical situations, acute bleeding needs to be dealt with in a calm and organised fashion. The parallels between a cardiac arrest situation or dealing with suspected anaphylactic shock are well made and the handling of acute bleeding can be optimised by the use and implementation of a massive haemorrhage protocol. There are a significant number of such protocols in practice but these are usually developed for local use as so many of the hospitals have rather unique features. When reviewing the various examples it becomes obvious that there are a number of similarities. It could therefore be possible to compile a protocol that can be used as a rather basic generic example to be customized by those hospitals that do not already use such emergency protocols.

The protocols produced in this way can contain the latest advice and evidence allowing personnel not familiar with such recommendations to follow an algorithm which helps them to immediately deliver best care.

These protocols need not be considered to be limiting the use of blood components but rather helping the overwhelmed and often nervous clinician to use such a valuable resource effectively and within guideline.

If timely use of blood components can be achieved together with concurrent monitoring of coagulation and physiological variables, the net result may be an improved clinical outcome and more rational use of blood components.

Sunday 18 October
ANZSBT ASTH Combined Symposium: Critical Bleeding

1600-1730
Hall B
1645

Damage Control Resuscitation - Coagulopathy of Trauma

Lena Napolitano

Abstract not received at time of going to print

Sunday 18 October
ANZSBT ASTH Combined Symposium: Critical Bleeding

1600-1730
Hall B
1710

The Role of Fibrinogen Concentrates in Managing Massive Transfusion

Benny Sørensen

Haemostasis Research Unit, Centre for Haemophilia and Thrombosis, Guy's and St Thomas' NHS Trust & King's College London School of Medicine, London, UK

Fibrinogen is a 300 kDa large protein produced in the liver. The average plasma concentration is 1.8-4.3 g/L. Fibrinogen plays a crucial role for haemostasis by i) facilitating platelet aggregation by bridging of glycoprotein IIb/IIIa receptors, and ii) fibrin polymerization trigger via thrombin generation. In addition, fibrinogen is an acute phase reactant. In principal, deficiency of fibrinogen can be inherited or acquired. Congenital fibrinogen deficiency is a miscellaneous coagulation disorder resulting in either hypo-fibrinogenemia causing bleeding symptoms or dys-fibrinogenemia resulting in bleeding or thrombosis tendency. Acquired deficiency of fibrinogen develops in conjunction with other disorders, such as liver disease, disseminated intravascular coagulation, and excessive bleeding.

The role of levels and function of fibrinogen as a haemostatic agent in management of peri-operative and traumatic haemorrhage are grossly underestimated. There may be several reasons for fibrinogen concentrate being overlooked as potent haemostatic intervention. For decades, haematologists have set the lower threshold level of fibrinogen at 1 g/L. Unfortunately, this level has never been clinically validated, yet mentioned again and again, although a series of publications have indicated that the critical level of fibrinogen may be significantly higher. A majority of patients experiencing excessive bleeding are treated with colloid plasma expanders for volume substitution. The presence of colloid plasma expanders or high levels of fibrin degradation product have been reported to induce artificial false high levels of fibrinogen when measure by the Clauss method. These phenomena may further have masked the recognizing and understanding the importance of fibrinogen in management of peri-operative/traumatic bleeding. Finally, the use of plasma expanders such as colloids, gelatine, or dextrans, is now known to induce a coagulopathy characterised by acquired hypo-fibrinogenemia and abnormal fibrin polymerisation. Moreover, experimental studies, animal studies, retrospective clinical surveys, as well as prospective randomised clinical studies have demonstrated excellent haemostatic effect of substitution with a fibrinogen concentrate.

The present presentation review laboratory aspects in evaluation of fibrinogen, the mechanisms of dilutional coagulopathy, and summarize clinical efficacy and safety outcome following intervention with fibrinogen concentrate.

Sunday 18 October

Nurses – Free Communications 1: Apheresis

1600-1730

Hall D

1600

O001

Trouble shooting the way through Therapeutic Plasma Exchange in a 2 year old boy with Thrombotic Thrombocytopenic Purpura (TTP)

Grainne Dunne

Clinical Nurse Consultant Apheresis SCH

Thrombotic Thrombocytopenic Purpura (TTP) is a complex disease process where the first line of management is apheresis, i.e. Therapeutic Plasma Exchange. To add to this complex disease is the challenge of managing an apheresis patient who is only 2 years old!

How do we fine tune apheresis issues such as fluid volumes and blood product replacement in a small body who is already so sensitive to these issues? How can we perfect the apheresis procedure so as to allow this young boy his greatest chance at survival?

There is not a lot of literature on paediatric Therapeutic Plasma Exchange. We therefore need to learn what we can from our own experiences and from our apheresis colleagues with regards to issues such as appropriate blood product replacement and maintaining suitable fluid balances when the body is at high risk of renal failure. Endeavouring to reduce or prevent additional complications such as fluid overload while using apheresis machines designed primarily for adult patients who are less sensitive to fluid changes.

These are some of the complex problems we encountered and examined during the management of this particular patient. Apheresis operators should constantly examine their apheresis practice and should continuously strive towards improved techniques when managing young children in apheresis. This case study also demonstrates the need for apheresis vigilance together with high quality apheresis training and experience.

No conflict of interest to disclose

Sunday 18 October
Nurses – Free Communications 1: Apheresis

1600-1730
Hall D
1615

O002

Managing the Complexities of Renal Patients during Therapeutic Plasma Exchange

Tracy Clarke

Prince of Wales Hospital, Randwick, NSW

Aim

Renal patients pose a unique set of complexities that need to be considered during apheresis procedures. There is an increasing number of renal patients undergoing apheresis particularly pre and post renal transplantation to reduce the risk of acute rejection. Our purpose is to explore these issues and identify safe management strategies for this patient population.

Method

170 procedures in 14 patients were performed for patients undergoing or having undergone renal transplantation or Haemolytic Uraemic Syndrome (HUS). Clinical condition pre and post procedure, complications experienced during the procedure, management strategies and response to treatment was documented and compared. Fluid balance requirements, urine output and dialysis requirements were considered in identifying procedural parameters and individual patient management strategies were developed to reduce the risk of adverse events and improve patient outcomes.

Result

Common toxicities experienced during apheresis were citrate toxicity and hypotension. The rate of citrate toxicity for this patient population was 9.4% compared to 8.1% overall. Interestingly, hypotension defined as a drop in BP of greater than 10% from baseline or systolic BP less than 100mmHg was documented in only 2.4% compared with 12% overall. Of greater significance was the additional adverse event related to transfusion of fresh blood products which was documented in 7 of the 14 patients and a reaction to promethazine was noted in 3 patients. Procedures were performed at varying fluid balances ranging from 80% to 100% fluid balance depending on patient needs and changes to individual patients run parameters were made following an adverse event with success in preventing further events.

Conclusion

Renal patients pose unique and different clinical challenges when undergoing apheresis procedures compared to other patient populations. Careful consideration of individual patient parameters, in particular electrolyte and fluid balance is required to successfully undertake apheresis while minimising adverse events.

No conflict of interest to disclose

Sunday 18 October
Nurses – Free Communications 1: Apheresis

1600-1730
Hall D
1630

O003

Plasma Exchange for treatment of Chronic Intractable Urticaria – A Single Case Experience

Fran Owen¹, Pauline Warburton¹, Robert Loblay²

¹ *Haematology Department, Wollongong Hospital, Wollongong, NSW, Australia*

² *Allergy Unit, Royal Prince Alfred Hospital, Sydney, NSW, Australia*

Aim

Chronic idiopathic urticaria is defined as recurring episodes of hives lasting more than 6 weeks. One third of patients have an autoimmune mediated urticaria, often experiencing more severe symptoms. Quality of life can be markedly affected. Management includes minimizing stress, overheating and alcohol. H1 and H2 antagonist drug therapies may be of benefit. Oral steroids may be used for severe exacerbations. Third line therapies including immunosuppressive drugs, intravenous immunoglobulin and plasmapheresis have been used in refractory cases. The use of plasmapheresis is rare and there is limited information in the literature regarding this treatment.

A 36 year old woman with an 18 year history of urticaria including angiodema was referred to our unit for a trial of plasmapheresis. Symptoms had improved during pregnancy and it was felt that hormonal factors were involved. Current treatment includes a progestogen implant and regular promethazine and doxepin. She presented intermittently to Emergency for management with adrenaline and steroids.

Method

Plasmapheresis was commenced using a one plasma volume exchange and Albumex 4% for replacement fluid. Treatments were given twice weekly for 4 weeks, weekly for 6 weeks, then second weekly (four months to date) with the aim to extend to monthly treatments if possible. An apheresis Hickman's catheter was inserted early due to poor venous access.

Result

Our patient has had a good response to plasmapheresis. She has stopped all oral medication. She experiences occasional mild urticaria/angiodema which is controlled by doxepin prn. Her quality of life has improved and she is keen to continue this treatment.

Conclusion

The use of plasmapheresis has resulted in a good clinical response in this patient to date. Chronic intractable urticaria is not an uncommon condition but treatment with plasmapheresis is rare as other measures are usually effective. Randomized trials are not feasible and reports of its use are generally anecdotal.

No conflict of interest to disclose

Sunday 18 October
Nurses – Free Communications 1: Apheresis

1600-1730
Hall D
1645

O004

Use of the Fresenius COM.TEC Cell Separator for PBOC Collection: Ongoing Need for Apheresis Operator Interventions

Jennifer Leutenegger, Kari L Mudie, Cheryl J Hutchins, Maree Bransdon, Alanna Geary, Glen A Kennedy
Royal Brisbane and Women's Hospital, Brisbane, Australia

Background

Historically, many transplant units have used the COBE Spectra (Version 6.1MNC) for collection of peripheral blood progenitor cells (PBPC). Recently, Pharmatel Fresenius Kabi has introduced a new technology, the COM.TEC autoMNC (Version 4.02) for PBPC collection. The Fresenius COM.TEC cell separator aims to decrease Apheresis Operator variability in PBPC collection via the autoMNC software programme, which predicts estimated CD34+ cell yield. The challenge for the Apheresis Operator is to adapt to this new technology without impacting on the quality of the PBPC product.

Aim

To compare the PBPC product collected on the Fresenius COM.TEC and the COBE Spectra.

Methods

A prospective study of 48 patients undergoing autologous PBPC collection following mobilisation with cytotoxic treatment and G-CSF. Collection was commenced when circulating peripheral CD34+ cell count was greater than or equal to $10 \times 10^6/\text{kg}$ body weight. Patients were alternatively assigned to have the 1st day of PBPC collection on either the Fresenius COM.TEC or the COBE Spectra cell separator.

Results

Overall, 20 patients had PBPC collected on the Fresenius COM.TEC and 28 on the COBE Spectra. Even though the Fresenius COM.TEC cell separator is a highly automated device, several variables were still found to influence the collection efficiency, including equipment performance, operator technique, institutional requirements and patient variables. Overall, the product collected using the Fresenius COM.TEC yielded similar CD34+ cell yields though a higher total red blood cell count, red blood cell volume and larger total collection volumes in comparison to collections performed on the COBE Spectra. This significantly impacted on laboratory processing post collection. Apheresis Operator interventions to overcome suboptimal product collection on the COM.TEC included manipulation of centrifuge speed, spillover volumes and buffy coat volumes. These interventions appeared to somewhat reduce cellular contamination and overall volume of the Fresenius COM.TEC collections.

Conclusion

Our experience highlights the need to formally assess collection efficiency of new technologies introduced in PBPC collection. Despite the aims of the Fresenius COM.TEC cell separator to decrease Apheresis Operator variability in PBPC collections, we still found that several factors influenced collection efficacy of these machines, and indeed an ongoing need for Apheresis Operators to manipulate machine parameters to reduce cellular contamination and collection volume on the Fresenius COM.TEC.

No conflict of interest to disclose

Sunday 18 October
Nurses – Free Communications 1: Apheresis

1600-1730
Hall D
1700

O005
Calcium Replacement in Apheresis

Andrew Scullion
Calvary Mater Hospital, Newcastle NSW, Australia

Aim

Citrate toxicity and the related effects of hypocalcaemia are an often experienced side effect of apheresis procedures.

The aim of my research was to develop an easy to navigate and functional tool for the apheresis operator to utilise that would aid in maintaining a safe apheresis environment for a haemodynamically stable patient free of or with minimal effects of citrate toxicity.

Method

A literature review of research papers relevant to this specific area of apheresis was undertaken to gain a comprehensive understanding of methods and dose ranges used in the intervention, treatment and management of side effects attributed to citrate toxicity in the apheresis setting. Reference material relating to the pharmacological aspects of treating hypocalcaemia was also reviewed to ascertain correct dosages for treatment pathways consistent with patient parameters.

Result

The result of the literary review formed the basis for the development of a flow chart using mechanical and pharmacological intervention as well as utilising prophylactic means to combat apheresis related citrate toxicity and the effects of hypocalcaemia. See flow chart as attachment.

Conclusion

The development of this flow chart for calcium replacement in apheresis gives the apheresis operator safe, research derived options and guidance for the treatment of citrate toxicity, from it's mild forms to more severe reactions, taking into account individual patient variances and the changing nature of an apheresis procedure.

No conflict of interest to disclose.

Sunday 18 October

Nurses – Free Communications 2: Discharge and Outpatient Care

1600-1730

Hall A

1600

O006

The Development and Implementation of a Nurse-Led Follow-Up Clinic for Patients Who have Undergone an Autologous Stem Cell Transplant (ASCT)

Trish Joyce¹, Linda Clark¹, Sharna Moloney¹, Meinir Krishnasamy¹, David Ritchie^{1,2}, Michelle Fleming³, Kirsten Herbert¹, John Seymour¹, Jenny Byrne³

¹ Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia. ² University of Melbourne, Parkville, Victoria, Australia. ³ Western and Central Melbourne Integrated Cancer Service, East Melbourne, Victoria, Australia

Introduction

The needs of individual patients following ASCT are highly varied. Patients commonly experience ongoing adverse effects such as fatigue, poor appetite, difficulties in resuming work, alterations in body image and sexuality issues. Evidence indicates that traditional medical models of follow-up care may fail to meet patients' psycho-social needs and are sub-optimally effective at management of late effects. Nurse led clinics (NLCs) have been shown to offer patients increased continuity of care, more individualised follow-up and improved psycho-social outcomes. In response to this, we obtained funding to undertake a pilot study to test a nurse-led follow-up clinic for patients who have undergone an ASCT.

Aim

This study set out to test the acceptability, feasibility and safety of the NLC. The aim of the paper is to describe the development of the NLC from its conceptualisation to implementation.

Method

A quasi-experimental pilot study was developed. Phase 1 involved the collection of baseline data to gain an appreciation of problems experienced by this group of patients at Peter Mac. This data was used to inform evidence-based interventions to be delivered in the NLC. Algorithms were developed to support the nurses working in the clinic to ensure safe and consistent practice. Standardised nursing assessment documentation was developed to record the issues presented by patients, the interventions delivered by nurses in the NLC and their efficacy. Caseload and quality assurance data will also be monitored. Phase 2 involves testing the acceptability, feasibility and safety of the NLC and this is now underway.

Conclusion

We believe this innovative model of care has the capacity to enhance the current model of follow-up for patients following an ASCT. We are testing this assumption using evidence, wherever possible, to inform the design, content and evaluation of our initiative.

No conflict of interest to disclose

Sunday 18 October

Nurses – Free Communications 2: Discharge and Outpatient Care

1600-1730

Hall A

1615

O007

An Integrated Outpatient Autograft Program: The Royal Hobart Hospital Model of Care

Gillian Sheldon-Collins, Louise Nicholson

Royal Hobart Hospital, Hobart, Tasmania, Australia

Aim

The Royal Hobart Hospital is the tertiary treatment facility for Tasmania. The Outpatient Oncology/Haematology Service at this hospital has managed an outpatient autologous transplant program for 11 years for patients with a variety of diagnoses. This presentation demonstrates that this model of care is safe and sustainable within the context of Australia's rapidly changing health care environment.

Method

A literature search was conducted and contact made with other Australian hospitals to investigate outpatient models. The Tasmanian Bone Marrow Transplant Data Base was investigated to reveal the number of patients selected for inpatient versus outpatient care, the distribution of transplant related deaths and length of hospital inpatient stay. Protocols supporting the outpatient model of care were reviewed including daily assessment by nursing, medical and allied health staff.

Result

The literature review reveals few published articles regarding models of outpatient care especially in Australia, although several hospitals provide outpatient programs. The Royal Hobart Hospital model demonstrates that patients can be safely supported in the community when ease of access to the tertiary treatment centre is assured. The review of the data base demonstrates the safety of outpatient care by drawing comparisons between transplant related deaths in the inpatient versus the outpatient group. The practice of accurately selecting outpatients without increasing risk is supported by the data.

Conclusion

The Royal Hobart Hospital demonstrates that patients can be carefully selected and safely managed in an outpatient autograft program. This model is adaptable and sustainable as the available human and material resources change over time. This presentation contributes to the available body of knowledge and growing trend toward outpatient services.

No conflict of interest to disclose

Sunday 18 October

Nurses – Free Communications 2: Discharge and Outpatient Care

1600-1730

Hall A

1630

O008

An Evaluation of a New Model Of Nursing Care in Queensland's Leading Haematology and Bone Marrow Transplant Unit

Emily Russell, Annette Barnes, Kylie Hilford

Royal Brisbane and Women's Hospital, Queensland, Australia

Aim

A 'New Model of Nursing Care' (NMNC) project was undertaken at the Bone Marrow Transplant and Haematology Unit, Royal Brisbane and Women's Hospital. This project included the implementation of three new leadership roles (two clinical Team Leaders (TL) one organisational Shift Coordinator (SC)). The aim of this evaluation was to determine if the new leadership roles arising from the NMNC enhanced patient care delivery, staff support and professional development.

Method

Forty-seven permanent nursing staff on the unit were invited to complete the NMNC questionnaire. Twenty three (49%) staff completed and returned the questionnaire. Both qualitative and quantitative data were collected to examine the perception of benefits associated to the introduction of NMNC. Results were categorised into three themes; organisational, clinical and educational.

Results

Organisational – The SC role aimed to manage organisational tasks such as patient flow and human resources. Staff generally reported feeling well supported by their SC, and felt the SC role allows other roles to focus on clinical tasks. However, 4 staff (17%) did not feel they had a good understanding of the SC role and suggested that succession management into the role would improve their understanding.

Clinical - The TL role was designed to lead a group of nurses in the delivery and coordination of patient care. A majority of staff agreed that they were more clinically supported by the TL (87%), and 91% believed the role improved basic nursing care. The presence of the TL in direct patient care was appreciated by 83% of nursing staff despite some variance in the perceived effectiveness of the specific individuals fulfilling the role.

Educational – Ninety-six percent of all staff agreed or strongly agreed that the clinical facilitators, clinical nurses and TL have been readily available to assist and facilitate their education needs. The improvement of staff education through the implementation of NMNC was evident through staff's ability to attend in-services, complete assessments, and attend ward meetings.

Conclusion

Overall, the response to the introduction of the NMNC has been positive. All staff agreed that their ability to provide holistic nursing care has improved and would like to continue working within the framework. Of note, 96% of staff stated that it has encouraged more effective teamwork.

Areas for improvement were identified as communication between the two TL and SC, discharge planning processes, and succession planning of staff into the SC role.

There is no conflict of interest to disclose

Sunday 18 October

Nurses – Free Communications 2: Discharge and Outpatient Care

1600-1730

Hall A

1645

O009

Cancer Outreach Team: Taking the Hospital Out of Myeloma

Kerrie Murphy

CNC Cancer Outreach Team, Prince of Wales Hospital, Randwick Sydney NSW 2031

With recent advances in the field of myeloma treatment patients are living longer with better health outcomes. Also treatment options such as Thalidomide provide the patient with the potential for less hospital stays. However the side effects of these treatments coupled with regular biphosphates infusions, venous access device care and the need for regular pathology tests ensures that the patient is required to attend the hospital setting.

The Cancer Outreach Team (COT) established in 2001 provides community based care for patients with oncological or haematological malignancies who are undergoing treatment at the Prince of Wales Hospital. Due to the changing nature of myeloma management COT has been able to provide a unique home based service that enables the patient to remain at home for the majority of their treatment. Services provided by COT in the home include:

- Venous access device care
- Zoledronic acid infusions
- Bortezomib administration
- Monitoring of oral therapies such as Melphalan, Thalidomide, Prednisone and Lenalidomide
- Triage service for febrile episodes
- Supportive care
- Allied health referral
- Pathology service
- Neulasta and GCSF administration
- Post chemotherapy and peripheral stem cell transplant support

This presentation will outline the unique home based care provided for patients with myeloma by COT at Prince of Wales Hospital.

No conflict of interest to disclose

Sunday 18 October

Nurses – Free Communications 2: Discharge and Outpatient Care

1600-1730

Hall A

1700

O010

The Haematology Step-Down Unit – A Novel Approach to Early Discharge and The Continuity of Care Through Care Co-Ordination

Sandra Liddell & Douglas Joshua

Institute of Haematology, Royal Prince Alfred Hospital, Camperdown, NSW Sydney, Australia

Aim

The Haematology Step-Down Unit (HSDU) was opened in February 2005 to promote and facilitate the early discharge of haematology patients that have undergone Bone Marrow Transplantation and/or high dose chemotherapy.

Method

The unit is a small ambulatory care area adjacent to the haematology inpatient unit. It comprises of 5 chairs and 1 bed. It is run by the Haematology Care Coordinator and supported by one other registered nurse. Its hours of operation are 0800hrs to 1700hrs on week days only. The HSDU provides a continuum of care through the transitional processes of inpatient to outpatient. It offers a haematology specific service: central line care, blood product support, bisphosphonate therapy, monoclonal antibody therapy along with counselling, education, support and pre chemotherapy assessments. The service allows for patients to be discharged before count recovery after treatment. The service also provides efficient and prompt triaging of the un-well haematology patient.

Results

The majority of patients (~ 50%) triaged in the HSDU were for febrile neutropenia. Other conditions included hypercalcaemia, nausea and vomiting post chemotherapy, symptom management, pain control and central line complications. In 2008 the unit saw approximately 180 patients per month. In 2008 76 patients avoid casualty by coming through the HSDU. The unit is cost effective returning about \$180 000 last financial year through Medicare.

Conclusions

The future direction is one of growth due to the ever increasing demands on our already strained public health system. The philosophy of Care Coordination aids in effective follow up and the early discharge of patients. The HSDUs capacity to provide these services could be enhanced by the addition of a nurse practitioner.

No conflict of interest to disclose

Sunday 18 October
BMTSAA Symposium

1600-1630
Meeting Rooms 1/2
1600

Cell Therapy Infrastructure: Development and Subsidized Access

Stewart Hay

Research Infrastructure Support Services, Level 6, 464 St Kilda Road, Melbourne, 3004

Research Infrastructure Support Services (RISS) is funded by the Federal Government to facilitate access for researchers to cGMP facilities for the manufacture of human cells for transplant, as well as supporting facilities to develop and maintain TGA licensing.

RISS supports cell therapy facilities at The Queensland Institute of Medical Research, The Children's Hospital at Westmead, The Royal Prince Alfred Hospital, Cell Therapies, The Institute of Medical and Veterinary Science and the Royal Perth Hospital. In the last two years RISS has provided approximately \$1.4 million to support cGMP related cell therapy research. This research has involved a variety of cell based approaches for treatment of cancer, inflammatory disorders, and infections.

The project administered by RISS is funded through the National Collaborative Research Infrastructure Strategy (NCRIS) and will run until 2011. The goals of NCRIS are to improve collaboration and to avoid unnecessary duplication of infrastructure.

Sunday 18 October
BMTSAA Symposium

1600-1630
Meeting Rooms 1/2
1610

Report from Australian Regional ISCT Meeting

John Rasko

Australian Regional Vice President, ISCT, on behalf of the Organising Committee

Following in the successful footsteps of the full International Society for Cellular Therapy meeting in Sydney in 2007, we have initiated a regional one-day ISCT meeting in Adelaide on Saturday 17 October 2009. Our program entitled “Cellular Therapies –Translational Medicine” was designed to emphasise the theme of providing a forum for national and international speakers to update us on the breadth and depth of clinical cellular therapies. Importantly we included a regulatory workshop and series of case studies for participants involving good manufacturing practices. Speakers include the President of ISCT, Mary Laughlin (Cord Blood Cells); Robert Deans (MSCs); Leslie Wolfe (chondrocytes); David Connell (tendon repair); Ineke Slaper-Cortenbach (ISBT-labeling standards); John Greenwood (skin); Stan Gronthos (bone); Giles Plant (neuronal repair) as well as talks on pluripotent stem cells and immunotherapies.

We hope to encourage all scientists and clinicians involved in the burgeoning field of cellular therapies to get involved and support this peak industry body.