Sunday 14 October **0900-1030**
HSANZ Symposium: Haemoglobinopathies **Arena 1B**

0900

Issues in Management of Sickle Cell Disease

Swee Lay Thein
King's College London School of Medicine and King's College Hospital, London UK

Sickle cell disease describes a group of inherited disorders caused by the presence of the sickle haemoglobin (HbS, *HBB* glu6val). Although most prevalent in individuals of African descent, due to recent population movements, SCD has become the most common and fastest growing genetic disease in many non-indigenous countries.

Patients with SCD have extremely variable characteristics, complications and prognosis despite having identical sickle genes. Management of SCD is one of the most challenging clinical problems facing healthcare professionals. Although much progress has been made in recent years towards understanding of the underlying pathophysiology, the mainstay of treatment remains preventative and supportive. Nonetheless, newborn diagnosis combined with long-term care programmes have a significant outcome on prognosis and patient survival. Life expectancy is increasing with an increasing recognition of specific complications of chronic organ dysfunction related to the disease. Major therapeutic options include blood transfusion, hydroxyurea and bone marrow transplantation. New therapeutic options include red cell ion-channel blockers, anti-adhesion and anti-inflammatory drugs, and drugs which normalise nitric acid (NO) metabolism. Relatively little progress, however, has been made in the management of acute pain.

Sunday 14 October **0900-1030**
HSANZ Symposium: Haemoglobinopathies **Arena 1B**

0940

High Throughput Screening for Haemoglobinopathies with Mass Spectrometry

Reinhard I Boysen, M Asif Alam, Donald K Bowden and Milton TW Hearn
ARC Special Research Centre for Green Chemistry, Monash University, Melbourne, Victoria, Australia

Haemoglobin (Hb) variants and isoforms result from genetic modifications (non-silent point mutations, deletions, insertions and translocations) or from chemical or biological pre-, co- or post-translational modifications (*i.e.* glycation, acetylation, carbamylation) of the expressed proteins. Existing methods to investigate haemoglobin disorders use gel electrophoresis and high performance liquid chromatography. However, the analysis of Hb variants frequently also requires DNA sequencing or high resolution mass spectrometry, since many Hb variants *i.e.* HbC, HbE and HbO-Arab, exhibit molecular mass shifts of as little as one amu and often no change in the charge status. Furthermore, the prevalent co-occurrence of multiple events such as sequence variations together with posttranslational modifications (*e.g.* glycation as marker for diabetes mellitus) and with different expression levels can present significant analytical difficulties.

We have developed methods that allow overcoming the present technological hurdles (lack of speed, economy and precision) for the large scale medical diagnostics of haemoglobin variants using Green Chemistry principles (*e.g.* the utilisation of degradable surfactants and reagent-economic procedures). The method consists of a surfactant-aided on-target proteolysis after either "separation free" sample preparation or after capillary liquid chromatographic separation and micro-deposition of intact haemoglobin variants and subsequent matrix-assisted laser desorption/ionisation-time of flight mass spectrometry (MALDI TOF MS). Workflows are presented with examples developed on more than 15 haemoglobin variants (including haemoglobin C, E, and S) of EDTA-treated human blood. Fast (< 3 min) on-target digestions of very small volumes of blood (≤ 200 nL) generate peptide mass fingerprints with very high sequence coverage and allow the rapid identification of amino acid sequence aberrations.

These new techniques are expected to significantly contribute to the development of fast, reliable and efficient high-throughput methods in biomedical diagnostics of haemoglobin variants or other applications in which protein variant identification is crucial for disease characterisation at the molecular level.

Acknowledgements: These investigations were supported by the Australian Research Council.

Sunday 14 October **0900-1030**
HSANZ Symposium: Haemoglobinopathies **Arena 1B**

1005

Recent Developments in Chelation Therapy

Donald K Bowden
Thalassemia Services, Monash Medical Centre, Melbourne, Australia

The care of patients with transfusional haemosiderosis is complex and resource intensive. Chelation with intramuscular desferrioxamine commenced in the 1960's and was initially given intramuscularly to patients with β thalassaemia major. Subcutaneous infusions were commenced in 1977-1978 at a dose of up to 60 mg/kg over 10 hours on five, six or seven days a week. Doses have varied widely in different centers. Compliance with this potentially effective regime has been particularly difficult for many patients, chiefly as a result of local toxicity at the site of injection where pain, swelling and scarring of skin and subcutaneous tissues is a common problem. Toxicity may be a more serious problem in young children and the elderly. However uncertainties remain about optimal chelation therapy. When should treatment commence? How rapidly should good control of iron loading be achieved? Can organ damage be prevented by earlier chelation? Complications of chronic hemosiderosis such as endocrine organ failure syndromes and cardiomyopathy are significant continuing clinical problems, the latter accounting for all but a few deaths in our patient group with β thalassaemia major. The availability of oral chelation treatment, initially with the introduction of deferiprone followed by deferiprone and desferrioxamine in combination and with the recent introduction of Exjade (ICL670), is a major development which offers the promise of greatly improved treatment outcomes. The monitoring of iron loading as a measure of the adequacy of the response to treatment has been a particularly significant problem in patient care. The serum ferritin does not give information about the iron content of individual organs. The introduction recently of the accurate measurement of liver and cardiac iron by MRI is therefore likely to greatly improve monitoring of the adequacy of chelation therapy hence allowing treatment to be tailored more accurately to the needs of the individual patient.

Sunday 14 October **0900-1030**
ANZSBT Symposium: Neutrophils **Central Room A**

0900

Structure and Clinical Significance of Human Neutrophil Alloantigens (HNA)

Jürgen Bux
German Red Cross Blood Service West & University of Bochum, Germany

Neutrophil antigens are implicated in a variety of clinical conditions including neonatal immune neutropenia, transfusion-related acute lung injury, refractoriness to granulocyte transfusions, febrile transfusion reactions, immune neutropenia after bone marrow transplantation, autoimmune neutropenia and drug-induced immune neutropenia. Seven alloantigens have been listed in the HNA system and are assigned to five antigen groups. Six antigens have been characterised biochemically and molecularly so that their primary structures are now known. As shown by regularly performed international granulocyte immunology workshops, a combination of granulocyte agglutination and immunofluorescence tests together with a panel of typed cells is currently the best means of detection. Since most of the HNA antigens have been well characterised, HNA typing as well as the detection of the corresponding antibodies are now reliably possible provided that the neutrophil laboratories regularly take part in national and/or international proficiency tests. This will improve diagnostics of neutrophil antibody-mediated clinical conditions as well as the prevention of transfusion-related acute lung injury (TRALI).

Sunday 14 October **0900-1030**
ANZSBT Symposium: Neutrophils **Central Room A**

0940

Neutrophils for Better or for Worse, in Sickness and in Health

Lin Fung
Research and Development, Australian Red Cross Blood Service, Brisbane, Australia

Neutrophils (PMNs) make up the largest proportion of leukocytes and are a critical part of innate immunity. In an infection, signals are disseminated from the site of infection in a concentration gradient that “activates” the microvasculature endothelium and PMNs. Selectins on the endothelium are up-regulated and form loose attachments with L-selectins on PMNs to slow the PMNs to a roll. As the PMNs get closer to the site of infection they become primed by chemokines, causing PMNs to be less deformable, more adhesive, have delayed apoptosis and have an augmented respiratory burst. These qualities allow the PMNs to transmigrate across the endothelium to the infection site in the tissue, where they phagocytise the microbial pathogens that are then destroyed by reactive oxidants and enzymes generated by the PMNs.

While the large surface area in the lung supports vital gaseous exchange it concurrently provides an area of contact with the external environment hence susceptibility to infections. As part of host defense 28% of PMNs are located in pulmonary capillaries. Importantly, migration of PMNs in pulmonary capillaries is different to migration in the systemic circulation as pulmonary capillaries are smaller (2-15 μm) and then PMNs (6-8 μm). Therefore PMNs are deformed into ellipsoid shapes as they traverse these capillaries, thus making the role of selectins redundant. The migration is relatively slow but this delay allows the cell to sense the environment for inflammatory signals. The next stage of adhesion may follow be either CD18 dependent or in dependent pathway and this is dependent on the stimuli.

Finally, it is important that the size of the microbicidal response match the size of the infection. As an inadequate response would not control the infection, and an excessive respond would result in injury to the surrounding tissue.

Sunday 14 October **0900-1030**
ANZSBT Symposium: Neutrophils **Central Room A**

1005

Transfusion-Related Acute Lung Injury (TRALI)

Christopher C Silliman
Bonfils Blood Center and Department of Pediatrics, University of Colorado School of Medicine, Denver, CO, USA

TRALI is the leading cause of transfusion-related death in the USA with an increasing incidence world-wide. Its pathophysiology is attributed to the transfusion of donor antibodies that target recipient HLA (class I or II) or granulocyte-specific antigens or biologic response modifiers (BRMs), which are a byproduct of storage. We **hypothesize** that TRALI is the result of two distinct events: the first being the clinical condition of the patient and the second the transfusion of a blood component that contains antibodies or BRMs that activate host neutrophils (PMNs) resulting in pulmonary endothelial damage, capillary leak and ALI.

Methods
In vitro methods include PMN priming, adhesion, and PMN-mediated damage of human pulmonary microvascular endothelial cells (HMVECs). *In vivo* methods include a two-event rat model of TRALI:
1) endotoxin (LPS) followed by 2) transfusion of heat-treated human plasma, antibodies against rat MHC class I, II or granulocyte antigens.

Results
Antibodies against PMN antigens (HNA-3a & 2a) caused priming of HNA-$2a^+$ & $3a^+$ PMNs, but not HNA-$3a^-$ PMNs. In a two-event model of HMVEC damage, LPS caused PMN adherence alone. Antibodies to HNA-3a caused PMN- (HNA-$3a^+$ only) mediated damage to LPS-, but not buffer-, treated HMVECs. *In vivo* modeling demonstrated that TRALI was the result of two events: rats pre-treated with LPS evidenced ALI, Evans blue dye leak, with plasma from stored but not fresh components and dose-dependent ALI: with antibodies to MHC class I antigens (OX18 or OX27) but not with antibodies to MHC class II. Antibodies to MHC class I, II, or PMN antigens, LPS, or stored components alone did not cause ALI. Granulocyte depletion also inhibited ALI.

Conclusion
TRALI is the result of two events, antibodies or BRMs must directly affect PMNs, and antibodies to MHC class II or to granulocytes, if they elicit neutropenia, do not cause TRALI.

Sunday 14 October **0900-1030**
ASTH Symposium: Haemophilia **Central Room C**

0900

Haemophilia – So Much Still Unknown

Alison Street
Haematology Unit, The Alfred, Melbourne, Victoria, Australia

The symptoms of haemophilia have been described from times of the Talmud. The genetic mutations responsible for the disorders have been studied since cloning of the genes for Factors IX and VIII in the 1980's. Recombinant technology has delivered pathogen-safe replacement therapy and there are products to bypass the acquired coagulopathy of factor inhibitors arising in response to Factor VIII and IX therapy.

There are still many areas for research into the natural history of "treated" haemophilia. We do not understand the clinical heterogeneity of bleeding patterns in patients with severe haemophilia (FactorVIII/IX <2%) though the phenotype correlates best with the age at first joint bleeding. Neither do we understand the variability of symptoms of joint bleeding and progression of joint pathology, now best studied by MRI in association with functional clinical assessment. There are novel small animal models of haemarthrosis and of standardised injury which allow histologic and molecular characterisation of the consequent patterns of inflammation. We do not know the optimum dose and duration of replacement therapy for surgery and other procedures or for prophylaxis. Should prophylaxis be continued into adult life and at what intensity? Studies are being devised to address this very important issue from "quality of life' and health economics perspectives.

There are products in development to extend factor half life in circulation, will they increase the risk of inhibitor development? Can other products such as transgenics be manufactured cost effectively to treat patients in those parts of the world that cannot conceive of recombinant therapy? And what of the safety and efficacy of gene therapy - with haemophilia such an "attractive" disorder for this treatment?

The pathophysiology and optimal treatment of haemophilia is still to be defined. There are many careers for haematologists still to be made!

Sunday 14 October **0900-1030**
ASTH Symposium: Haemophilia **Central Room C**

0945

Inhibitors in Haemophilia: What Have We Learnt?

Claude Negrier
Hôpital Edouard Herriot; University of Lyon, France

Inhibitors raised against the clotting factor concentrates currently represent the most serious complication of therapy. They are more frequent in haemophilia A (HA) than in haemophilia B (HB) and mainly concerns severe cases (FVIII:C/FIX:C<1 IU/dL). Up to thirty percent of severe HA patients and 6 % of severe HB patients develop inhibitory antibodies after a median of 10-15 exposure days. The antibodies may be transient, or can permanently neutralize the exogenous clotting factor when the titre, expressed in Bethesda units per ml (BU/mL), is high enough. The fact that not all haemophiliacs develop such antibodies is dictated by several factors which are inherited and acquired. Among the inherited risk factors the mutation type plays a significant role and deletion affecting multiple domains and other important gene disruptions are associated with a higher incidence of inhibitors. Recent work also pointed out the role of several genes intervening in the immune response (interleukin 10, TNF alpha), as well as racial background and family history. In addition, multiple environmental factors probably modulate the inherited risk: treatment regimen (prophylaxis, on-demand), mode of administration (bolus or continuous infusion), type of concentrate (purity, recombinant or plasma-derived origin, presence of large amount of vWF), reasons for initial treatments (prophylaxis, large bleedings, surgical intervention, concomitant diseases) or stimulatory signals associated with treatment (inflammatory states, surgical interventions, vaccinations). When the inhibitor titre is more than 5-10 BU/mL, one can barely achieve haemostasis with high dose factor VIII/factor IX, and bypassing agents that can trigger thrombin and fibrin formation may be used. Another possibility is to eradicate the inhibitor by immune tolerance induction, probably through the deletion of memory B cells. There still are multiple unanswered questions regarding this therapeutic modality, and several clinical trials are currently underway to address the main issues.

Dr Claude Negrier sponsored by CSL Bioplasma

Sunday 14 October **0900-1000**
Nurses Symposium: Adolescents and Young Adults **Meeting Room 5**

0900

Treatment Paths and Options: Why be Age Specific

Ross Pinkerton

Abstract not received at time of going to print

Sunday 14 October **0900-1000**
Nurses Symposium: Adolescents and Young Adults **Meeting Room 5**

0940

Benefits of an Adolescent / Young Adult Unit

Danielle Tindle
Leukaemia Foundation of Australia, Brisbane, Queensland, Australia

It has been internationally recognised that adolescents and young adults (AYA) with cancer are a poorly understood patient group. Compared with older adults and younger children, research and services for this group are lacking, and treatment outcomes have not improved in the past twenty years. However, the process of improving service provision for AYAs has commenced in some Western countries and headway is being made into understanding the needs of this demographic. Given the developmental life stage of AYAs, this patient group faces unique issues which affect their cancer experience. The creation of an area specifically designed for AYAs ensures their requirements are more adequately met, thereby improving quality of life. As such, a separate adolescent unit provides the infrastructure and specialised care which assists the AYA to receive both age-appropriate treatment and psychosocial care which reflects his or her unique needs. Furthermore, by treating young people together, peer support is facilitated and many factors identified in paediatric or adult hospitals are mitigated, such as isolation and inability to identify with older or younger patients. Although Australia is lagging behind many countries in addressing this gap in age-appropriate care, changes to practice are slowly being made in some major hospitals. Critical mass justifying separate AYA units remains an obstacle to the development of specialised units. However, given the success of AYA units with both patients and practitioners in the United Kingdom, the benefits of these units can no longer be ignored. Indeed, it is necessary for treating centres around Australia to address the gap in age-appropriate care for AYAs, thereby providing specifically designed spaces and specialised multi-disciplinary teams to care for this patient group.

Sunday 14 October **0900-1030**
BMTSAA: BMT Laboratory Workshop 1 **Meeting Room 7**

0900

Quality Management Systems for Cell Therapy Laboratories

R Rodwell, J Ramsay, E Wolf, P Johnson, D Baldry, B Taylor, R Bacajewski, A Ridge, A Misra
Queensland Cord Blood Bank At The Mater, Brisbane, QLD, Australia.

Cell Therapy Laboratories are required to maintain a Quality Management System (QMS) and must operate in accord with the code of Good Manufacturing Practice (cGMP) a prerequisite for licensing with the Therapeutic Goods Administration (TGA) and Netcord/FACT accreditation. Usually this requires enhancement of existing QMS to meet the stringent requirements of the regulatory codes. The organisation's Quality Manual should define policies with respect to quality management. GAP audits against the regulatory codes are necessary to identify required improvements. Preliminary discussion with external service providers are required to define specifications and the required level of documentation. Commonly many areas need enhancement. These include the development of systems and documentation for the management of contracts, equipment management and validation incorporating the concepts of Installation Qualification (IQ), Operational Qualification (OQ) and Process/Performance Qualification (PQ). Critical materials, batch management, validation of computer software, processes and labels should be examined. Staff training and competency assessment, documentation, change control, environmental monitoring, management of improvements, complaints and non-conformances, quality assurance and control procedures with inclusion of trending of data must also be addressed. Risk management must be incorporated into the organisation's operations. Development and use of template forms greatly assist in the preparation and management of documentation and facilitates otherwise time-consuming tasks. Regular internal audits are necessary to ensure ongoing compliance; external audits identify deficiencies and areas for improvement. Management meetings and review are necessary to maintain ongoing control of the QMS and operations and regulatory compliance.

Sunday 14 October **0900-1030**
BMTSAA: BMT Laboratory Workshop I **Meeting Room 7**

0930

New Standards for Cellular Therapy – Terminology, Coding and Labelling

Paul Ashford

ISBT 128 is an international coding and labeling standard. Already in widespread use for blood transfusion, it has been adopted by the Cellular Therapy community to provide global consistency in coding and labeling. New standards for terminology of CT products have recently been published. This presentation will provide a summary of the ISBT 128 system, and of the new standards.

Sunday 14 October **0900-1030**
BMTSAA: BMT Laboratory Workshop 1 **Meeting Room 7**

1000

Validating the Analysis of CD34+ Fresh and Cryopreserved

Annette Trickett, Mel Chimenti
Sydney Cord Blood Bank, Sydney, NSW, Australia

Although dual platform (DP) CD34 analysis has been shown to yield reproducible results for enumeration of fresh haemopoietic progenitor cells (HPC), it is well recognised that this methodology may give erroneous results in thawed samples. The single platform (SP) method incorporates a pre-determined number of fluorescent beads into the sample and facilitates quantitation of CD34+ cells from the ratio of cells and beads, without the need of a WBC count.

The SP CD34 method was based on standard operating procedures developed by the BMT Network of NSW, with gating strategies based on published methods developed by the International Society of Haematotherapy and Graft Engineering (ISHAGE).

Comparison of viable CD34+ cell number in 28 fresh cord blood (CB) samples demonstrated a highly significant correlation, with the average DP result being 2.3 CD34/µL greater than the SP result. In 8 thawed CB samples, there was also a highly significant correlation, however the average DP result was 58 CD34/µL greater than the SP result. Triplicate acquisition of CB samples yielded CVs of 6.8 ± 4.1% for fresh CB (n = 17) and 7.2 ± 2.7% for thawed CB (n = 4). Stability studies demonstrated no significant change in CD34+ cell number over time from staining ($p = 0.99$, $r^2 < 0.001$), however greater variability in CD34 count was observed after overnight storage (18 hours post lysis). Inter-laboratory comparison of 4 thawed CB samples by SP CD34 analysis revealed an excellent correlation between the two laboratories, with the SCBB lab on average 8.8 CD34/µL higher than the external laboratory.

The SP viable CD34 assay appears to be accurate, reproducible and stable. There is excellent agreement with the DP method for fresh samples, but lower results are obtained with the SP

Sunday 14 October **1100-1200**
HSANZ Symposium: Difficult Diagnostic Issues **Arena 1B**

1100

Diagnosing and Subtyping Amyloidosis

Hugh Goodman
Department of Haematology, Waikato Hospital, Hamilton, New Zealand

The systemic and localised amyloidoses are an uncommon group of disorders caused by deposition of protein as abnormal fibrillar aggregates. Many widely different proteins may form the unique fibrillar structure that is amyloid: these may be normal proteins in normal (eg transthyretin) or increased (eg serum amyloid A, beta-2 microglobulin) concentration, or variant proteins, either hereditary (eg fibrinogen A-alpha chain, TTR) or acquired (eg immunoglobulin light chains). The amyloidoses are then defined by the main constituent protein, for example AL (immunoglobulin **L**ight chain) or AFib (**Fib**rinogen).

The amyloidoses have notoriously protean effects and present to diverse specialties; however, the commonest syndromes are renal involvement (proteinuria and / or renal impairment), cardiac involvement (diastolic heart failure) and neuropathy (peripheral and / or autonomic). A high index of suspicion is required to obtain a diagnosis at an early point in the disease. Targeted or screening biopsies may be appropriate in various situations.

There is also substantial phenotypic heterogeneity within, and overlap between, the various systemic amyloidoses. Correctly establishing the source of the amyloid protein is vital for correct treatment which may range from chemotherapy for AL amyloidosis to organ transplantation in hereditary amyloidoses. One must not, therefore, rely on the phenotype and associated disease alone in order to establish a subtype. A range of immunohistochemical and genetic assays are available to confirm the amyloid protein or exclude alternatives.

Sunday 14 October **1100-1200**
HSANZ Symposium: Difficult Diagnostic Issues **Arena 1B**

1130

WHO-EORTC Cutaneous Lymphoma Consensus Classification – Should Haematologists Care?

Debra Norris
Queensland Medical Laboratory, Brisbane Australia

Up until 2005, cutaneous lymphomas were classified using either the EORTC classification or the WHO classification, neither of which was ideal. In addition, the literature concerning cutaneous lymphomas is conflicting and difficult to understand, beset by complex, eponymous and often inaccurate methods of classification. If the distinctive histological and clinical features of primary cutaneous lymphoma are not recognized by both pathologists and oncologists alike, these patients may be overtreated with aggressive chemotherapy. This lecture will present the EORTC-WHO consensus classification and highlight in particular, differences in the classification of cutaneous T-cell lymphomas other than mycosis fungoides; CD30+ cutaneous lymphoproliferative disorders and the classification and terminology of different types of cutaneous B-cell lymphomas that have resulted in considerable debate and confusion and have significant treatment and prognostic implications. The WHO-EORTC classification for cutaneous lymphomas represents a significant step forward, and should contribute to a more uniform diagnosis and hence more uniform treatment of patients with cutaneous lymphoma.

Sunday 14 October: **1100-1200**
ANZSBT Symposium: Risk Management in Transfusion **Central Room A**

1100

Current and Future Vector-borne Disease Threats to Australia

Scott A Ritchie
Tropical Population Health Network, Queensland Health, Cairns QLD, Australia

Despite its relatively dry environment, Australia is host to an array of mosquito-borne diseases that impact human health. Historically, Australia, especially coastal areas that received ample rainfall, was subject to outbreaks of dengue fever, malaria, encephalitis and even filariasis. Today, however, many of these pathogens no longer occur endemically in Australia. Currently, the zoonotic viruses Ross River virus and Barmah Forest virus are collectively responsible for several thousand human cases/year. Murray Valley encephalitis, which used to cause sporadic outbreaks of lethal encephalitis in SE Australia, in now limited to sporadic cases occurring nearly annually in far NW Australia. Malaria was eradicated from Australia in 1981, and only rarely now do small outbreaks occur in tropical Queensland. Currently, the dengue viruses are the greatest risk to Australia, with almost annual outbreaks in the tropical urban areas of north Queensland. What will the future bring? The threat of global warming, and especially the tangible effects of drought, has increased the storage and hording of water at home. This has created a "back to the future" scenario harkening to the first half of the 20th century when rainwater tanks, the dengue mosquito *Aedes aegypti*, and large epidemics of dengue virus were common throughout much of urban eastern Australia. In addition to an increased risk of dengue fever, Australia is also potentially vulnerable to exotic viruses, such as the Chickungunya virus that ravaged the Seychelles and India the last two years, that are but a short plane ride away.

Sunday 14 October: **1100-1200**
ANZSBT Symposium: Risk Management in Transfusion **Central Room A**

1130

Pathogen Reduction in Blood Safety – Seeking a Consensus

Richard J Benjamin
American Red Cross Blood Services, Washington, DC, USA

Pathogen reduction technologies offer a new paradigm in blood safety by providing blanket protection to a wide range of pathogens in a prospective fashion. Following early adoption of a number of systems directed at plasma products, technologies have been developed that target nucleic acid for inactivation of pathogens and residual leukocytes that may contaminate platelets and red blood cells. Unfortunately, each technology has a price in terms of cost, practicality, effectiveness, side effects and/or loss of product efficacy. Increasing implementation of pathogen reduction technologies is underway in Europe and national blood services now need to consider their approach to these new technologies. A consensus conference was held in Toronto, Canada in March 2007 to bring together research, clinical and regulatory experts from a variety of countries. This presentation will review the highlights of these considerations and the recommendations that they engendered.

Sunday 14 October **1100-1200**
ASTH Symposium: Haemostasis Research **Central Room C**

1100

De-encryption of Tissue Factor

Philip J Hogg
UNSW Cancer Research Centre, University of New South Wales, Sydney, NSW, Australia

Tissue Factor is a plasma membrane glycoprotein that initiates the blood coagulation cascade when it binds coagulation factor VIIa. It will only bind VIIa productively, however, when it has undergone a transition from cryptic to active form. The nature of this transition involves an allosteric disulfide bond in the membrane-proximal domain of the cofactor. Allosteric disulfides control protein function by breaking or forming in a precise and often dynamic way [1]. The Tissue Factor allosteric disulfide is cleaved in the cryptic form of the co-factor and formed in the active state [2].

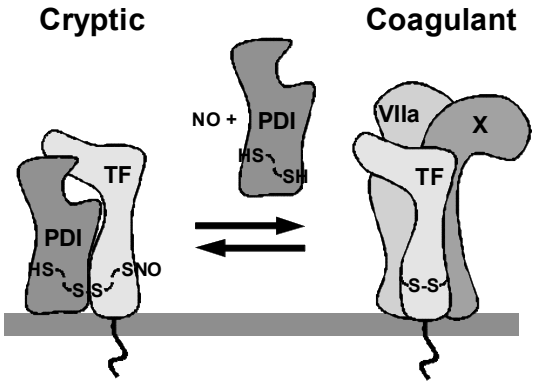

Figure 1. Proposed model for the mechanism of de-encryption of Tissue Factor

Both the oxidoreductase, protein disulphide isomerase, and the thiol alkylator, NO, have been implicated in control of the redox state of the Tissue Factor bond (3). Specifically, PDI cleaves the allosteric disulphide forming a mixed disulphide between Tissue Factor and PDI which renders Tissue Factor cryptic. S-nitrosylation of the unpaired Tissue Factor thiol appears to control the stability of this complex. Denitrosylation of Tissue Factor by an unknown mechanism leads to resolution of the Tissue Factor-PDI complex with formation of the Tissue Factor allosteric disulphide and coagulant TF (Figure. 1).

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Sunday 14 October **1100-1200**
ASTH Symposium: Haemostasis Research **Central Room C**

1130

The Ever Growing Complexity of Platelet Aggregation

Shaun P Jackson
Australian Centre for Blood Diseases, Melbourne, VIC, Australia

Platelet aggregation, the process by which platelets adhere to other platelets at sites of vascular injury, has long been recognized to be critical for hemostatic plug formation and thrombosis. Until relatively recently, platelet aggregation was considered a straightforward process, involving the non-covalent bridging of integrin αIIb β3 receptors (GPIIb-IIIa) on the platelet surface by the dimeric adhesive protein fibrinogen. However, with recent technical advances enabling real-time analysis of platelet aggregation *in vivo*, it has become apparent that this process is much more complex and dynamic than previously anticipated. Over the last decade it has become clear that platelet aggregation represents a multi-step adhesion process involving distinct receptors and adhesive ligands, with the contribution of individual receptor-ligand interactions to the aggregation process dependent on the prevailing blood flow conditions. It now appears that at least 3 distinct mechanisms can initiate platelet aggregation, with each of these mechanisms operating over a specific shear range *in vivo*. The identification of specific shear-dependent mechanisms of platelet aggregation has raised the possibility that vascular-bed specific inhibitors of platelet aggregation may be developed in the future that are safer and more effective than existing antiplatelet agents.

Sunday 14 October **1100-1200**
Nurses Symposium: Impact of Innovations in Haem/BMT **Meeting Room 5**

1100

Giving the Punters What They Want – Transplants in the Hotel Setting

Anthony Goldstone
North London Cancer Network, University College Hospital, London, UK

Since December 2004, the initiation of an Ambulatory Care (AC) initiative at UCH has seen over four hundred patients receiving haematology treatments in a hotel adjacent to the hospital, treatments previously delivered as in patients. A primary aim of the AC Service is to safely transfer the delivery of inpatient treatments to the Ambulatory setting. The objectives have been:

- to define eligibility of patients for outpatient/ambulatory transplant.
- to identify and minimise risk factors when adapting inpatient transplant for the ambulatory setting.
- to determine reasons for and the potential median day of transferred hospital for specific inpatient treatments.

155 patients have received either autologous or low intensity allogeneic transplantation (LI) in AC. 77 or 50% have received a BEAM autograft, 45 or 29% an autograft with an alternative conditioning regimen and 33 or 21% a LI allogeneic transplant.

Results
Almost all patients are ultimately transferred back from the hotel to the hospital at some point. Reasons for hospital transfer from AC fall into seven categories.

1. GI symptoms
2. Febrile neutropenia
3. Non neutropenic fever
4. Fatigue
5. Anxiety
6. Drug reactions
7. Carer issues

Patients go to the hotel from the initiation of the chemotherapy high dose regimen or before it. The median day of rehospitalisation is day +3 for BEAM autograft patients, day +4 for high dose Melphelan and day +4 for LI allogeneic transplants. 15 (10%) have required out of hours hospital admissions. 5 (38%) due to febrile neutropenia, 3 (23%) due to GI symptoms, 3 (23%) due to drug reactions, 1 (8%) due to non neutropenic infection and a further 1 due to anxiety.

Robust out of hours policies, risk management and infection control procedures are fundamental in order to provide a safe AC Service. Efficiencies in inpatient bed use is a cost saving and is advantageous to the service.

Sunday 14 October **1100-1200**
Nurses Symposium: Impact of Innovations in Haem/BMT **Meeting Room 5**

1130

Impact of Relocation

Pam McGrath
International Program of Psycho-Social Health Research (IPP-SHR), Central Queensland University, PO Box 1307, Kenmore QLD 4069, Australia

In most states in Australia specialist treatment for haematological malignancies is situated in the major metropolitan areas. Consequently, patients from regional, rural and remote locations have to leave the comfort of their homes and relocate for the specialist care that is not available locally. This presentation draws on the findings from a number of research studies conducted by the International Program of Psycho-Social Health Research (IPP-SHR) that explore the experience of relocation. Families who have to relocate are challenged by a multiplicity of issues including the need to leave immediately without preparation or knowledge of how long they will be away, uncertainty with regards diagnosis and treatment, problems with maintaining the family home in absentia, disorientation and unfamiliarity with the metropolitan hospital and surroundings, the distress of family separation, divided loyalties between the patient and well family members, a sense of life being on hold, a sense of lack of choice, an unmet desire for normalcy, travel and accommodation problems, financial impact and problems with work and education. The issue is especially poignant in Australia at the moment, where ongoing problems with travel and accommodation support for relocated families have created the necessity for a Senate Affairs Committee Inquiry into Patient Assisted Travel Schemes. Detailed recommendations of practical ways to assist families affected by relocation will be provided.

Sunday 14 October **1100-1200**
BMTSAA BMT Laboratory Workshop II **Meeting Room 7**

Developments in Regulation of Haemopoeitic Progenitor Cells 1100

Albert Farrugia
Blood and Tissues Unit, Therapeutic Goods Administration, Australian Government, Canberra, Australia

Haemopoeitic progenitor cells (HPCs) are therapeutic goods subject to the TGA's oversight under the Therapeutic Goods Act (1989). Initially HPCs were defined as blood components and the majority of products were exempt from regulation as their governance was seen to be through clinical rather than manufacturing provisions. Over the past years a new regulatory framework for biologicals has been developed which includes a class of therapies which are similarly governed. This presentation will review the integration of HPCs in this framework and discuss how the regulation of HPCs within the international transfer of these products can be progressed.

FACT Accreditation – Discussion Forum 1130

Nicola Lumley, QLD; Sushi Narayan, QLD; Josephine Ritchie, QLD

Discussion on the current approach undertaken by various facilitites to implement an effective Quality Management System and comply with the NPAAC & FACT Stem Cell regulatory requirerments by Queensland Health. Early wins and challenges will be presented for clinical, collection and the laboratory areas.

Sunday 14 October **1200-1300**
ASTH Barry Firkin Oration **Arena 1B**

Life as a Clot

John Lloyd
Institute of Medical & Veterinary Science, Adelaide, SA, Australia

Abstract not provided

Sunday 14 October **1400-1530**
HSANZ/BMTSAA/Nurses Symposium: Clinical BMT **Arena 1B**

1400

Immune Modulation and the Control of Graft vs Host Disease following Non-myeloablative Transplantation

Robert S Negrin
Stanford University Medical Center, Stanford, CA, USA

Graft-versus-host disease (GVHD) remains a critical obstacle in the clinical application of allogeneic hematopoietic cell transplantation (HCT). A number of different strategies have been attempted to reduce GVHD risk. A particularly attractive approach has been to utilize natural regulatory mechanisms in an attempt to modulate an over exuberant immune reaction characterized by GVHD. In murine models developed by Dr. Samuel Strober, they have demonstrated that recipient mice treated with total lymphoid irradiation and anti-thymocyte globulin (TLI/ATG) results in the reduction of GVHD risk such that nearly 1,000 times the number of donor derived allogeneic T cells can be injected into these animals without GVHD. This concept has been translated to the clinic using the TLI/ATG approach where we have treated over 100 patients with hematologic malignancies. Patients must be over the age of 50 years or have co-morbid medical conditions which preclude the use of myeloblative conditioning. Following preparation with TLI (800 cGy) and ATG (Thymoglobulinœ®, rabbit ATG 7.5 mg/kg today dose) patients are transplanted with unmanipulated G-CSF mobilized PBPC collections from either fully matched related or unrelated donors. GVHD and rejection prophylaxis consists of CSA and MMF. The results indicate that acute GVHD risk is ~5% with chronic GVHD of ~25-40%. These patients appear to maintain graft-versus-tumor responses as evidenced by an excellent long term outcome, especially for patients treated in minimal disease. The mechanisms underlying the beneficial effects in reduction of GVHD risk appear to be similar to those observed in murine models. This approach is being explored in a variety of different disease treatment options including patients with malignancy, for preparation of non-myeloablative haploidentical transplantation, for the treatment of autoimmune disorders, as well as induction of tolerance for combined solid organ transplantation. An update of the clinical results will be presented in detail.

Sunday 14 October **1400-1530**
HSANZ/BMTSAA/Nurses Symposium: Clinical BMT **Arena 1B**

1445

The Role of Allogeneic Stem Cell Transplantation in Acute Myeloid Leukemia

Jean-Luc Harousseau
Department of Hematology, University Hospital Hotel-Dieu, Nantes, France

In the absence of randomized studies the role of allogeneic stem cell transplantation (SCT) has been evaluated in prospective multicenter studies by donor/no donor analysis. When overall results are considered, allogeneic SCT is superior to other types of post remission therapies (Autologous SCT or intensive consolidation chemotherapy) in terms of DFS but not always in terms of OS due to a shorter survival after relapse. However in the past few years, this situation has changed.

- Results of allogeneic SCT have improved mostly due to a better management of GVHD and infectious complications. As a consequence the age limit has increased from 40 to at least 50 years.
- For patients older than 50, the use of reduced intensity conditioning is increasing rapidly
- Studies of large groups of patients have allowed a better selection of patients who are candidates for allogeneic SCT based on simple prognostic factors. Age is an important factor and results of myeloablative allogeneic SCT are better in patients under the age of 35-40. Cytogenetics is a major factor to be considered in the decision. Not only M3 AML but also CBF AML: t(8;21) and inv (16) are no longer considered an indication of upfront allogeneic SCT since the outcome is not superior to that achieved with less aggressive strategies. More recently it has been show that patients with NPM1 mutated/FLT 3 negative AML have a relatively good prognosis with conventional chemotherapy and the role of allogeneic SCT is currently discussed in this subgroup of AML. These questions will be discussed in the light of the GOELAMS experience in the last 20 years.

Dr Jean-Luc Harousseau sponsored by Pharmion

Sunday 14 October **1400-1530**
ANZSBT Symposium: Immunohaematology **Central Room A**

1400

Molecular Studies of Blood Groups

Geoff Daniels
Bristol Institute for Transfusion Sciences, NHSBT, Bristol, UK

The molecular genetics era of blood groups began in 1986 with the cloning of the gene for the MN protein. Now the genes for all but one of the 29 blood group systems have been cloned and the molecular backgrounds to almost all clinically important blood group polymorphisms have been identified. This makes it possible to predict blood group phenotypes from genomic DNA with a high level of accuracy. Most of the blood group polymorphisms arise from single nucleotide polymorphisms (SNPs), though other mutations or SNPs elsewhere in the gene or in another gene can affect antigen expression. The Rh system is very complex, with a large variety of RhD variants resulting from different mutations in *RHD* and *RHCE*.

The main applications of molecular genetics to red cell blood grouping include: the prediction of fetal blood groups in pregnant women with blood group antibodies in order to determine whether the fetus is at risk from HDN; prediction of clinically important blood groups of multiply-transfused, transfusion-dependent patients so that matched blood can be provided to assist in the prevention of blood group antibody production; defining RhD and RhCcEe variants, predicting blood group phenotypes on red cells coated with immunoglobulin (DAT+); and confirming zygosity in the production of reagent red cells.

High-throughput methods for detecting the SNPs and other gene sequence variations associated with blood group polymorphism will make it possible to genotype most donors and patients for all clinically significant blood groups, enabling electronic matching, which would reduce immunisation and the prevalence of haemolytic transfusion reactions. The Bloodgen project in the UK has led to the development of a DNA microarray for 176 allelic variants from 10 blood group systems, including 87 *RHD* genotypes, which has a very high level of accuracy for predicting blood group phenotypes.

Sunday 14 October **1400-1530**
ANZSBT Symposium: Immunohaematology **Central Room A**

1445

Antenatal Testing for RhD: Non Invasive Prenatal RhD Gene Assessment (NIPA)s

C Hyland[1], H Davies[1], R Flower[2], J Hyett [3], G Gardener [4]
[1]Australian Red Cross Blood Service, Brisbane. [2]PALMS, Royal North Shore Hospital. [3]Royal Brisbane and Womens Hospital. [4]Mater Health Services

Prenatal blood group gene assessment using invasive sampling methods, such as amniocentesis, has been performed by specialized laboratories since the mid 1990s to assist clinicians manage RhD negative pregnant women who are iso-immunised to the RhD antigen and at high risk for hemolytic disease of the new born (HDN). For such cases prenatal fetal RHD blood group gene tests using PCR can assess the RhD status for the unborn baby. Babies assessed as D gene positive are monitored further, and if necessary, transfused with RhD negative blood in utero to prevent HDN.

The discovery by Lo et al in 1997 that cell-free fetal DNA is detectable in the circulation of pregnant mothers has opened pathways for non-invasive prenatal blood group testing using a sample of the mothers blood which avoids the risks inherent in invasive sampling procedures. A few laboratories have since described the efficacy for assessing the fetal RHD gene status using RHD PCR tests on free fetal DNA isolated from maternal blood samples.

Under an ANZSBT scholarship we have adapted a qualitative assay to assess the fetal RHD gene status using cell free DNA isolated from maternal plasma. Free fetal DNA has been detected in 30/30 RhD negative maternal plasma samples collected between 11 and 39 weeks gestation. RHD and or SYR gene sequences were detected by Real Time (RT) PCR in all samples except for three. For these 3 samples, the presence of a fetal-specific epigenetic marker was assessed by follow up testing and confirmed that ffDNA was indeed present.

The assay permitted an accurate RHD genotype assessment for all pregnancies that since delivered. The assay can detect low copy numbers of target input DNA per reaction which is important as low copy numbers of ffDNA may be present in maternal plasma.

The data gathered from this first phase will contribute to a large scale quantitative analysis on the test methodology to measure the accuracy and the power of the test when applied to both high and low risk RhD negative pregnancies.

In the future a safe and simple blood group test in pregnancy could assist all RhD negative women, both at low and high risk for HDN, as currently all RhD negative women receive prophylactic anti-D injections at 28 and 32 weeks of pregnancy although only those carrying RhD positive babies need the injection. Such a test could ensure that precious anti-D immunoglobulin resources are available for those pregnancies truly at risk and eliminate the need for unnecessary administration of a blood derived product for a large number of RhD negative pregnant women.

Sunday 14 October **1400-1530**
ASTH Symposium: Fibrinolysis **Central Room C**

1400

Clot Busters vs Clot Builders

Paul Coughlin
Australian Centre for Blood Diseases, Monash University and Department of Haematology, Box Hill Hospital, Melbourne

Vertebrate vascular integrity is protected by a sophisticated hemostatic mechanism which, when activated by trauma, leads to the formation of a fibrin rich clot. Simultaneously the fibrinolytic system is activated to begin the process of remodelling and removing the clot during tissue repair. Fibrinolysis is initiated by trace quantities of tissue plasminogen activator (tPA) derived from endothelial cells. In the presence of fibrin, tPA efficiently cleaves the zymogen plasminogen to form plasmin, which mediates clot lysis. Plasmin binds avidly to fibrin and cleaves it repeatedly to yield soluble degradation products. The fibrinolytic enzymes are constrained by regulatory factors including plasminogen activator inhibitor-1 (PAI-1), antiplasmin and the thrombin activated fibrinolysis inhibitor (TAFI). All of these pro-fibrinolytic enzymes and their regulators operate in the physical context of the fibrin mesh. Finely tuned interactions between domains of the enzymes, inhibitors and fibrin lead to a co-ordinated sequence of events leading to local lysis of haemostatic clots while preventing a systemic lytic state.

Sunday 14 October **1400-1530**
ASTH Symposium: Fibrinolysis **Central Room C**

1430

Measuring Fibrinolysis in Clinical Practice – Role of the Global Coagulation Assays

Jennifer Curnow
Northern Blood Research Centre, Royal North Shore Hospital, Sydney, NSW, Australia

The fibrinolytic enzyme system is involved in prevention and/or removal of fibrin deposits from blood vessels. Increased activity, due to antiplasmin deficiency or PAI-1 deficiency, may produce a bleeding tendency. Reduced activity, associated with thrombotic risk, is more common and may occur due to plasminogen deficiency, reduced tPA production or storage or increased inhibition due to elevated PAI-1 levels. Hereditary abnormalities in the fibrinolytic system have been described but acquired defects are more common. These include hyperfibrinolysis which may occur in liver transplantation or postpartum haemorrhage. The thromboelastogram can be used in these acute settings to indicate the degree of lysis and need for antifibrinolytic therapy. Thrombelastographic parameters correlate with markers of activation and markers of the fibrinolytic system (t-PA, PAP and PAI-1). Studies of fibrinolytic system parameters have shown reduced fibrinolytic activity in the settings of malignancy, insulin resistance, myocardial infarction and venous thromboembolism. However fibrinogen, PAI-1 and d-dimer may also be affected by the acute phase response seen in these conditions. Measurement of fibrinolytic parameters may be time consuming, complex and in most cases is not routinely performed. Furthermore, although mean levels are higher in patient groups, studies show a large overlap of results with normal ranges which may limit the utility of such parameters in interpreting an individual patient's risk. Use of a global assay, such as the overall haemostatic potential, provides a simple, reliable means of measuring fibrinolysis in the individual patient. It combines this information with detection of a hypercoagulable state and therefore identifies patients with both increased fibrin generation and reduced fibrinolysis, who are likely to be at greatest risk of thrombosis.

Sunday 14 October **1400-1530**
ASTH Symposium: Fibrinolysis **Central Room C**

1500

Advances in Acute Stroke Management: Thrombolysis and Other Therapies

Christopher Bladin
Eastern Melbourne Neurosciences, Box Hill Hospital, Melbourne, VIC, Australia

There have been significant advances in the management of acute stroke over the past decade. At present there are three key therapies, with level one evidence, to support their use: Stroke Units, aspirin (anti-platelet) therapy, and stroke thrombolysis.

Stroke Units (SUs) have been present in Australia since 1977. They represent one of the most cost effective “therapies” for the management of acute stroke with an NNT (number needed to treat) of 20. However, SUs are primarily located in metro areas and are therefore only available to about 30% of the population; in Australia there is only 1 stroke unit per 1000 stroke patients.

Aspirin administered early has been demonstrated to benefit patients with acute ischaemic stroke, with prevention of further stroke events. The soon to be completed PROFESS trial may give further insights into the benefits of clopidogrel and aspirin/dypiridamole in this regard.

tPA for thrombolysis of acute ischaemic stroke was licensed in Australia in 2003. The goal is to achieve cerebral reperfusion at the earliest opportunity and salvage the ischaemic penumbra (brain tissue that is hypoxic and ischaemic, but not yet infarcted). The use of tPA is within a 3 hour time window and treatment therefore depends on quick recognition that a stroke has occurred, rapid transport to hospital, and brain imaging. Randomised controlled trials indicate that tPA therapy for acute ischaemic stroke has an NNT of about 8 to achieve a good to excellent recovery. Importantly, the results of clinical trials appear similar to those achieved in every day clinical practise. tPA is one of the most effective acute stroke therapies currently available.

There are a number of new therapies that are being investigated for acute stroke. These include novel thrombolytic agents (derived from the vampire bat, and the Malaysian pit viper), “gelatin” type agents (recombinant Factor 7a) for intracerebral haemorrhage, as well as mechanical devices with cork-screw like wires to remove blood clots. These represent exciting advances in future acute stroke therapy.

Sunday 14 October **1600-1730**
HSANZ Symposium: Leukaemia **Arena 1B**
Session sponsored by Novartis

1600

MRC/ECOG Adult ALL Study: Lessons Learnt and Where Next in Adult ALL

Anthony Goldstone
North London Cancer Network, University College Hospital, London, UK

Background
An international collaboration was set up to prospectively evaluate the role of sibling allogeneic transplantation for adults with ALL and compare autologous transplantation with standard chemotherapy.

Methods
Patients received 2 phases of induction and, if in remission, were assigned to allogeneic transplantation if they had a compatible sibling donor. Other patients were randomized to chemotherapy for 2.5 years versus an autologous transplant.

Results
A donor versus no donor analysis showed that Philadelphia chromosome-negative patients with a donor had a 5-year improved overall survival (OS), 53% (95% CI=48-58%) versus 45% (95% CI=40-49%) (p = .01) and the relapse rate was significantly lower (p = <.0001). The survival difference was significant in standard risk patients (62% versus 52% for the donor versus no donor, respectively,p = .02), but not in high-risk patients (41% versus 35% p = .2) with a high non-relapse mortality rate in the high risk donor group. Patients randomized to chemotherapy had a higher 5-year OS (46%; 95% CI=39-53%) than those randomized to autologous transplant (37%; 95% CI=31-44%, p = .03)

Conclusions
Matched related allogeneic transplants for ALL in first complete remission provide the most potent anti-leukemic therapy and considerable survival benefit for standard-risk patients. However, the transplant-related mortality for high-risk older patients was unacceptably high and abrogated the reduction in relapse risk, so that benefit was restricted to the standard risk group as defined in this study. There is no evidence that a single autologous transplant can replace consolidation/maintenance in any risk group.

Sunday 14 October **1600-1730**
HSANZ Symposium: Leukaemia **Arena 1B**
Session sponsored by Novartis

1640

New Approaches and Insights into the Genomics of Acute Leukemia

Charles Mullighan
Pathology, St Jude Children's Research Hospital, Memphis, TN, USA

A major challenge in leukemia research is the identification of the full complement of genomic abnormalities required for the establishment of the leukemic clone. The hope is that this will identify rational targets against which novel therapies may be developed. The advent of the human genome project has facilitated the development of several microarray platforms that allow interrogation of genomic abnormalities in cancer at very high resolution. These include single nucleotide polymorphism (SNP) and oligonucleotide arrays that allow detection of copy number abnormalities (CNAs) and loss of heterozygosity (LOH) at a resolution of below 5 kb. At St Jude, we have used SNP arrays examining over 615,000 markers in over 500 acute leukemia samples including *de novo* acute lymphoblastic and myeloid leukemia samples, and samples obtained at relapse. Corresponding germline samples were also examined in the majority of cases to distinguish somatic changes from inherited copy number variations. Complementary high-throughput methylation analysis and cancer gene resequencing has also been performed. Overall, there are marked differences in the frequency and nature of CNAs and LOH between AML and ALL, and across leukemia subtypes. The most striking abnormalities were observed in ALL, where 40% of B-progenitor ALL cases harbor focal, recurring deletions, amplification, translocations, or point mutations in genes encoding regulators of normal B cell development, indicating that mutations targeting this pathway are a key step in the pathogenesis in B-ALL. The most commonly involved genes were the transcription factors *PAX5*, *EBF, IKZF1* (Ikaros), and *LEF1*. Furthermore, several abnormalities are strictly associated with disease subtype, and integrated analysis with gene expression data has identified the genetic basis of a novel subtype of ALL. Other ALL subtypes, such as *MLL*-rearranged and *TCF3-PBX1* leukemias harbor fewer abnormalities, suggesting these lesions require fewer cooperating events to induce leukemia. Sequencing of the genomic breakpoints at sites of recurring deletion has provided novel insights into the mechanisms of deletion, and indicates that many lesions arise from specific mechanisms, such as aberrant V(D)J recombination, rather than generalized genomic instability. The frequency of CNAs and copy-neutral LOH is much lower in AML, and the pattern of CNAs and recurring point mutations differs significantly between AML subtypes. These analyses have provided important insights into the mechanisms of leukemogenesis, and will serve as a foundation for the design of high-throughput screens for the development of novel therapies in acute leukemia.

Sunday 14 October **1600-1730**
HSANZ Symposium: Leukaemia **Arena 1B**
Session sponsored by Novartis

1705

CML: Biomarkers of Disease Progression and Response to Treatment

Junia V Melo
IMVS, Adelaide, SA, Australia

Abstract not available

Sunday 14 October **1600-1730**
ANZSBT/ASTH Symposium: TTP **Central Room A**

1600

TTP Pathogenesis and Management

Thomas Raife
University of Iowa Department of Pathology, Iowa City, IA, USA

In the broadest sense thrombotic thrombocytopenic purpura (TTP) comprises a heterogeneous group of acute microvascular thrombosis syndromes characterized by multiorgan failure and high risk of mortality. There has been much recent progress in understanding the pathogenic underpinnings of several forms of TTP. Elements of endothelial injury and dysregulation of hemostasis are central to the pathophysiology. Plasma exchange is the only well established treatment, although its utility is not understood in some forms of TTP. Recent evidence reveals a critical role of von Willebrand factor (VWF)-mediated platelet thrombosis and deficient activity of the regulatory enzyme ADAMTS13 in the pathogenesis of many cases of TTP. In vitro studies and studies in ADAMTS13 knockout mice have established a pathogenic model of TTP microvascular thrombosis in which stimulated endothelium combined with unregulated VWF-platelet binding result in microvascular thrombosis. TTP associated with ADAMTS13 deficiency is increasingly recognized as a distinct clinical entity. The etiological role of anti-ADAMTS13 autoantibodies as a cause of this form of TTP, and the therapeutic benefit of replacing ADAMTS13, support new approaches to treatment. Immunomodulation with newer agents like rituximab has gained currency in recent years, despite a lack of controlled clinical trials. ADAMTS13 deficiency is an important pathogenic factor, but not the sole cause, of TTP microvascular thrombosis. Current investigations seek to identify additional pathogenic factors, including other enzymes that may regulate VWF.

Sunday 14 October **1600-1730**
ANZSBT/ASTH Symposium: TTP **Central Room A**

1645

ADAMTS13 Testing

Ian Mackie
Haemostasis Research Unit, Haematology Department, University College London, UK

The use of ADAMTS13 assays in thrombotic thrombocytopenic purpura (TTP) has been limited by the rarity of the disease, technical difficulty and time taken. First generation activity assays involved incubation of plasma with VWF and measurement of residual VWF. Assays using electrophoretic detection of VWF multimers are difficult, lengthy, with limited sensitivity and precision, since they depend on resolution of multimer bands. Analysis of residual VWF in a ristocetin aggregation system has performed well, but precision can be poor and throughput is limited. Assays based on the binding of residual VWF to collagen are also time consuming, but the ELISA principle allows high throughput, with better sensitivity and precision. However, there are numerous potential sources of error. Second generation activity assays employ peptide substrates based on the ADAMTS13 cleavage site in VWF. These are rapid, producing results within a few hours, with high throughput, good precision and sensitivity. However, these assays may fail to detect certain inherited ADAMTS13 defects, since they measure metalloprotease activity independent of exosite interactions with other VWF domains. Inhibitor tests are generally simple mixing studies with normal plasma, followed by an activity assay and are often unreliable with dilution artefacts and time dependency. Heat inactivation provides some improvement, but then basically only IgG is being detected. Many patients have antibodies with complex reaction kinetics, so that Bethesda units cannot be applied. Direct antibody assays are available for IgG and yield rapid results, assays for IgM and IgA have been reported, but the clinical significance is uncertain. ADAMTS13 antigen methods vary depending on coating and detection antibodies; some are specific for full length protein, while others detect proteolysed forms. Antigen assays have limited clinical utility, since the majority of TTP patients have immune complexes, however they can be helpful in differentiating congenital TTP. Activity assays confirm the diagnosis of TTP and allow treatment to be monitored. IgG anti-ADAMTS13 assays are also useful in this respect, particularly when immunosuppressive therapies are utilised.

Sunday 14 October **1600-1700**
Nurses Symposium: Transfusion in the Haematology Setting **Meeting Room 5**

1600

Reporting of Adverse Events in Transfusion – A Victorian Experience

Lisa Stevenson[1,3], David Beilby[3], Karen Botting[1,3], Julie Domanski,[3] Chris Hogan[3], Geoff Magrin[3], Ellen Maxwell[3], Richard Rogers[3], Carole Smith[3], Neil Waters[2,3], Deane Wilks[4], Erica Wood,[2,3] Larry McNicol[1]
[1]*Better Safer Transfusion Program, Department of Human Services, Melbourne*
[2]*Australian Red Cross Blood Service, Melbourne, Victoria, Australia*
[3]*Better Safer Transfusion Program – STIR Expert Group, Department of Human Services, Melbourne, Victoria, Australia*

Background
Transfusion adverse events: what should we report? Haemovigilance is an important part of the transfusion improvement process; it enables review of systems and procedures and allows a focus on problem areas. A working group of Better Safer Transfusion (BeST) Program developed the Serious Transfusion Incident Reporting (STIR) system so that Victorian health services can report centrally. It was designed so that health services firstly report and investigate transfusion incidents internally and then, as an adjunct, report to STIR for a statewide review.

Method
The system is a two-layer process: an initial notification of the incident to BeST and then a follow-up investigation by the health service using STIR forms to guide the process. The initial forms were paper based and are now in electronic format online. The system captures ten clearly defined serious hospital transfusion incidents (including near misses), relating to pre-transfusion samples and fresh blood components, namely red cells, platelets, fresh frozen plasma and cryoprecipitate. Incidents are reported by a health service nominated contact through the Clinical Governance or Clinical Risk management of the health service.

Results
The system was piloted in 2006 and a total of 42 incidents meeting STIR criteria were reported. At the conclusion of the pilot project, 39 of these reports had been investigated by the health service and reviewed by a STIR Expert Group that advises the BeST program.
The types of reports received are outlined in the following table.

Near miss events, including wrong blood in labelled pre-transfusion sample	18 (43)%
Acute and delayed reactions	18 (43%)
Possibly transfusion-related acute lung injury	2 (5%)
Suspected bacterial contamination	2 (5%)
Incorrect blood component transfused	2 (5%)

Conclusion
Victoria has developed a central reporting system with tools for health services to report serious transfusion incidents. The aim of the system is to measure and monitor these incidents and make recommendations for better, safer transfusion processes for implementation within individual health services across the state.

Sunday 14 October **1600-1700**
Nurses Symposium: Transfusion in the Haematology Setting **Meeting Room 5**

1620

HLA Platelets – The Who, When and Why of Ordering, Collecting and Administration

Bev Quested[1] & Kaylene Huxtable[2]
[1] ARCBS, Adelaide, SA. [2] ARCBS, Brisbane, QLD, Australia

For haematology patients undergoing treatment Platelet transfusions are often an essential part of supportive treatment. In patients who fail to adequately increment after a standard platelet transfusions the next step is to move to HLA matched platelets. HLA platelets rely on having time to locate a matched donor who is available to donate as well as for the patient to have HLA typing to be matched against. Anecdotal evidence indicated that clinician knowledge of the steps required in obtaining HLA matched platelets is lacking at times. The appointment by ARCBS of Transfusion Nurse Consultants by ARCBS seeks to address to some of these issues as well as streamline the ordering process in each of the states. This paper explores some of the efforts undertaken to improve the process for requesting HLA platelets, finding suitable HLA matched donors and their clinical use across Australia.

Sunday 14 October **1600-1700**
Nurses Symposium: Transfusion in the Haematology Setting **Meeting Room 5**

1640

Granulocyte Transfusions – What, When, How?

Christine Akers
The Alfred, Melbourne, Victoria, Australia

The major complication in patients with prolonged disease, or therapy-related neutropenia is an increased risk of infection. [1] Granulocyte transfusions (GTX) have been recognised as one possible way of treating these patients. However this is a controversial treatment due to limited evidence from randomised controlled trials of effectiveness and the logistical problems associated with obtaining a therapeutic product. [2]

There are no central pools of granulocyte donors and institutions must recruit donors and conduct their own assessment of eligibility to donate which may be less rigorous than that applied to volunteer red cell donors. Donors need to be educated about the risks of the procedure, be tested for infectious disease markers and provide consent, all of which can take time to organise. The collection procedure calls for priming of donors and the use of a sedimenting agent which is not without risks.

Due to the limited life span of granulocytes long term storage is not possible requiring daily collections, good liaison between the collection centre and the ward and the availability of a number of donors.

GTX administration is an uncommon procedure leading to limited experience and knowledge of staff infusing the product. While GTX may be complicated to organise it may still provide benefit to selected patients as a treatment modality or as a prophylactic therapy.

Reference

1 Dale, DC, Lilies, WC, Price, TH. 'Renewed interest in granulocyte transfusion therapy'. British Journal of Haematology 1997; 98:497.
2 Bishton, M and Chopra, R. 'The role of granulocyte transfusions in neutropenic patients'. British Journal of Haematology 2004; 127: 501-508.

Sunday 14 October **1700-1730**
Nurses Symposium: Transfusion Education and Staff Updates **Meeting Room 5**

1700

Blood Safe E-learning

Bev Quested
ARCBS and BloodSafe, Adelaide, Australia

Education of all clinicians about the appropriate handling, transport and administration of blood products is a key plank of transfusion safety. A brief overview of the e-learning tool developed by BloodSafe for all Australian clinicians to undertake to improve their transfusion knowledge will be given as well as feedback from users of the package. Furthermore, local and international transfusion education packages currently being developed for clinicians in specialty areas will be covered.

Sunday 14 October **1700-1730**
Nurses Symposium: Transfusion Education and Staff Updates **Meeting Room 5**

1715

Training Transfusion Nurses in Victoria: What Have We All Learnt?

Karen Botting[1, 2], Neil Boyce[2], Judy Forsyth[3], Larry McNicol[4], Erica Wood[2]
[1]Better Safer Transfusion Program, Quality and Safety Branch, Department of Human Services, Melbourne, Victoria, Australia, [2]Australian Red Cross Blood Service, Melbourne, Victoria, Australia, [3]Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia, [4]Austin Health, Melbourne, Victoria, Australia.

Aim
To describe the entry level graduate certificate course developed in Victoria, Australia and used to develop the specialist transfusion nurse role. This role is an important mechanism for achievement of clinical transfusion practice improvements, including the implementation of national clinical practice guidelines.

Method
The course was developed in 2002 and first delivered in 2003 as a combination of face to face lectures/tutorials, self-directed learning and practical work. It is now conducted entirely online to improve access. The course is accredited by The University of Melbourne School of Nursing, administered by the Australian Red Cross Blood Service and coordinated by the Education Department at Peter MacCallum Cancer Centre. Course content is based on existing Australian transfusion guidelines. Participant numbers are limited, with the aim of providing individualised support to students. Training is a requirement for funding of the public hospital transfusion nurse positions in Victoria, Australia. Course content includes four subjects (~40 topics), including quality management. Annual content updates have been informed by regular student evaluations.

Results
The course provides students with knowledge and skills to stay up to date, such as familiarity with obtaining information electronically and encouraging learning from peers through dialogue and information sharing. Overall satisfaction with the course has been 78 per cent (2004–2006). Past students' comments include: "The course is invaluable for those wishing to be a transfusion nurse consultant" and "I have recommended this course to others". Initially set up to assist transfusion nurses, participants have subsequently included Australian and international scientific and medical professionals.

Conclusion
Academic training is desired and valued by transfusion nurses for practical reasons including increasing their transfusion knowledge and gaining recognition for the role. The online environment ensures national and international access. Further development will ensure evolution to meet changing needs. More information is available at: www.health.vic.gov.au/best/tools/cert.htm.