P43
Experience on the Utilisation of Palifermin in Peripheral Blood Stem Cell Transplant (PBSCT)

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A problem of PBSCT not overcome by stem cell reinfusion is damage to the mucosal lining of the gastrointestinal tract (GIT) with potential for substantial morbidity. Palifermin a human keratinocyte growth factor (KGF) that results in the growth and differentiation of epithelial cells has the potential to overcome the significant GIT complication associated with PBSCT. Experience of PBSCT in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM) who have received palifermin compared to controls will be reported. A total of 24 PBSCT patients palifermin =12 (NHL = 7, MM = 5) v controls = 12 (NHL = 7, MM = 5), median age of 55 yrs palifermin (range 46-75) v controls 56.5yrs (range 42-68) were analysed. Patients were administered (palifermin v controls) BEAM = 7 v 7, Melphalan= 2 v 5, CVB=3 v 0 and were reinfused a median CD34 dose of palifermin 5.5 $x10^6$ (3.1-14.1): controls 5.7 $x10^6$ (3.6-12.3). Engraftment data (palifermin v controls) in days (median) was: neutrophils >0.5 (10 v 10.5); platelets >50 $x10^9$/L (14 v 26.5); blood transfusions (5.5 v 6); platelet transfusions (4 v 10); hospital days from "day 0" (18 v 24). Oral mucositis was mild/moderate in 66% of palifermin patients and in 42% of controls. Diarrhoea was moderate/severe in 8% of palifermin and 33% of control patients. In those with GIT toxicity (palifermin v control), neutropenic enterocolitis was seen in 1 v 5 and total parenteral nutrition was administered in 1 v 6. The palifermin course was completed in 75% of patients. The major toxicity with palifermin administration was skin rash (8/12 patients). Although this is a small patient group, palifermin has reduced GIT toxicity and therefore can improve the tolerability of high dose chemotherapy for patients. A randomised trial using the agent in common conditioning regimens would be appropriate.

P44
Management of Autoimmune Thrombocytopenia with Rituximab: A Report of Our Experience at Monash Medical Centre

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Introduction: Autoimmune thrombocytopenia (AT) is characterised by antibody-mediated platelet destruction and can be idiopathic or secondary. Traditionally AT is managed with immunosuppression, intravenous immunoglobulin (IvIg) and splenectomy. (1) Despite these measures many patients remain refractory to treatment or suffer intolerable side effects. Rituximab an anti-CD20 monoclonal antibody is a novel therapy utilised in idiopathic AT with encouraging results.(2,3) The data on secondary AT is limited to case reports.(4,5) We would like to report our experience at MMC in managing AT with rituximab.
Method: Retrospective analysis of patients with AT treated with rituximab. All information was obtained via medical records.
Results: Five patients had rituximab since 2002; four had chronic refractory AT. All were female; age range 19-80 years. Two patients had idiopathic AT; three had underlying lupus or low-grade lymphoma. Four patients received prior treatments with prednisolone/IvIg; two also received azathioprine, cyclophosphamide or methotrexate. All four had transient responses to IvIg (i.e. platelet count>$50x10^9$). Three patients were splenectomised with response duration ranging from 4-72 months. The fifth patient (with follicular lymphoma) had no prior treatment.
Rituximab was administered at 375mg/m^2/wk for 4 weeks. Three patients had booster doses 3-6 months later despite normal platelet counts. Treatment was well tolerated. Concurrent prednisolone was administered to four patients; one (underlying lupus) also received azathioprine and another (underlying follicular lymphoma) received one dose of intravenous cyclophosphamide/vincristine/IvIG and further oral cyclophosphamide. All patients responded; response time ranging from 2-84 days. Two patients relapsed

at 6 and 21 months; both were retreated successfully and remain in complete remission (platelets>100x10^9) 7-8 months later (one patient is still on prednisolone/azathioprine). The remaining three patients are in complete remission 18+ months later. These 3 were weaned off prednisolone/cyclophosphamide between 5-7 months post infusions.
Conclusion: Rituximab is an effective, well tolerated agent producing durable remissions in patients with AT.

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P45
Cryopreserved Ovarian Tissue from Patients with Hodgkin Lymphoma: Factors Predictive of Oocyte Yield and Examination for Disease Contamination

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Introduction: Ovarian cryopreservation is a promising strategy for fertility preservation in patients pre-chemotherapy. However there is concern regarding disease reimplantation, as murine studies demonstrate that reimplanted ovarian tissue can transmit lymphoma. Another difficulty is identifying those patients with an adequate number of ovarian follicles in harvested tissue.
Aims: To examine harvested ovarian tissue for subclinical involvement by Hodgkin lymphoma (HL) by morphology/immunohistochemistry, and to define patient and treatment factors predictive of oocyte yield.
Method: Retrospective analysis of 25 cryopreserved ovarian tissue samples harvested from women with HL. Histology, immunohistochemistry (CD15/CD30) and follicle density (number/mm^3) was examined by a single expert pathologist. Disease status and pre-harvest chemotherapy details were obtained via questionnaires to treating physicians on 20 patients. Mann-Whitney U-test and Pearson's correlation-coefficient were calculated using Minitab software.
Results: Median age was 22 years (range 13-29). Ten of 20 patients had infradiaphragmatic disease at diagnosis or at time of harvest and 9/20 patients had B symptoms at diagnosis. Eight of 20 patients had received chemotherapy pre-harvest (ABVD=6, other regimens=2), and one radiation only (excluding pelvis). The 6 receiving ABVD (median number cycles=6) showed no difference in follicle density compared to patients not receiving chemotherapy (n=12) (median=2375, range 45-4512 vs 1620, range 375-2840 p=0.67). Follicle density measurement showed no correlation with patient age (R-squared=0.01, p=0.94). There was no evidence HL involvement by morphology or immunohistochemistry in the 25 samples examined (95% CI for "true" rate of involvement=0-11%).
Conclusion: Subclinical involvement of HL has not been identified in ovarian tissue, even when patients have infradiaphragmatic disease or B symptoms at diagnosis. Quality of tissue harvested does not appear to be adversely affected by patient's age or prior ABVD chemotherapy, and thus should be considered in patients with relapsed disease prior to salvage therapy or high-dose therapy.

P46
Effect of the "Hyper-CVAD" Chemotherapy Regimen on Female Fertility

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Introduction: Hyper CVAD–MTX/HiDAC, a dose-intensive regimen consisting of cyclophosphamide/doxorubicin/vincristine/dexamethasone alternating with methotrexate/cytarabine has been used with encouraging results in mantle cell and lymphoblastic lymphoma, and leukaemia and is under investigation by the Australasian Leukaemia and Lymphoma Group for the initial therapy of poor-prognosis diffuse large-cell lymphoma. The acute side-effects of this regimen are well-documented. However, long-term effects on fertility have not been explored. Therefore the aim of this study was to assess the impact of Hyper-CVAD on female fertility.
Method: Retrospective analysis of women <40 years of age who received Hyper CVAD-MTX/HiDAC as initial chemotherapy at two centres. Menstrual pattern (off hormonal agents) and pregnancy were used to define ovarian function and fertility.
Results: Twelve patients were identified, however 5 were inevaluable (early death in 3, and continuous oral contraceptive use in 2). Of the 7 evaluable patients, 2 had acute lymphoblastic leukaemia (and also received prednisolone/vincristine/mercaptopurine/methotrexate maintenance), 2 diffuse large-cell lymphomas, 1 anaplastic lymphoma, 1 primary mediastinal lymphoma and 1 lymphoblastic lymphoma. Median age was 25 years (range 19-35). Median number of Hyper-CVAD and MTX/HiDAC cycles administered was 4 and 3 respectively. Of the 7 patients, 6 maintained their fertility, as evidenced by return of regular menstrual cycles off hormonal agents, or by naturally achieving pregnancy (n=3). The time to resumption of regular menstruation ranged from 1-15 months post cessation of chemotherapy. One patient (age 35) remains amenorrhoeic at 6 months post completion of chemotherapy.
Conclusion: Resumption of regular menstrual cycles is probable after Hyper CVAD- MTX/HiDAC chemotherapy. Multiple successful natural pregnancies have been achieved. Future studies are required to corroborate these findings and to accurately define the percentage of women in who ovarian function will be retained.

P47
Improved Clinical Management of CML Patients Following Allogeneic Bone Marrow Transplant Using Quantitative Real-Time PCR

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Aim: Chronic myeloid leukaemia (CML) is a clonal proliferative disorder that is characterised in most cases by the presence of BCR-abl mRNA, an ideal molecular target for monitoring disease in patients. Many techniques have been developed to detect this target, most recently, quantitative real-time PCR (Q-PCR). This assay provides superior disease monitoring by indicating the actual level of disease. Increasing Q-PCR results are now considered prognostic of emerging relapse and can be used as a basis for therapeutic intervention. We report the application of Q-PCR to monitor BCR-abl levels in CML patients post allogeneic bone marrow transplant (BMT) resulting in improved clinical management.
Method: Q-PCR using Taqman technology on the Applied Biosystem 7700 Sequence Detection System was used to monitor BCR-abl levels in 19 CML patients post BMT at various time intervals.
Results: 14/19 patients achieved and maintained undetectable BCR-abl post BMT whilst in haematological and cytogenetic remission. Interestingly eight patients demonstrated a transient low level of BCR-abl in plateau, despite no change in treatment, after 12 months post BMT. 5/19 patients demonstrated persistence or re-emergence of BCR-abl post BMT that progressively increased in level, signifying molecular relapse. This was confirmed by cytogenetics up to 3 months later in 3 patients.

Relapsed patients were given imatinib with or without donor lymphocyte infusion (DLI). Q-PCR clearly indicated the decrease in BCR-abl levels allowing precise modulation of therapy.
Conclusion: Q-PCR to monitor BCR-abl levels in CML patients post BMT provided the earliest indication of patients at risk of disease relapse and a superior means of monitoring disease response to treatment, improving patient outcome.

P48
Progressive Hepatic Lymphoma Successfully Treated with Regional Chemotherapy Through a Hepatic Artery Catheter

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Introduction: Patients with intermediate or high grade non-Hodgkin's lymphoma (NHL) presenting with progressive disease despite optimum therapy pose a major clinical problem, especially when involving multiple sites or a major organ such as the liver. This report describes successful treatment to progressive hepatic lymphoma with regional chemotherapy.
An 82 year old gentleman presented with generalized lymphadenopathy and was found to have small cell follicular lymphoma on inguinal lymph node biopsy. Staging investigations showed stage IV disease with multiple sites of gallium avidity above the diaphragm. The liver was normal on CT examination, as were the liver function tests. He was commenced on Rituximab-CHOP chemotherapy.
One month post commencement of chemotherapy, his liver function tests became deranged and there was rapid development of massive hepatomegaly and palpable nodules. A repeat CT scan showed multiple hypoechoic lesions throughout the liver but reduction in the size of the previously described lymphadenopathy. Core biopsy of the liver showed B-cell NHL of intermediate to large cell type.
More aggressive systemic combination chemotherapy or radiotherapy was deemed unsuitable because of his age and the widespread hepatic disease. Regional chemotherapy with cytarabine (500mg in 1L normal saline given as a 24 hour infusion) was administered via a hepatic artery catheter (HAC) thrice during the first week with prompt and significant response. This was repeated at 3-weekly intervals, along with concurrent systemic treatment (R-CHOP). Both modalities were well tolerated. He remained well and in remission for six months but succumbed to aspiration pneumonia at ten months from diagnosis.
Administration of chemotherapy via HAC has been used for hepatic colorectal metastases and hepatocellular carcinoma. To the best of our knowledge this is the first report of this approach for malignant lymphoma.

P49
Occult Chronic Lymphocytic Leukaemia (CLL) in Patients with Aggressive Non-Hodgkin's Lymphoma: The "Reverse Richter's Syndrome"

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Richter's syndrome (RS) refers to the development of high grade non-Hodgkin's lymphoma (NHL) in patients with CLL or small lymphocytic lymphoma (SLL). The reported incidence ranges from 2-8%. It is not clear if RS represents a clonal evolution or an independent neoplasm. In this report we describe a series of four patients seen during the past three years in out institution who presented with aggressive NHL and on staging investigations were found to have a sub-population of cells with classical CLL phenotype- CD5+, CD19+, CD20+, CD23+, CD10-.

Age/Sex	NHL		CLL			Outcome
	Histology	Stage	Peripheral blood	Bone marrow	Lymph node	
70 yo Female	DLBCL- para-aortic lymphadenopathy IPX: CD15-, CD20+, CD79a weak, CD30++, CD45++, CD3-	Stage III	-	+	-	NHL in CR, CLL still occult at 3 yrs
74 yo Male	Burkitt's lymphoma of gastric mass IPX: CD10+++, 20++, 23-, CD5-, BCL2-, sIg+, Ki67+	Stage IV	+	+	-	NHL in CR, CLL still occult at 1 yr
58 yo Male	DLBCL- mesenteric mass IPX: CD79a, CD20+, LCA+	Stage III	-	+	-	NHL relapse resulting in death at 15 months
79 yo Male	DLBCL- bone marrow CD19++, CD20+, CD22+,5-, 10-, FMC7++, 79b++, 38+, 103-,kappa ++	Stage IV	+	+	-	Death due to disease w/n 4 weeks

DLBCL = diffuse large B cell lymphoma
CR= complete remission

Conclusions: These patients represent the opposite or the reverse side of the syndrome originally described by Richter. We will be interested to hear of any similar cases from other Australasian centres; collation and analysis of all these cases may enable a better insight to the to the relationship between these two entities.

P50

Preliminary Results of the Caspofungin Case Study Project: a Retrospective Study of the Clinical Experience of Cancidas® (caspofungin acetate) for Invasive Fungal Infections in Adults in Selected Australian Hospitals

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Cancidas® is approved for use in a number of settings. The Australian caspofungin case-study project is an ongoing retrospective study exploring the post-marketing use and efficacy/safety of Cancidas® in a variety of non-comparative settings.
Six hospitals are participating in this study. For inclusion, patients must have received caspofungin between January-June 2004. A standardised data collection form is used.

By May 2005, data from 14 patients had been received. The mean age was 52 years and 64% (n=9) were male. In 13 patients, caspofungin has been used in symptomatic patients with possible/probable/proven invasive fungal infection. Risk factors were: HIV-infection (n=1), indwelling central lines (n=2), septic shock (n=1) chemotherapy (+/- neutropaenia) for haematological malignancy (n=6) and immunosuppression for bone marrow transplant-related graft-versus-host-disease (n=3). In one patient caspofungin was used as primary fungal prophylaxis. Seven of nine patients with a current/past history of haematological malignancy had used either fluconazole (n=3) or itraconazole (n=3) as primary prophylaxis; one had used voriconazole as secondary prophylaxis. In the haematology group, caspofungin was used to treat definite (n=1) and possible (n=5) invasive pulmonary aspergillus; 2 patients received caspofungin for possible invasive candida. Caspofungin was used as first-line treatment in 5 of these 8 patients. Mean duration of use was 13 days (range 3-21 days); the drug was well tolerated. Five of these 8 patients responded, despite this 2 still died. Overall 5 patients died, 2 due to underlying disease and 3 to fungal disease progression (2 proven).
This small study demonstrates the diversity of Cancidas® use in Australia. The drug was well tolerated in all patients. While the majority of haematology patients responded to caspofungin, 5 out of 8 died, 3 due to fungal disease. This outcome is only too common in this setting and is a source of ongoing frustration for clinicians caring for these patients.

P51
A Case of Severe Transfusion-Dependent Congenital Dyserythropoietic Anaemia Type II. Pitfalls in the Diagnosis Revisited

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The congenital dyserythropoietic anaemia's (CDA) are rare inherited disorders characterised by ineffective erythropoiesis and distinct morphological abnormalities of erythroblasts seen on bone marrow examination. There is significant genetic/phenotypic heterogeneity manifested as a variable degree of clinical severity between the recognised forms. Precise diagnosis may be delayed in these patients as result of clinical and laboratory pitfalls. It remains imperative to pursue an accurate diagnosis in order to guide management and further document the natural history of these rare disorders.
An 18-year-old female presented with severe bi-ventricular cardiac failure in the setting of transfusion associated haemosiderosis. She had previously been diagnosed with CDA type IV at age 6, following investigation for anaemia. At initial diagnosis, she was icteric with hepatosplenomegaly and a facies consistent with marrow expansion from ineffective erythropoiesis. Bone marrow cytology was suggestive of CDA type II. However, CDA type IV was diagnosed consequent to a negative acidified-serum test, and the clinical severity of her anaemia. The patient remained transfusion dependent on desferrioxamine until her recent presentation. Following aggressive iron chelation she stabilised clinically and the diagnosis of CDA was revisited. Raised levels of serum transferrin receptor, erythropoietin, and biochemical features of intramedullary haemolysis confirmed ineffective erythropoiesis. Bone marrow cytology again showed features of CDA type II. Repeat acidified-serum test with 10 donors was shown to be positive in two, and repeat testing with anti-i sera revealed agglutination at a very high titre. The patient has been reclassified as CDA type II. Whilst the clinical severity and transfusion dependency is inconsistent with previously described cases, this is likely to represent genetic heterogeneity and is an important addition to the documented clinical spectrum of this disorder. The patient is currently considering a splenectomy, which is reported to be efficacious in other patients with CDA type II.

P52
Controlled Patient Drives - Adding Diversity to the ABMDR

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Finding a stem cell donor for a patient relies on matching tissue types. Tissue types are dependent on one's ethnic background. The Northern Caucasian group is very well represented on the Australian Bone Marrow Donor Registry (ABMDR) and in most donor registries internationally. There are currently over 162,000 donors on the ABMDR, over 47,700 being registered in NSW and ACT alone. At least 74% of donors on the ABMDR classify themselves as Northern Caucasian. The aim of the ABMDR is to encourage other ethnic groups such as Asian, Middle Eastern and Southern Caucasian to join the registry so that our registry reflects the multicultural patient population. The ABMDR is often flooded with donors after a public appeal for volunteers. There are enormous problems with patient drives if they are uncontrolled public drives, the consequence often being inappropriate volunteers e.g. over 40 years of age, female Northern Caucasoid donors. What the registry needs is younger, male and ethnically diverse donors.

The family of an 11 year old girl newly diagnosed with CML had contacted the ABMDR-NSW/ACT coordinators for information on how to recruit more donors. The child was from a Eurasian background (Caucasian father, Chinese Asian mother). After consultation with the coordinators from the ABMDR-NSW/ACT office a media fact sheet was prepared outlining the requirements for this patient drive. The media are always keen to promote a story with what they perceive as a good cause especially if it is about a young child who is in need of a bone marrow transplant.

The requirements for this drive were donors (preferably Eurasian/Asian) aged between 18-40 years of age.

For the duration of the drive (3 months) a total of 102 volunteer donors were recruited onto the ABMDR. Of these, 43 were male and 59 were female with an average age of 29. The number of donors entered as "Multiple Race" were 47; Northern Caucasian as 41; Asian as 10 and "Other" as 4.

In conclusion, it is important for the ABMDR coordinators to work closely with a family when the patient is from a minority ethnic community so that its' members are encouraged to join the registry. This makes it more likely that a matched donor will be found. This also ensures that the drive is controlled and appropriate volunteers are targetted. This way the ABMDR becomes genetically diverse.

P53
Pure Red Cell Aplasia After Major ABO-incompatible Allogeneic PBSCT Treated Successfully with Plasma Exchange

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Purpose: To explore the effectiveness of plasma exchange in the treatment of patients with pure red cell aplasia (PRCA) who are resistant to treatments such as intravenous gammaglobulins, steroids and subcutaneous erythropoietin after major ABO-incompatible allogeneic peripheral blood stem cell transplantation.

Methods: Plasmaphereses were performed using the cell separator COBE Spectra to exchange the patients' plasma with the group A or group B fresh frozen plasma and albumin solutions

Results: All three patients achieved a clear improvement of their anemic symptoms within a very short time after a single large volume plasmapheresis. Anti-A and anti-B isoaggutinins titres dropped immediately. Reticulocyte counts rose significantly within seven days after plasma exchange. Bone marrow aspirate demonstrated normal cellularity with a higher erythroid percent. Hb level returned to normal, without further treatment. Blood groups were converted from O to A or B.

Conclusions: Plasma exchange is an effective therapeutic method for patients with PRCA following major ABO-incompatible allogeneic stem cell transplantation especially when patients exhibit resistance to treatment such as intravenous gammaglobulin, steroids and subcutaneous erythropoietin. On the other hand, the successful treatment with plasmapheresis suggests an alloantibody mediated etiology.

P54

Corticosteroid-Responsive Central Nervous System Graft Versus Host Disease Complicating a Non-Myeloablative Allogeneic Stem Cell Transplant for Non-Hodgkins Lymphoma

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Central nervous system (CNS) graft versus host disease (GVHD) is rarely reported after allogeneic stem cell transplantation. We report a case of a 48-year-old man with probable CNS GVHD that responded to high dose corticosteroids.

The patient had a history of multiply-relapsed follicular centre cell non-Hodgkins lymphoma (NHL) diagnosed at age 29. Following multiple courses of treatment he had myeloablative chemotherapy with autologous stem cell transplant at age 40. Further relapse with high-grade transformation at age 47 was treated with an HLA-matched, volunteer unrelated donor, allogeneic stem cell transplant with reduced intensity conditioning. At no stage did he receive cranial irradiation or intrathecal chemotherapy.

Post-transplant complications included GVHD of skin and bowel, treated with corticosteroids and cyclosporin. Cyclosporin intolerance required substitution with sirolimus after four months.

In the absence of apparent GVHD, immunosuppression was weaned at 1-year post transplant. At fourteen months the patient developed progressively worsening headaches associated with fevers, personality change and global cognitive dysfunction. Hospital admission was necessitated on two occasions following neurological events consistent with complex partial seizures. He was commenced on phenytoin. Testing for infection including cerebrospinal fluid (CSF) analysis for herpes and JC-viruses was negative. CSF demonstrated normal glucose, a mildly increased protein (0.73 g/L) and lymphocytosis (10 x 10^6 cells/L), without evidence of malignant phenotype on flow cytometry. Vasculitic screen was negative. Electroencephalogram was consistent with encephalopathy. Magnetic resonance imaging (MRI) demonstrated diffuse deep white matter change with a periventricular predominance. Complete remission from NHL was confirmed by negative whole body positron emission tomography scanning.

He was treated empirically with 1mg/kg of methylprednisolone followed by maintenance oral prednisolone. There was an immediate improvement in headaches and cognition allowing him to return home and recommence work. The MRI appearances after 2 months of therapy were markedly improved.

The development of a corticosteroid responsive CNS syndrome following cessation of immunosuppression supports the diagnosis of an atypical manifestation of GVHD.

P55

Evaluation of CD34+ Selection T-cell Depletion of Bone Marrow and Peripheral Stem Cell Grafts using the CliniMACS™ Device

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Aim: To evaluate clinical and laboratory outcomes in paediatric patients undergoing haematopoietic stem cell transplantation receiving grafts that were CD34 selected using the CliniMACS™ device. This procedure achieves a 3-4 log T-cell depletion, with the objective of reducing graft-vs-host disease (GVHD) in patients receiving grafts from matched unrelated donors and in patients with primary immunodeficiency receiving haploidentical grafts.

Methods: Consecutive paediatric T-cell depleted stem cell transplants were evaluated for CD34+ recovery, purity, T-cell content, kinetics of engraftment and GVHD.

Results: Twenty-two grafts were evaluated, 15 from bone marrow (BM) harvests and 7 from peripheral blood (PB) stem cell collections. Donors were related to the recipient in 7 cases, and were unrelated in 15.

The median age of the recipient was 8.9 years (range: 2 months to 18 years). Indications were malignant (n=10) and non-malignant (n=10) disease. The median recovery efficiency of positively selected CD34+ cells was 49% (BM: 49%, PB: 53%) with a purity of 96.4% (BM: 94.6%, PB: 97.4%), a residual T-cell content of 0.08 x 10^5/kg (BM: 0.06 x 10^5/kg, PB: 0.2 x 10^5/kg). A median of 3.5 x 10^6/kg (BM: 1.9 x 10^6/kg, PB: 26.1 x 10^6/kg) of CD34+ cells was infused. One patient failed to engraft. The remainder engrafted at a median time of 16 days (BM: 16 days, PB: 12 days). One patient developed severe GVHD.
Conclusion: These results compare favourably with published data. The grafts collected by bone marrow harvest demonstrate an adequate CD34+ cell recovery, purity and T-cell depletion. As expected, the CD34+ cell dose was lower and the time to engraftment was 4 days longer than following PB stem cell collections. These data support the feasibility of bone marrow and peripheral blood CD34+ cell selection.

P56
The Successful Treatment of Primary Cardiac Lymphoma with a Dose Dense Schedule of Rituximab-Plus-CHOP

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Primary cardiac lymphoma (PCL) is a rare and often fatal malignancy with a varied clinical presentation. Despite the well-documented clinical course, little consensus exists on management of this lymphoma including the best modality of medical imaging for diagnosis and monitoring. We report the first case of the combination of rituximab and CHOP-14 as successful therapy for PCL and highlight the integral role of cardiac MRI and PET in guiding diagnosis, management and monitoring of this condition.
A previously well 76-year-old woman presented with syncope and progressive dyspnoea. Investigations for suspected pulmonary embolus with CTPA revealed a large pericardial effusion and right atrio-ventricular mass. Transoesophageal echocardiography and cardiac MRI confirmed an extensive intramyocardial mass involving the right atrium, right ventricular free wall and encircling the pulmonary artery trunk. Surgical biopsy revealed the histology of diffuse large B-cell lymphoma (DLBCL; CD20 and CD79a positive). Approximately 80% of the cells expressed Ki67. Complete staging confirmed the lymphoma to be confined to the heart. The anatomical extent and metabolic activity of the lymphoma was well demonstrated with the combination of cardiac MRI and PET. Laboratory findings demonstrated an elevated LDH of 1056 U/L. Serum electrolytes, cardiac biomarkers, full blood count and blood film were all normal. HIV serology was negative. The ECOG score at presentation was 2 resulting in a high-intermediate IPI. The potential for cardiac rupture following chemotherapy was assessed using cardiac MRI which revealed the muscular integrity of the right atrium and ventricle to be intact and contractile. The patient received a 14-day interval dose dense schedule of R-CHOP with growth factor support utilising pegylated-GCSF. Chemotherapy was completed with a median of 16 days between treatment cycles. Re-staging following the fourth cycle of chemotherapy demonstrated complete remission. The patient remains asymptomatic with no evidence of disease recurrence eight months following the original diagnosis.

P57
Myeloid/Natural Killer Cell Precursor Acute Leukaemia: A Case Report

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We report the presentation and management of a very rare form of leukaemia with a mixed Myeloid and T cell Natural Killer phenotype.
A 27 year old man presented in May 2004 with a one month history of dyspnoea and right upper quadrant abdominal pain and was found to have bilateral pleural effusions, pericardial effusion and large anterior

mediastinal mass. Peripheral blood demonstrated Hb 126g/l, WCC 4.6 x 10^9/l, neutrophils 3.7x10^9/l, lymphocytes 0.3x10^9/l, monocytes 0.5x10^9/l, eosinophils 0.1x10^9/l and platelets 238 x 10^9/l. Bone marrow aspirate demonstrated 22 % blast cells with L2 features. Flow cytometry demonstrated positivity for CD 34, CD117, HLA-DR, CD13, CD9, CD19, CD79a CD2, CD7, CD56. The clinical presentation, blast cell morphology and flow cytometry results (with the exception of the expression of two B cell antigens) were considered to be consistent with myeloid / NK precursor acute leukaemia as originally reported by Suzuki *et al*, *Blood*. 1997; 90(6):2417-2428. This rare condition carries a very poor prognosis but responds best to AML treatment. Having been started on the day after presentation with an ALL regime for impending superior vena caval obstruction his treatment was changed to an AML regime comprising 2 courses of DAT chemotherapy. His bone marrow was in remission after his first induction treatment. He subsequently received 20cGy of mediastinal irradiation when he was noted to have persisting adenopathy in his mediastinum. He subsequently had two further courses of combination chemotherapy. A PET scan of his mediastinum after this demonstrated that he had no residual disease. He underwent reduced intensity allogenic matched unrelated donor (MUD) peripheral blood stem cell transplantation with fludarabine and melphalan conditioning and has subsequently remained in remission. This patient represents one of the few cases of this rare malignant disease and demonstrates to date that a favourable response can be achieved using aggressive AML type chemotherapy.

P58
Comparison of Tc-99m MIBI (SestaMIBI) Uptake by Transformed and Multiple Myeloma (MM) Plasma Cells

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Introduction:Tc-99m MIBI (SestaMIBI) is used for myocardial imaging, but found to be preferentially (and reversibly, if high p-glycoprotein expression) taken up by malignant cells in breast, brain, thyroid tumors and MM. Significant correlation has been demonstrated in MM patients between % BM plasma cells and increased SestaMIBI uptake of BM in areas of active disease. Percentage of infiltrating plasma cells in the BM is an index of disease activity and can be measured since BM myeloma cells are strongly CD38/138+.
Aim: Our aim was to investigate the binding sestaMIBI to transformed cell lines compared with enriched 138+ BM cells from MM patients.
Method: Malignant plasma cells from the BM of MM patients were CD138+ enriched using MACs separation. Selected CD138+ cells and the following cell lines were plated in equal numbers: myeloid leukaemia cells (KG1a), erythroleukaemic cells (K562), myeloma cells (H929), and the 138-ve cells from the patient samples. Cells were incubated with 100KBq of Tc-99m-SestaMIBI for various MIBI dilutions/time periods/cell concentrations prior to harvesting, collecting both the cell pellet and the washes and radioactivity of both counted. Percentage of radioactivity retained by the cells was compared with the total radioactivity added.
Results: Conditions for optimum SestaMIBI uptake by the cell lines were determined. Variables included time of exposure, dilution of SestaMIBI and non-specific binding to plastic.. The myeloma cell line H929 bound more (average 30 fold) SestaMIBI (fold increase of % bound compared with control) at all times of exposure; followed by K562 (av.10 fold) KG1a (av. 6 fold). BM CD138+ve plasma cells bound 2-3 fold the corresponding CD138-ve fractions.
Conclusion: Myeloma line H929 bound significantly more SestaMIBI than the other transformed cells and the CD138+ BM cells more than double the CD138- cells. Further experiments will aim at elucidating the dynamics of uptake, correlation with p-glycoprotein expression, and compare uptake with patient scans and disease status.

P59
POEMS Syndrome - A Case Report with Poor Prognostic Features

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POEMS syndrome is a rare plasma cell dyscrasia characterised by polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes. Prognosis is generally favourable with overall median survival of 13.7 years in Mayo clinic series (Dispenzieri *et al*, *Blood*, 2003).

We report a 62-year old male who was initially diagnosed with chronic idiopathic demyelinating polyneuropathy of a relapsing course predominantly affecting his lower limbs. No paraprotein was detected at the time. He was unresponsive to IVIG or plasma exchange except high dose corticosteroid. Sixteen months later, he was wheelchair bound and admitted with hyperglycaemia (BSL of 37.9mmol/L) and endocrine screen revealed hypogonadism (testosterone of 1.8nmol/L). Incidentally, he was found to have multiple sclerotic lesions affecting L3 vertebra, right scapula, sternum and ribs, histologically proven to be sclerotic plasmacytoma. Further investigations demonstrated 3g/L serum monoclonal IgG (Lambda) and 3% plasma cells in bone marrow. Other clinical features included pulmonary hypertension, peripheral oedema and skin haemangioma. Organomegaly was absent. He fulfilled the major diagnostic criteria for POEMS syndrome. He was treated with 3 cycles of doxorubicin and dexamethasone followed by radiotherapy to sclerotic lesions. This had lead to a brief six-month period of symptomatic improvement in his peripheral neuropathy. Normal serum free light chain ratio was noted during follow-up. He subsequently developed finger clubbing, marked generalised oedema and gynecomastia. Further studies revealed worsening pulmonary hypertension and mild thrombocytosis. He developed acute respiratory failure with bilateral diaphragmatic palsies demonstrated by fluoroscopy. He continued to deteriorate with pseudo-bowel obstruction and died from multi-organ failure.

This case highlights several poor prognostic features reported in the literature: pulmonary hypertension, clubbing and oedema. Diaphragmatic palsies have not been previously described in POEMS syndrome.

P60
Cutaneous Squamous Cell Carcinoma Behaves Aggressively in Patients with Chronic Lymphocytic Leukaemia

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Aim: Cutaneous squamous cell carcinoma (CSCC) occurring in patients with chronic lymphocytic leukaemia (CLL) may present with locally invasive or regional metastastic disease and may be loco-regionally recurrent. We describe a series of patients with CLL who have developed locally aggressive or regional metastatic CSCC.
Methods: Patients with CLL who developed locally advanced or regional metastatic CSCC were identified from existing databases in the Department of Haematology and Oncology, Princess Alexandra Hospital, Australia from August 2001-May 2005. Patient demographics, tumour characteristics and treatment received were reviewed from the clinical records.
Results: We identified 11 patients with CLL who developed locally invasive or regional metastatic head and neck CSCC: 10 locally invasive and 6 with lymph node metastases. The median age was 72 (range 49-88) and 8 patients were male. The median time to CSCC development was 55 months (range 0-169months) after the diagnosis of CLL. In 6 patients who received purine analogue therapy (fludarabine or cladribine) median time to development of CSCC from treatment was 12 months (range 1-39 months). 8 patients were Rai stage III or IV. 7 of 8 patients with documented IgG levels had hypogammaglobulinemia (median 3.4g/L). All patients had extensive surgical resection and 10 had post-operative radiotherapy. Despite this, three developed loco-regional recurrence (range 6-12 months). 10 patients had numerous CSCC (>5) excised prior to the diagnosis of a locally invasive or regional metastatic lesion.

Conclusions: Patients with CLL are at risk of developing locally invasive and regional metastatic CSCC of the head and neck region leading to significant morbidity and cosmetic disfigurement. Radiotherapy plays an important role as adjuvant or definitive treatment, particularly in unresectable cases. These patients are at high risk of loco-regional recurrence and require close surveillance and early excision of cutaneous lesions. Cellular and humoral immunodeficiencies from CLL and its chemotherapy treatment may predispose patients to aggressive CSCC.

P61
Hereditary Fibrinogen A Alpha-chain Amyloidosis

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Aim: Hereditary fibrinogen A alpha-chain amyloidosis is an infrequently described clinical entity with a characteristic disease phenotype. We describe the first case from Australia.
Case Report: A 62 year old male was seen following a diagnosis of nephrotic syndrome in August 2004, after presenting with marked peripheral and sacral oedema, hypertension and proteinuria. There was no family or personal history of renal disease, hypertension or proteinuria. His only medication was prednisolone which had been started for Polymyalgia Rheumatica two months prior. Examination revealed hypertension (170/90 mm Hg), marked peripheral and sacral oedema but no hepatomegaly, macroglossia or peripheral neuropathy. Full general physical examination was otherwise normal. Significant investigations revealed proteinuria of 5.22g per 24 hours, occasional cellular casts on midstream urine, serum creatinine of 100umol/L, albumin 32g/L and cholesterol 8.9mmol/L. Full blood count, alkaline phosphatase and coagulation screen were unremarkable. Serum and urine electrophoresis and immunofixation did not demonstrate a monoclonal protein. Serum free light chain assay was normal. Renal ultrasound revealed abnormally echogenic kidneys of normal size. There was no evidence of other organ involvement.
Renal biopsy revealed large glomerular deposits of amorphous eosinophilic material without tubular or interstitial deposits that stained positive with congo red and exhibited apple green birefringence under polarized light. Immunofluorescence staining was strongly positive for lambda (subsequently demonstrated to be false positive), but not kappa light chains or AA amyloid. On review the biopsy showed patchy uptake with fibrinogen. His fibrinogen A alpha-chain gene sequencing revealed a valine for glutamic acid substitution at position 526 (Glu526Val), the most common mutation associated with hereditary fibrinogen amyloidosis.
Conclusions: This case demonstrates the diagnostic expertise required to identify hereditary fibrinogen amyloid. Accurate diagnosis can prevent futile and potentially hazardous treatment aimed at eradicating an underlying plasma cell dyscrasia and may allow appropriate alternative therapies such as renal or hepatic transplantation.

P62
EBV-Related Haemophagocytic Lymphohistiocytosis in a Previously Well Adult: A Rare Entity Treated with Immunochemotherapy

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Introduction: Haemophagocytic Lymphohistiocytosis (HLH) is a syndrome of fever, hepatosplenomegaly, CNS dysfunction, cytopenias, coagulopathy and hypertriglyceridaemia due to hypercytokinemia and organ infiltration by phagocytosing histiocytes. It is a rare entity which is mostly described in children. When it

occurs in adults, it is mostly associated with immunosuppression or malignancy. While HLH may resolve spontaneously, severe cases are associated with a high mortality. We present a case report and review of the literature.
Case Report: A previously well 22 year old woman presented with a week's febrile illness and constitutional symptoms as well as some confusion. She was found to be neutropenic and thrombocytopenic, with hepatitis and disseminated intravascular coagulation, as well as a high ferritin. Her bone marrow aspirate showed haemophagocytosis. She had a minor response to high dose intravenous steroids and IVIG, but ultimately was treated with and responded to a paediatric protocol consisting of etoposide, cyclosporin and dexamethasone. She was found to have active EBV viraemia, and preliminary investigation has shown reduced natural killer cell activity. There was no evidence of malignancy.
Conclusions: This is a case of severe EBV-related HLH highlighting the importance of early aggressive therapy of this potentially fatal condition. This approach is supported by clinical trial data.

P63
Primary Skeletal Muscle Marginal Zone Lymphoma with Persistent Tissue Tropism and PET-Avidity

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Introduction: Primary skeletal muscle lymphoma is a rare entity that has been reported to be associated with a poor prognosis. Extra-nodal marginal zone lymphoma of MALT type, is not uncommon, and accounts for 7-8% of all cases of NHL. However, even among this histologic entity skeletal muscle involvement is rare, as evidenced by no instances in a recent series of 180 patients with non-gastric marginal zone lymphomas.
We now report a patient with marginal zone lymphoma and an unusual pattern of disease with multiple recurrences in skeletal muscle. It is noteworthy that ^{18}F-fluoro-deoxy-glucose positron emission tomography (FDG-PET) scanning was found to be the most useful modality in surveillance and disease staging.
Case Report: A 56 year-old man presented with an infiltrative mass of the muscles of the right forearm. Biopsy showed an extra-nodal marginal zone. Staging investigations including FDG-PET revealed multiple sites of soft tissue involvement. The patient received six cycles of standard-dose CHOP chemotherapy and achieved complete remission.
Eight months after completing chemotherapy repeat PET scanning showed increasing abnormal tracer consistent with relapsed disease. This relapse was eventually treated with local radiotherapy.
This was followed by a clinically local relapse, demonstrated by FDG-PET scanning to involve multiple skeletal sites. The patient then received six cycles of fludarabine, cyclophosphamide and rituximab and achieved complete remission. He remains in complete remission to date.
Discussion: To our knowledge, this is the first case report of primary skeletal muscle marginal zone lymphoma, showing an interesting tissue tropism and suggesting a helpful role for FDG-PET in disease staging, which has not been highlighted in the past. This case also responded extremely well to fludarabine-based therapy, with a durable remission after only short-lived responses to other therapies including CHOP and local radiotherapy suggesting this combination is especially useful in this disease.

P64
Treatment of Adult Acute Lymphoblastic Leukaemia: The 2001-2004 Royal Brisbane and Women's Hospital (RBWH) Experience

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Aims: To review the outcome of adult ALL treated at our institution based on local guidelines.

Methods: Records of all patients >15 and <65yrs diagnosed with ALL between January 2001 and December 2004 were retrospectively reviewed. Patients with Burkitt's leukaemia (ALL-L3) were excluded. PFS, EFS and OS were calculated using the Kaplan-Meier method. RBWH treatment guidelines for ALL allow for a choice of induction protocols, depending on consultant preference. Local guidelines also recommend allogeneic stem cell transplantation (SCT) in CR1 for patients with poor risk clinical features if a matched sibling donor is available, and for patients with poor risk cytogenetics (as per CALGB guidelines) with either matched related or unrelated donors. For patients without an allogeneic donor, autologous SCT is permitted at individual patient / consultant discretion.
Results: In total 13 ALL patients (8M and 5F) were identified. Median age was 39yrs (range 24-63). At presentation, 8 patients (62%) had poor risk clinical features (age >50, extensive extra-medullary disease, WCC >300 and / or pro-B phenotype) and 6 (46%) poor risk cytogenetics (+8 in 2 cases; t(4;11) in 2; del7 in 1; and Ph+ in 1). Primary therapy was Hyper-CVAD in 10 patients, GMALL 4/89 in 2, and LALA 94 in 1. Four patients (31%) were refractory to initial therapy, with 2 (15%) rapidly dying of progressive ALL. At median FU of 19mths (range 9 to 39), median PFS, EFS and OS are 12mths, 12mths and 18mths respectively. Of the 6 patients who received SCT in CR1 (5 allogeneic and 1 autologous), 5 remain alive in ongoing remission at median FU 19mths post SCT (range 12 to 30). For patients who did not receive SCT in CR1, 3 of 5 relapsed within 6mths of completion of primary chemotherapy.
Conclusions: Our experience highlights the need for ongoing development of new therapeutic approaches for adult ALL. Our results also suggest that, based on current chemotherapy approaches, SCT continues to have an important role in the initial management of adult ALL.

P65
Successful Desensitisation Protocol for Methotrexate Hypersensitivity Encountered During the Treatment of Primary CNS Lymphoma

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Aims: We present a case of methotrexate (MTX) hypersensitivity occurring during treatment of primary CNS NHL, and describe a successful desensitisation protocol enabling safe completion of multiple cycles of high dose MTX-based chemotherapy.
Case: A 22yr male with primary CNS ALK+ ALCL was commenced on BFM-90 chemotherapy, including administration of x4 cycles of IV MTX 5gm/m2 and recurrent intrathecal MTX (12mg) injections. Within 5mins of commencing initial IV therapy, the patient developed an urticarial rash, angio-oedema and wheeze. The reaction recurred on re-exposure to MTX later the same day despite heavy pre-medication with corticosteroids and anti-histamines.
Results: A desensitisation protocol for MTX was developed, in which corticosteroids (prednisolone 1mg/kg/day), anti-histamines (ranitidine 300mg bd and loratidine 10mg od) and anti-leukotrienes (montelukast 10mg od) were administered 3 days prior, during and 2 days after MTX exposure. To allow close haemodynamic monitoring, each cycle of MTX chemotherapy was administered in intensive care. IV MTX was given as a continuous infusion over 24hrs, commencing at 0.1% of total dose. In the absence of any reactions, at the end of each hour the infused hourly MTX dose was incrementally increased to 0.5%, 1%, 1.5%, 2%, 3% and 4% of total dose, with the remaining dose then infused over the next 17hrs. Folinic acid rescue was administered as per normal BFM-90 protocol. IT MTX was administered post completion of IV MTX, such that in any cycle of chemotherapy <24hrs had elapsed between repeat MTX exposures. The desensitisation protocol was repeated for each cycle of MTX-based chemotherapy. The patient suffered no further reactions to MTX and completed his chemotherapy without significant complications.
Conclusions: For patients with hypersensitivity to chemotherapeutic agents desensitisation can allow safe administration of specific chemotherapy drugs and thus should be considered whenever practical.

P66
Isolated Central Nervous System Relapse of Acute Promyelocytic Leukaemia Confirmed by Fluorescence In-Situ Hybridisation in a 15 Year Old Male Treated with All-Trans Retinoic Acid

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Aim: We describe a case of isolated central nervous system relapse of acute promyelocytic leukaemia (APL). Although rare, this complication has been increasingly described in the era of ATRA therapy, and we review potential mechanisms and risk factors for this phenomenon.
Case Report: A 15 year old male presented with a fever, bruising, and gingival haemorrhage. His full blood count revealed an elevated white cell count of $40.3x10^9$/L with a 90% blast population demonstrating classic morphologic features of acute promyelocytic leukaemia. The presence of t(15;17) was confirmed by standard karyotyping and RT-PCR for the PML-RARA transcript. Induction therapy with ATRA, daunorubicin and standard dose infusional cytarabine led to morphologic and cytogenetic remission, although the PML-RARA transcript remained detectable until after completion of consolidation with two cycles of ATRA plus daunorubicin. CSF examination following induction revealed no leukaemic infiltrate. Maintenance therapy consisted of oral 6-mercaptopurine, methotrexate, and second weekly ATRA. At nine months following presentation a diagnostic lumbar puncture was performed for persistent headache. The CSF contained small numbers of immature cells consistent with malignant promyelocytes, and fluorescence in-situ hybridisation (FISH) confirmed the presence of the t(15;17) translocation. Bone marrow examination remained morphologically normal with negative cytogenetic analysis and RT-PCR for PML-RARA.
Conclusion: CNS relapse of APL has historically been regarded as extremely rare, however increasing reports have appeared since the widespread use of ATRA. Potential factors contributing to this phenomenon include the markedly improved survival with ATRA, biologic changes to leukaemic promyelocytes induced by ATRA which may facilitate passage across the blood brain barrier, and the trend toward omission of cytarabine in induction and/or consolidation therapy. An elevated white cell count at presentation appears to be the most consistently identified risk factor. We also highlight the utility of FISH applied to CSF samples to rapidly confirm leukaemic involvement.

P67
Rituximab Use in Paediatric ITP

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Aims: To review the indications, efficacy and safety of rituximab (anti-CD20 monoclonal antibody, Mabthera®, Roche Pharmaceuticals) in children with immune-mediated thrombocytopaenia treated at a tertiary children's hospital.
Methods: A search of the pharmacy database was conducted for all children who had received rituximab for ITP prior to June 2005
Results: Four cases were identified in which rituximab was used primarily for treatment of ITP. All patients had severe ITP at the time of treatment (platelet count <30 x 10E9), and had either failed conventional therapy (corticosteroids, pooled human immunoglobulin, anti-D, splenectomy etc) or had developed unacceptable side-effects as a result of treatment with steroids. A "standard" rituximab dosing schedule was used in all cases (375mg/m2 weekly for four weeks) and patients received premedication with promethazine, hydrocortisone and paracetamol. Rituximab was well tolerated, and apart from one patient in whom arthralgia and malaise occurred after the second dose of rituximab no adverse effects were documented. Three patients (75%) responded (platelet count >50 x 10E9), 2 achieving complete response (CR: platelet count >150 x 10E9), and 1 patient achieving partial response (PR: platelet count 50-150 x

10E9). All responses occurred within 4 weeks of commencement of therapy. The one PR patient had subsequent relapses at 11 months and 26 months post therapy, but responded well to repeat doses of rituximab with normalisation of platelet counts.
Conclusions: Rituximab appears to be safe in paediatric patients, and may have a role in the management of complicated ITP in this population.

P68
Zoledronic Acid Prevents Bone Loss After Allogenic Haematopoietic Stem Cell Transplantation

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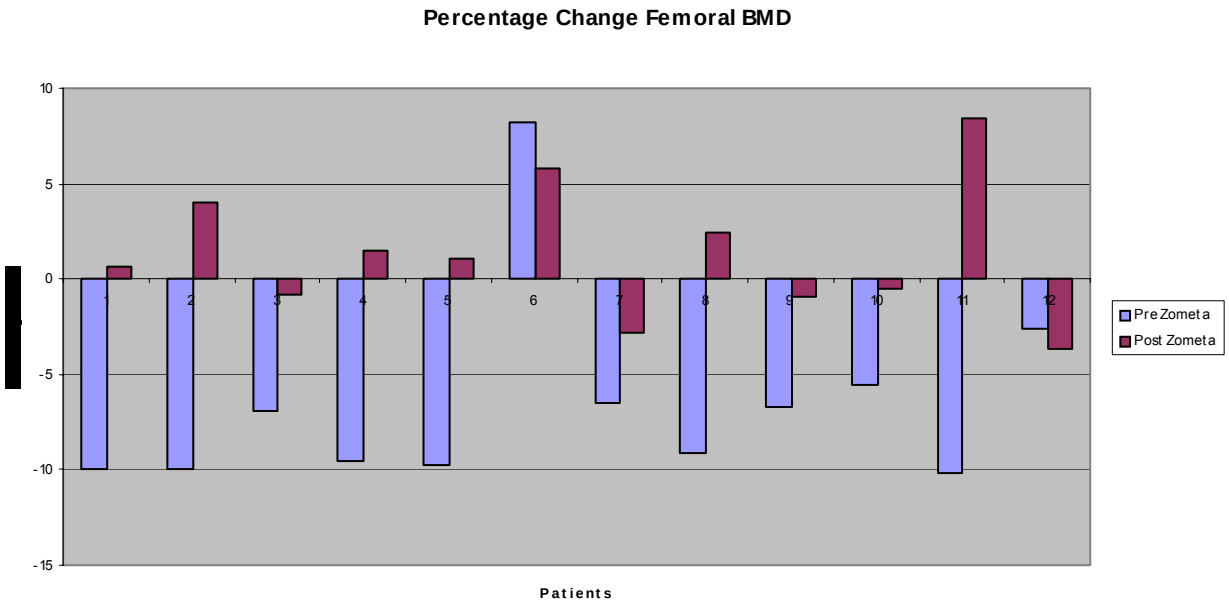
Background: Allogeneic haemopoietic stem cell transplant (alloHSCT) recipients are at increased risk of osteoporosis. Zoledronic acid (ZA) is a potent intravenous bisphosphonate, however, there are few data on ZA use after alloHSCT.
Aim: To examine the effect of a single 4mg ZA infusion in alloHSCT patients with either osteoporosis (T score < -2.5) or rapid bone loss post-alloHSCT.
Method: An uncontrolled, prospective study of twelve consecutive patients receiving ZA, predominantly within the first year post-HSCT. BMD was measured by dual-energy x-ray absorptiometry (DXA) at the spine and proximal femur pre-transplant, pre-ZA and post-ZA.
Results: The median annualised percentage change in total hip (TH) BMD between the pre-transplant scan and the scan immediately prior to ZA was –13% (range –51% - +3.6%). After ZA treatment, the TH-BMD increased by a median of +3.3% (range -20.4% - +14.8%) in 75% of patients. The median annualised percentage change in femoral neck (FN) BMD between the pre-transplant scan and the scan immediately prior to ZA was –13.2% (range –40% - +1.0%). Post-ZA, FN-BMD increased by a median of +1.4% (range –22.2% - +33.6%). Only one patient continued to lose bone from the FN post-ZA infusion. The median annualised percentage change in spinal BMD pre-transplant was – 12.5% (range –38% - +6.9%). Post-ZA, spinal BMD decreased by a median of –2.8% (range –27.6% - +24.4%). Four patients continued to lose bone from the spine post-ZA.
Conclusion: ZA reduces bone loss in most patients after alloHSCT. Our data now require confirmation in a larger prospective, randomised study.
Figure: Individual patient femoral bone density pre and post Zoledronic acid infusion.



P69
Morphology, Cytogenetics and Chimerism Analysis in a Case of Ph+ AML Treated with BMS-354825 Following Relapse after Reduced Intensity Allogeneic Stem Cell Transplant

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Ph+ AML is a rare diagnosis with the largest series of 10 cases being recently described.
Our patient presented with a right femoral lytic lesion, which on biopsy revealed a chloroma consistent with acute myeloblastic leukaemia (AML). Subsequent bone marrow biopsy confirmed AML complicated by marked fibrosis and panmyelosis. Cytogenetic assessment revealed the Philadelphia chromosome positivity by both metaphase banding and fluorescent in situ hybridisation (FISH). Reverse transcriptase polymerase chain reaction (RT-PCR) revealed the BCR-ABL p190 fusion gene with the rare e6a2 breakpoint.
Morphological, cytogenetic and molecular remission was achieved following induction with Idarubicin and ARA-C and Imatinib mesylate 400mg/day, and two cycles of consolidation chemotherapy were completed. Imatinib mesylate was initially escalated to 600mg/d and later reduced to 300mg/d due to recurrent bone marrow suppression. Serial bone marrow assessment revealed ongoing morphological and molecular absence of AML and significant reduction in the fibrovascular stroma.
A reduced intensity matched-sibling allogeneic stem cell transplant (SCT) undertaken in first complete remission. Complete donor myeloid and lymphoid chimerism was confirmed on day100. Graft versus host disease has not occurred. Imatinib mesylate was reintroduced at day 30 post SCT, however marked gastrointestinal side effects and profound marrow hypoplasia at day 100 required its cessation. Molecular studies performed at day 160 indicated AML relapse, which was confirmed on repeat marrow examination.
The patient was subsequently started on the tyrosine kinase inhibitor BMS-354825. To date this agent has been well tolerated. Serial peripheral blood and marrow assessment has shown a further morphological and molecular remission in the setting of ongoing 100% donor chimerism. This case demonstrates that, in

a similar fashion to Imatinib mesylate, BMS-354825 is capable of inducing molecular remission from Ph+ leukaemia and allows marrow repopulation by donor haematopoiesis.

P70
Extramedullary Relapse of t(4:14), 13q$^-$ Myeloma Following Autologous Stem Cell Transplant Presenting with Gastric and Skin Plasmacytomas

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Background: Extramedullary manifestations of myeloma are rare, particularly gastric involvement. However, extramedullary relapse is being increasingly reported following high-dose chemotherapy and autologous stem cell transplantation. To date, there is no recognised association between cytogenetic abnormalities and patterns of extramedullary relapse but, as our understanding of the various cytogenetic abnormalities in myeloma improves, such associations may become evident.
Method/Results: We describe a patient with myeloma with t(4:14) and 13q$^-$ who relapsed less than six months after an autologous stem cell transplant with gastric and cutaneous plasmacytomas. This occurred with only modest marrow disease and a very small rise in serum paraprotein. His disease proved refractory to intensive systemic salvage chemotherapy. Fortunately, some degree of symptomatic relief was achieved with palliative radiotherapy to the stomach.
Only five cases of multiple myeloma with gastric involvement have been reported in the literature in the last 25 years. Loss or deletion of chromosome 13 and t(4:14) are both well-recognised poor prognostic cytogenetic abnormalities. However neither are significantly correlated with extramedullary disease.
Conclusion:
1. Gastric myeloma is rare and therefore a high degree of clinical suspicion is required to make the diagnosis.
2. Extramedullary disease at any site can occur without a significant rise in serum or urinary paraprotein.
3. Radiotherapy is a useful palliative tool in the management of aggressive chemoresistant myeloma.

P71
PET Is a Useful Tool in The Staging of Castleman's Disease

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Background: Castleman's disease (CD) is an uncommon lymphoproliferative disorder that can be classified both histologically (hyaline vascular *vs* plasma cell variants) and by extent of disease involvement (unicentric *vs* multicentric). Positron emission tomography (PET) is being increasingly used in the management of malignant lymphoma. There is very little information in the literature regarding the use of PET in the context of CD.
Method/Results: We describe our experience of using ^{18}F-fluorodeoxyglucose (FDG)-PET as an imaging modality in six patients with CD. FDG-PET was used to assist in staging the patients: Unicentric CD (one hyaline vascular variant and one plasma cell variant) was confirmed in two patients by excluding involvement in other nodal sites seen on computed tomography, and two patients had additional sites detected and "up-graded" to multicentric CD (both hyaline vascular variants). Two patients with known multicentric plasma cell CD (one with POEMS syndrome) had disease sites confirmed by FDG-PET. These latter two patients achieved a good clinical response to systemic chemotherapy and radiotherapy respectively. However, post-treatment PET imaging remained positive in both cases.
Conclusions: 1. PET is useful in differentiating unicentric from multicentric CD.
2. PET was not consistently useful in assessing response to therapy.

However, small patient numbers in this series do not allow for more definitive conclusions and further studies are required.

P72
Mesenchymal Stem Cell Isolation From Human Placenta

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Aims: To determine if mesenchymal stem cells (MSCs) can be isolated and cultured from human placenta.
Methods: Placentas were obtained at elective caesarean section from normal term pregnancies. Working from the foetal side, approximately 1 cm^3 pieces of placenta were excised and washed thoroughly in HBSS. Excised tissue was digested with collagenase I for 3 hours at 37°C. After passing through a 40 μm cell strainer, cells were centrifuged on a Percoll density gradient and the interface placed in culture in DMEM (low glucose) with FCS. After 24 hours, non-adherent cells were removed and the remaining cells cultured until 90 % confluent . At this stage the cells were passaged and further cultured changing media every 3-4 days. After two or more passages, the cells were analysed by flow cytometry. Bone marrow derived MSC were obtained from iliac crest of healthy volunteers and were purified by density gradient and plastic adherence as for placenta.
Results: Using this technique, placental plastic-adherent cells could be maintained and greatly expanded in culture for long periods in a manner similar to bone marrow-derived MSC. After three passages placenta-derived cells were large, plastic-adherent and exhibited an elongated, fibroblast-like morphology. In terms of phenotype, the cells had a similar phenotype to bone marrow derived MSC, being positive for CD29, CD44, CD73, CD90, CD105 and CD166, whilst negative for CD34, CD45 and MHC class II expression. However differences were noted in the expression of CD90 and CD49d. As with bone marrow derived MSC, the placental cells were also shown to be capable of differentiating into cells of the mesenchymal lineage, namely osteocytes, chondrocytes and adipocytes.
Conclusions: The placenta-derived cells exhibited a mostly characteristic MSC morphology and phenotype and thus may be a therapeutically useful source of MSC.

P73
Optimisation of Rat and Mouse Mesenchymal Stem Cell Growth

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Aim: To optimise the culture conditions required for the expansion of bone marrow-derived rat and mouse mesenchymal stem cells (MSCs).
Method: Bone marrow-derived MSCs were isolated by plastic adherence in expansion cultures. After several passages the cells were tested for mesodermal differentiation ability and leukocyte contamination by flow cytometry. The *in vitro* proliferation of rat cells was tested in different media, FCS concentrations, with and without FCS heat inactivation, at several seeding densities and when media was replaced either partially or fully.
Results: Rat (DA) cells adhered to plastic and exhibited an elongated, fibroblast-like morphology. The cells expressed CD59 and CD90, but not the macrophage and leukocyte markers CD11b and CD45. Murine (Balb/c and C57BL/6) cells were more difficult to isolate by plastic adherence. At an early passage the murine MSC cultures had a heterogeneous morphology with CD45+ cell contamination. However, by the third passage CD45+ cell contamination was minimal. Rat and mouse cells differentiated into osteocytes, chondrocytes and adipocytes. Rat cells proliferated more rapidly in alpha-MEM than DMEM-LG. Rat cell proliferation increased as the concentration of FCS in culture increased. Prior heat inactivation of FCS had little effect on MSC proliferation rate. Cells seeded at 10 cells/cm^2, 100 cells/cm^2,

and 1000 cells/cm^2 proliferated at the same rate. However, cells plated at higher densities underwent fewer population doublings to generate the same number of cells. There was no difference in cell proliferation when culture media was replaced either partially or fully every 3-4 days.
Conclusions: Rat MSCs were easily isolated and cultured from bone marrow. Murine MSCs were more difficult to isolate using the same method, but homogeneous populations were obtained after several passages. The cultured rat and mouse cells exhibited characteristic MSC morphology, phenotype and differentiation ability. Rat MSCs are now cultured in alpha-MEM with 10 % (v/v) non-heat inactivated FCS, cells are seeded at 1000 cells/cm^2 and half the culture media is replaced every 3-4 days.

P74
Matrix Metalloproteinase Production by Monocytes in Pre-eclampsia

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Background: Migration of monocytes (Mo), which are key factors in the inflammatory response of pre-eclampsia, from the circulation is mediated by matrix metalloproteinases (MMPs). Activated protein C (APC), which has anti-inflammatory properties and low circulating levels in pre-eclampsia, modulates MMP production in endothelial cells but its effect on Mo MMP production is unknown. This study tested the hypothesis that in pre-eclampsia there is up-regulation of MMP production by Mo, which can be modulated by APC.
Aims: To examine MMP production by monocytes from non-pregnant, pregnant and pre-eclamptic women; to assess the effect of APC on MMP production by monocytes and to localise placental bed APC expression.
Methods: Peripheral blood monocytes were isolated from normal non-pregnant (n=10), normal pregnant (n=10) and pre-eclamptic (n=10) women. MMP production by these Mo was measured by zymography and ELISA under basal conditions and with different concentrations of APC. Statistical analyses were performed using the General Linear Model of Variance and Pearson's correlation test. Immunohistochemistry was used to localise APC in placental bed biopsies.
Results: This study demonstrates significant increases in both MMP-7 ($p<0.01$) and MMP-9 ($p<0.005$) in pre-eclamptic women compared with normally pregnant women. There was no significant difference in production of MMP-7 and MMP-9 by monocytes from non-pregnant and normally pregnant women. APC did not significantly affect MMP production by Mo. APC expression in leukocytes and endothelial cells within the placental bed was lower in pre-eclamptic women than in normally pregnant women.
Conclusion: This study is the first to report that MMP-7 and MMP-9 production by Mo is increased in women with pre-eclampsia, suggesting a role in the inflammatory process. However, there was no evidence that APC modulates Mo secretion of MMPs. Low expression of APC in placental bed biopsies from women with pre-eclampsia is consistent with the inflammatory response.

P75
Gene Expression Profiling in Multiple Myeloma Cells Treated with the Novel Anti-myeloma Agents Zoledronate and Fluvastatin

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Aim: We have recently shown *in vitro* that multiple myeloma (MM) cells can be destroyed by treating them with the mevalonate pathway inhibitors zoledronate and fluvastatin. While the efficacy of these

compounds singly and combination have been demonstrated, their exact modes of action remain largely unknown. The present study aimed to use microarray and quantitative real-time PCR (QRT-PCR) techniques to analyse gene expression in treated myeloma cells to identify novel genes and pathways involved in the anti-myeloma action of these compounds.
Methods: The human MM cell line NCI-H929 was treated with zoledronate and fluvastatin singly and in combination. RNA was extracted and used to interrogate oligonucleotide microarrays consisting of 19,000 features representing known and unknown genes. Quantitative real-time PCR was subsequently used to confirm the expression of several genes of interest. Flow cytometry with Annexin V FITC staining was used to detect apoptosis.
Results: Genes related to apoptosis (caspases and p53-related genes), cell cycle control (cyclins), GTPase signalling (Rabs), and growth and proliferation (growth factors) were particularly affected by zoledronate and fluvastatin, and some of these genetic effects were synergistic when a combination of zoledronate and fluvastatin was used. QRT-PCR confirmed the effects on the caspase- and p53-related apoptotic pathways, and these effects were correlated with increased apoptosis in the myeloma cells.
Conclusions: The mevalonate pathway inhibitors fluvastatin and zoledronate are highly efficient at killing MM cells, and their effects appear to be synergistic. Our microarray and QT-PCR analyses demonstrated that the expression of specific groups of genes important to the survival and proliferation of myeloma cells are affected by these compounds. p53 and caspase-dependent pathways appear to be the key apoptotic cascades stimulated. Insights into the mechanisms of these novel therapeutics are important as they might help to define their roles in the treatment of multiple myeloma.

P76
Recurrent Malignant Melanoma Post Non-Myeloablative Stem Cell Transplant.

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Aim: To report two cases of recurrent malignant melanoma (MM) following HLA-identical sibling non myeloablative stem cell transplant.
Case 1 was a 45 year old man with follicular centrocytic B cell lymphoma (stage IV) diagnosed in 1999. Following 7 different treatment regimens and 4 progressions he had a very good partial response to 6 courses of oral fludarabine, completed in June 2004, and he underwent NMAT in October 2004 following conditioning with fludarabine (90mg/kg) and low dose TBI (2Gy) and GVHD prophylaxis with cyclosporin and mycophenolate mofetil. A lymph node biopsy 4 weeks prior to transplant confirmed follicular lymphoma only. He had had recurrent malignant melanoma (MM) on the right ear from 1990 with excision of the lesion last performed in 1995 without evidence of further recurrence. He developed an atypical illness starting 10 days post transplant which was eventually diagnosed 4 weeks later as metastatic MM, the patient died 3 months post NMAT from fulminant MM. CT scanning had shown widespread tumour deposits not seen pre-transplant and tissue biopsy was consistent with metastatic MM. *Case 2* was a 53 year old man with IgG Myeloma diagnosed in August 2004. He received treatment with VAD x5, high dose melphalan (200mg/m^2) in February 2005 and HLA identical sibling NMAT in May 2005. He had a previous MM of left thigh in 1994 with full excision which was stage 1B (T1bM0N0) and considered good prognosis. A new skin lesion of MM was noted 3 weeks post NMAT and was completely excised.
Conclusion: There are no previous reports of recurrent MM in association with recent NMAT, although this has been recognised in solid organ transplantation and might be predicted in the setting of immunosuppressive therapy associated with NMAT. Further prospective study of effects of NMAT on patients with a prior history of MM is warranted.

P77

Hypereosinophilic Syndrome with Cardiac Involvement - A Case of Identification of FIP1L1-PDGFRA and Imatinib Response

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Recently cases of idiopathic hypereosinophilic syndrome (HES) and chronic eosinophilic leukaemia (CEL) have been reported to be responsive to imatinib despite being negative for BCR-ABL. A different tyrosine kinase fusion gene mutation FIP1L1-PDGFRA has been identified as potentially pathogenic. We present a case of successful identification of the genetic abnormality and response to imatinib in HES with cerebral and cardiac involvement.

A 37 year old man presented in May 2005 for investigation of a 3cm hypodense lesion in left frontal lobe manifesting as speech difficulty and confusion. Full blood examination revealed Hb 5.8g/L, WCC 19.9 $x10^9$/L and platelets 20 $x10^9$/L. Blood film showed marked eosinophilia (5.7 $x10^9$/L) without basophilia. Bone marrow aspirate and trephine demonstrated erythroid and granulocytic hyperplasia with eosinophilia of 13% and increased mast cells (c-kit positive). There were no features of a secondary cause of eosinophilia. Echocardiogram revealed left ventricular mural thrombus.

The patient's condition deteriorated and high dose steroids were commenced on day 2 and imatinib 400mg daily on day 6, reduced to 200mg daily 3 days later. By day 12 the eosinophil count had decreased to 0.1 $x10^9$/L and he had resolution of B symptoms. Follow up at 8 weeks revealed full haematological remission on imatinib 100mg daily. Anticoagulation was possible after resolution of thrombocytopenia.

Cytogenetic analysis was normal and FIP1L1-PDGFRA transcripts were detected by RT-PCR (confirmed with DNA sequencing). The breakpoint identified for FIP1L1 was 3' of exon 13 and the PDGFRA breakpoint was within exon 12.

Although not all cases of HES respond to imatinib and only a proportion of these have the identifiable FIP1L1-PDGFRA mutation, this case highlights the potential for rapid and significant response to low dose imatinib. Further investigation is required to allow the reclassification of eosinophilic syndromes, document remission and organ damage reversal rates and potential resistance/mutation patterns.

P78

Corticosteroid Responsive Encephalopathy Post Allograft – A Potential Case of Hashimoto's Encephalopathy

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The Hashimoto's encephalopathy or "corticosteroid-responsive encephalopathy associated with autoimmune thyroiditis" has been described as an association between neurological manifestations, positive antithyroid antibodies and responsiveness to steroid therapy. We report a 51 year old male allograft recipient with possible Hashimoto's encephalopathy.

APML was diagnosed in 1998 and remission achieved with idarubicin and ATRA. First relapse in 1999 was treated with arsenic. A sibling allogeneic transplant was performed in March 2003 for second relapse and was complicated by severe GVHD. He relapsed soon after the allograft and was salvaged with ATRA and arsenic. He has remained in molecular remission with 100% donor chimerism. Other medical history included occipital lobe stroke, ophthalmic division HSV, hepatitis C, TCC bladder, DVT and depression.

In October 2004 he presented with altered conscious state, myoclonus, ocular tremor and seizures requiring intubation. MRI showed old posterior infarct with mild encephalopathic pattern on EEG. Lumbar puncture showed elevated protein and antithyroglobulin antibodies were markedly raised at titre of 25600 and microsomal antibodies at titre of 400. TSH was mildly reduced and FT4 normal. Extensive infectious, metabolic, toxicology and connective tissue screens failed to provide an alternative diagnosis. There was no evidence of GVHD or drugs implicated. Despite antibacterial, antiviral and antituberculous treatment

he failed to improve. Possible Hashimoto's encephalopathy was diagnosed and high dose steroids commenced. The patient's mental state markedly improved and was discharged 5 weeks later.
At follow up, titres of antithyroglobulin antibody decreased to 6400 and microsomal to 100. Steroids were weaned and he has maintained normal cognitive function thereafter. The allograft donor is negative for antithyroglobulin and microsomal antibodies.
This case highlights the diagnostic dilemma of encephalopathy and the potential usefulness of steroid therapy. Altered immune function post allograft and/or GVHD are potential mechanisms implicated in the pathogenesis in this case.

P79
Parvovirus Associated Pure Red Cell Aplasia with Giant Pro-normoblasts in Two Patients Following Pancreato-Renal Transplantation

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Aim: We describe the clinical and bone marrow features of parvovirus associated Pure Red Cell Aplasia in two patients following combined pancreas and renal transplantation.
Methods: 2 patients were identified through the Consultative Liason Haematology service at Princess Alexandra Hospital, Brisbane Australia. A review of clinical history from inpatient charts was undertaken. Bone marrow aspirate and trephine biopsy results for both patients were also reviewed.
Results: Patient One presented with anaemia following pancreato-renal transplantation at another institution seven weeks prior. Patient Two also presented with anaemia following pancreato-renal transplantation at the same institution within four days of Patient One. Both patients underwent investigation of their anaemia and were found to be positive for parvovirus B19 serologically (IgM) and on peripheral blood and bone marrow PCR. Both patients underwent bone marrow aspiration and trephine biopsy (BMAT). BMAT on Patient One was consistent with pure red cell aplasia and characteristic giant pro-normoblasts were demonstrated on both aspirate and trephine biopsy. BMAT on Patient Two showed marked reduction in erythroid progenitors, with dysplastic changes in the remaining erythroid cells and characteristic giant pro-normoblasts. This was felt to be consistent with Pure Red Cell Aplasia. Both patients had a reduction in immunosuppression and received five days of intravenous globulins (0.4 mg/kg/day) and both responded, with their haemoglobin returning to the normal range.
Conclusion: We describe the clinical and bone marrow features of two patients with parvo-virus related Pure Red Cell Aplasia who underwent pancreato-renal transplantation within four days of each other. Both had bone marrow features consistent with the diagnosis of pure red cell aplasia, including the presence of giant pro-normoblasts.

P80
A Retrospective Cohort Study of Polycythaemia Vera in NZ Maori and Polynesians

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Polycythaemia Vera (PV) is a chronic myeloproliferative disorder affecting predominantly the elderly patient. Little is available in the literature on PV in NZ Maori and Polynesians. The aim of this study was to define the age at presentation, incidence of thromboembolism and disease progression within these particular ethnic groups.
The files of 28 NZ Maori / Polynesians and 36 Caucasians / others diagnosed with PV at a single centre between 1987-2005 were reviewed. The age at presentation, ethnicity, PV diagnostic criteria, treatment modality, occurrence of thrombosis, acute leukaemia (AL) and myelofibrosis, as well as survival were recorded.
Although the overall mean age at presentation was 63 years, it was 55 and 70 for the Maori/Polynesian and Caucasian groups respectively ($p<0.0001$). Overall complication frequencies were comparable

between the two arms (n=14/28 versus 19/36 respectively, not significant). Among 26 patients (40%) developing 34 thromboembolic events, 11 were Maori/Polynesians and 15 Caucasians (difference not significant). Progression into AL and myelofibrosis has occurred in 1 and 2 respectively of the 28 Maori/Polynesians versus 2 and 2 of 36 Caucasians to date. Median overall survivals are 170 months (Maori/Polynesians) and 108 months (Caucasians); p=0.55. Median life expectancies are not significantly different between the two groups (82.2 and 83.3 years respectively).
Despite presentation of PV at a significantly younger age in the Maori / Polynesian group, their risk of complications and disease progression appear comparable to Caucasians. Their longer median life expectancy compared to published figures for their ethnicity may conceivably reflect a survivor effect, or the effect of more intensive medical surveillance. Further data will follow to elucidate whether there are molecular differences between these two groups.

P81
Improvement in Quality of Life Correlates with Haemoglobin Improvement following Erythropoetin Therapy in Patients with Anaemia due to Haematological Malignancies

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Aim: Studies on quality of life in patients receiving Erythropoetin preparations for anaemia associated with cancer have been inconclusive and controversial. We wished to demonstrate that patients in a routine clinic responding to erythropoetin therapy demonstrated an improvement in quality of life.
Methods: A prospective audit was carried out between February 2003 and December 2004. Forty-seven patients were studied and received either epoetin Alpha usually 40,000 units weekly or darbepoetin, usually 150mcg weekly. Assessment was by quality of life tool (EORTC QOL 32) at Day 0, Day 28, Day 56 and Day 84. It consisted of five questions on quality of life and the patients rated their score on a scale of 0 to 10. Sixteen patients had lymphoma receiving chemotherapy, five patients had multiple myeloma receiving chemotherapy, seven had various myelodysplastic syndromes and twenty-one patients had miscellaneous conditions (AML, CML, CLL).
Statistical analysis was performed using SPSS Ver 11.5 software, and used Pearson correlation coefficients.
Results: A complete response (defined as a rise in haemoglobin of 20g/L) was seen in 71%. Comparing the group who responded versus the non-responders, there was a significant improvement in quality of life at four, eight and twelve weeks (P.014).
Conclusions: Erythropoetin therapy results in a significant response rate in correcting anaemia associated with haematological malignancies and in those who respond there is a significant improvement in quality of life. Erythropoetin is a preferable alternative to blood transfusion and warrants consideration in this group of patients.

P82
Cytomegalovirus Viraemia After Allogeneic Transplant: A Prospective Study of a Risk-Adapted Strategy in a Single Transplant Unit

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Aim: CMV infection causes significant morbidity and mortality following allogeneic transplantation. In 2003 the NSW BMT network adopted a uniform CMV prevention policy. This prospective study aimed to evaluate the impact of the policy on the rate, management and outcome of CMV reactivation in allogeneic transplant recipients at St Vincent's Hospital, Sydney.

Methods: All patients at high risk for CMV reactivation (recipient and/or donor CMV seropositive pre-transplant) had weekly blood samples screened using nucleic acid tests for CMV RNA and DNA. Patients with a related donor were screened from day +21 to +84 post-transplant and received antiviral treatment for CMV only if reactivation was detected. Patients with an unrelated donor received ganciclovir 5mg/kg 3x/week from day +21 to +84, in addition to screening tests.
Results: Between October 2003 and June 2005, 40 patients (median age 44 years, range 20-67) received allogeneic transplants, with 21 (53%) originating from an unrelated donor. Thirty-six (90%) patients were high risk for CMV disease and 13 (33%) developed CMV viraemia at a median of 39 days (range 16-101) post-transplant. Six of the 13 (46%) PCR positive patients had unrelated donors, and three had severe, steroid resistant GVHD requiring monoclonal antibody therapy. The median CMV viral load was 3200 copies/mL (range 870 to >100,000) and three of the 13 patients had CMV disease (all biopsy-proven CMV enteritis). All viraemic patients were treated with ganciclovir 5mg/kg BD for a median of 2 weeks, with clinical improvement and reduction in viral load in 10 patients. Overall survival of the CMV viraemia group was 85% at a median of 303 days follow up, compared with 78% for the whole group (p = NS).
Conclusion: The described risk-adapted CMV preventive strategy is associated with acceptable rates of viral reactivation and low morbidity and mortality post-allogeneic transplant.

P83
The 8p11 Syndrome – A Case Report

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Aim: We describe a case characteristic of the rare 8p11 syndrome
Method: We describe the case of a patient with a peripheral T cell lymphoma in conjunction with a myeloproliferative disorder. Cytogenetic analysis of bone marrow and subsequently a lymph node demonstrated a translocation between chromosomes 8 and 13 (46, XY t(8;13)(p11.2;q12))
The 8p11 syndromes are a rare group of disorders thought to result from a mutation in a pluripotent lymphoid/myeloid stem cell. They are biphenotypic syndromes in which a myeloproliferative disorder is frequently associated with a T cell or less commonly a B cell Non Hodgkin Lymphoma. Eosinophilia is often a feature.
The mechanism of disease in these syndromes relates to the FGFR 1 (Fibroblast Growth Factor Receptor 1) gene located at 8p11. FGFR 1 encodes a receptor tyrosine kinase for fibroblast growth factors and is fused with various partner genes in the 8p11 syndromes. Aberrant tyrosine kinase activity with constitutive activation of FGFR 1 signal transduction pathways results from the fusion gene.
Our patient's presentation, pathology and progress will be described.
Results: Our case demonstrates many of the features of this syndrome, including short-lived response to therapy
Conclusions: The 8p11 are a rare group of disorders with characteristic features that result from the translocation of the FGFR 1 gene.

P84
A Case of Gemcitabine Related Pulmonary Radiation Recall After Salvage Chemotherapy for Relapsing Hodgkin's Lymphoma Post Autologous Stem Cell Transplant

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Aim: Radiation recall is an inflammatory reaction in previously irradiated areas following chemotherapy, often involving the skin. The use of gemcitabine is increasing in patients with relapsing/refractory

Hodgkin's lymphoma. There are few reported cases of gemcitabine induced radiation recall with lung involvement. There are also no reported cases of FDG-PET imaging in the setting of pulmonary radiation recall.
Method: We present the case of a patient with relapsing Hodgkin's disease with clinical and radiological evidence of gemcitabine related pulmonary radiation recall, without skin involvement.
Result: A 30 year old man with primary refractory FDG-PET positive Hodgkin's disease underwent an autologous stem cell transplant, followed by consolidation radiotherapy to the lower neck and mediastinum. The patient subsequently relapsed with FDG-PET positive, biopsy proven left axillary lymphadenopathy, 4.5 months after completion of radiotherapy. Gemcitabine and vinorelbine were administered. The patient then developed mild dyspnoea on exertion and a cough over 4 weeks upon cessation of chemotherapy. CT scanning demonstrated acute pneumonitis and lung function tests demonstrated a significant reduction in diffusion capacity. FDG-PET scan demonstrated new thoracic uptake in the previous radiation field likely to be attributable to radiation recall. There was significant resolution clinically and on CT scan a month later without therapy.
Conclusion: This is one of the first reported cases of gemcitabine induced pulmonary radiation recall. Given the increasing used of gemcitabine in relapsed/refractory Hodgkin's lymphoma, pulmonary radiation recall needs to be considered as a diagnosis , and as a factor in planning future treatment Radiation recall is also a potential cause of false positive findings on FDG-PET.

P85
Tandem High Dose Melphalan (HDM) and HLA Identical-sibling Allogeneic Non Myeloablative Stem Cell Transplant (NMAT SCT) for Multiple Myeloma. A Single Centre Experience

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Aim: We present data on all patients receiving tandem HDM/NMAT SCT for multiple myeloma at a single centre in NZ.
Results: The tandem HDM/NMAT SCT approach was offered to all patients with myeloma and an HLA identical sibling donor who were considered suitable for the procedure from 2000 onwards (n=12). Following induction, most patients received high dose melphalan (200mg/m^2) with autologous stem cell rescue except for three who received 140mg/m^2 melphalan without stem cell rescue. Patients then proceeded directly to NMAT SCT conditioned with fludarabine 3x30mg/m^2 + TBI 200cGy. Median age at NMAT was 50 years (range 34-63 years) and median follow up post NMAT was 22 months (range 2-56 months). All patients engrafted but one case initially showing poor and decreasing donor T-cell chimerism was rescued using pentostatin and donor lymphocyte infusion. Of 10 patients evaluable for disease response and GVHD, 5 subsequently achieved complete remission (CR), one of these patients achieving CR after being treated for progressive disease with thalidomide and withdrawal of immunosuppression. Two patients achieved partial response and 3 have shown progressive disease, one of whom died at day +120 post NMAT. Seven of the 10 patients developed grade II-IV acute and/or extensive chronic graft versus host disease (GVHD). Overall 11/12 patients remain alive.
Conclusions: The use of tandem HDM/NMAT SCT in multiple myeloma remains investigational and the outcomes of comparative trials are awaited. Our data shows a low 1 year TRM (10%) with acceptable outcomes in terms of disease control (CR+PR=70%) and incidence of manageable GVHD (70%).

P86
99m-Technetium Aprotinin Scintigraphy in Amyloidosis

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Aim: To assess the validity and safety of 99m-technetium aprotinin scintigraphy in the detection of amyloid deposits in a sample of patients with biopsy-proven amyloidosis.
Method: Seven patients with biopsy-proven primary amyloidosis were recruited for a pilot study. 700MBq of 99m-technetium aprotinin were injected intravenously. Immediately following tracer injection a 30 minute dynamic study of the abdomen was performed. At 90 minutes whole-body scans and SPECT tomograms were obtained. The scans were correlated with the patient's symptoms and signs, other clinical data and biopsy results. Patients were monitored for any adverse events.
Results: 33 lesions were identified in the 7 patients. Three of these lesions were biopsy-proven (bowel, bone marrow, carpal tunnel). One patient with known muscle involvement had equivocal uptake in the gluteal regions. Uptake in the myocardium was seen in 3 patients. Two of these patients had clinical presentations suggesting cardiac involvement with amyloid. The third patient did not have clinical symptoms and had a normal echocardiogram, but had an elevated brain natriuretic peptide and unexplained low voltage on an ECG. Diffuse pulmonary uptake was seen in one of the patients with cardiac involvement. This patient had restrictive changes on lung function testing, but was unsuitable for an open lung biopsy. All patients showed uptake in the liver, however, only two of the patients had clinical evidence of liver involvement with markedly deranged liver function tests. There were no serious adverse events.
Conclusions: 99m-technetium aprotinin scintigraphy is a safe and non-invasive technique for the detection of amyloid deposits. The preliminary results from our study support the observations of other groups that it has utility in detecting cardiac involvement with amyloid, as well as lesions at other sites, however may be poorly specific in assessment of the liver. Longer term follow up of this cohort of patients is needed to provide corroborative evidence for 'silent' lesions at other sites.

P87
Successful Allogeneic Stem Cell Transplantation of Two Patients with Prolonged Severe Neutropenia and Invasive Fungal Infection Treated with Granulocyte Transfusions and Antifungal Therapy

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Aim: Invasive fungal infections are associated with a high mortality in patients with prolonged neutropenia. We describe two patients with disseminated fusariosis and invasive *Aspergillus* infection whose infections were successfully controlled with granulocyte transfusions and anti-fungal therapy such that potentially curative allogeneic stem cell transplantation could be performed.
Method and results: A 45 year old man was diagnosed with acute myeloid leukemia in March 2005, on the background of a four month history of myelodysplasia. Following induction chemotherapy he developed disseminated *Fusarium anthophilum* infection at day 14. In spite of treatment with voriconazole he remained septic with persistently positive blood cultures and was started on high-dose liposomal amphotericin and intensive granulocyte transfusions. He failed to recover from chemotherapy. Despite a 10 week period of severe neutropenia, his sepsis resolved and fungal infection remained under control with intermittent granulocyte infusions and combination antifungal treatment. He was able to receive a potentially curative allogeneic transplant with low intensity conditioning from his HLA-compatible brother. He has had successful engraftment with no evidence of residual leukaemia.
A 48 year old man was diagnosed with severe aplastic anemia in March 2005. He failed treatment with ATGAM, cyclosporin and prednisone. He remained profoundly neutropenic for 5 weeks and became septic with a chest infection due to *Aspergillus fumigatus*. He was started on voriconazole but was persistently febrile and was changed to high-dose amphotericin. In view of his poor clinical condition and continuing neutropenia, granulocyte transfusions were commenced and continued approximately twice

per week. He went on to receive an allogeneic transplant from his HLA-matched sister. He successfully engrafted, remains well and has returned to work post-transplant.
Conclusion: In these two patients with prolonged severe neutropenia, the combination of antifungal therapy and augmentation of host response with granulocyte transfusions enabled control of serious invasive fungal infections. Control of infections in this manner enabled potentially curative allogeneic stem cell transplantation to be performed. This approach may be applicable to other profoundly neutropenic patients with active fungal infections requiring stem cell transplantation.

P88
Collaborative Establishment of New Autograft Centres by GMTT, a Clinical Network in NSW

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In June 2001 the Greater Metropolitan Services Implementation Group (GMSIG) was established to address equity of access to quality services in metropolitan NSW hospitals. GMSIG was a group of clinicians, administrators and community representatives reporting directly to the NSW minister for Health. GMSIG made 162 recommendations across a wide range of hospital services including the finding that "…autologous bone marrow transplantation …be provided by all tertiary haematology units."
A group of haematologists, haematology nurses and transplant scientists began meeting in October 2002 regarding a broad range of transplant issues with a subgroup of haematologists from the proposed new centres developing a joint funding proposal and implementation plan by January 2003.
Prerequisites identified included stem cell apheresis, CD34 counts, transplant co-ordination, safe transplant of apheresis product and cryopreserved stem cells, cryopreservation and storage at a central laboratory. The collaborative multi-centre nature of the group was critical to resolving these issues, development of documented protocols for key aspects of patient management and providing appropriate professional development and support for nursing staff.
From July 2003 to June 2005, 57 autologous haemopoietic stem cell transplants (AHSCT) have been performed in the 4 new centres: Concord (14), Gosford (17), Nepean (15), Wollongong (11). AHSCT indications were similar to those reported nationally to the Australasian Bone Marrow Transplant Recipient Registry: Myeloma (31), NHL (24), ALL (1), Amyloid (1). 8 deaths have been reported, 6 with progression of primary disease at 3-13 months from transplant, 1 early procedure related death with diffuse GIT bleeding in a patient with amyloid and 1 death with renal failure 9 months post autograft.
The autograft group has consolidated to include representatives from all transplant centres in NSW with an agenda including agreed best practice and relevant clinical research. We report this successful implementation to highlight the strengths of multidisciplinary, multicentre clinician directed planning and implementation of a complex clinical service.

P89
PCAB Chemotherapy Prior to Stem Cell Mobilization Adversely Affects CD34 Yield in Patients with Multiple Myeloma

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Aim: Autologous stem cell transplant is standard of treatment for patients with multiple myeloma below 65 years of age. Various factors affect stem cell yield .We have conducted this study to find effect of PCAB treatment on stem cell mobilization.

Methods: Forty-seven patients with multiple myeloma were mobilized with intermediate dose of cyclophosphamide (4 gm/m^2) and GCSF. Leukaphereses were planned to start between Day 9 to Day15 after chemotherapy. G-CSF was started on D-4 prior to start of collection and was continued until collection was completed.
Patients were classified further depending on prior treatment with PCAB or not (Prednisone 60 mg/m^2 D1-5, Cyclophosphamide 600 mg/m^2 on D1, Doxorubicin 30 mg/m^2 D1and BCNU 30 mg/m^2 D1; repeated every 28 days).
Results: There were 26 patients who did not have prior exposure to PCAB [NO PCAB] and 21 patients had prior exposure to PCAB [PCAB]. Median no of cycles PCAB was 6 (4 to 12). There was no statistical significant difference in two groups for various demographic variables and disease parameters
CD 34+ stem cell yield is shown in the table I

CD34 Cell yield	NO PCAB	PCAB	P
Total CD 34/kg Median (Range)	7.71 (0.06-9.33)	2.66 (0.06-9.33)	> 0.0001
Total CD34/kg/L Median (Range)	1.07 (0.01-3.77)	0.30 (0.01-1.17)	> 0.0001
CD34 /kg on D1 Median (Range)	5.11 (0.04-15.9)	0.97 (0.04-4.85)	> 0.0001
No of pts CD 34 > 2 x 10^6/Kg)	24	15	0.061
No. of Leukapheresis Median (Range)	2 (1 –3)	3 (2-5)	> 0.0001

There was significant increased in toxicity during stem cell mobilization in PCAB group Vs. NO PCAB
Conclusion:

- Patients with prior exposure to PCAB had worse mobilization and there was also significant increased toxicity in PCAB group during stem cell mobilization.
- Hence patients who are planned for stem cell transplant should not be treated with PCAB prior to stem cell mobilization.
-

P90
A Rare Case of Primary Bone Lymphoma in Chinese Woman

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Case Report: A 78-year-old female had history of aortic valve replacement done for chronic rheumatic heart disease and coronary artery bypass graft surgery for coronary artery disease. She presented with progressive swelling of left leg for four months. Radiography of left leg showed soft tissue swelling involving primarily the distal end of left tibia with extension to the surrounding soft tissue. Ultra-sonogram showed left ankle effusion and subcutaneous edema. MRI showed large mass in the left ankle with extensive soft tissue and bony involvement consistent with lymphoma. Ultrasound-guided biopsy confirmed diagnosis of diffuse large B cell lymphoma. Staging including CT showed no evidence of disease elsewhere. Bilateral bone marrow aspiration and trephine biopsy showed no evidence of lymphoma involvement. In view of the underlying heart disease, she was treated with 60% CEOP(Cyclophosphamide 750mg/m2 + Epirubicin 60mg/m2+ Vincristine 1.4 mg/m2+ Prednisolone 100mg/m2) followed by local radiotherapy to the left ankle. She achieved good response with dramatic shrinkage of the local tumor.
Discussion: Primary lymphoma of the bone is rare. It accounts for approximately 3% of malignant bone neoplasms and comprise less than 5% of all extranodal Non-Hodgkin's lymphoma. Primary lymphomas of bone are characterized as "mottled" or moth-eaten" radiolucencies, corresponding to regions of marrow and cortical replacement by lymphoma cells. Pathologic fracture may be present in approximately one quarter of the cases.
At pathology, primary osseous lymphoma is typically of the diffuse B-cell subtype. A mixed-cell infiltrate or variation in cell size and shape can be seen in most bone lymphomas.
Overall survival is good with more than 50% of patients survive at 5 years for those with single bone involvement. Treatment typically involves a combination of radiation and chemotherapy. It remains to be seen whether monoclonal antibodies against CD20 will become a mainstay of treatment for bone lymphoma.

P91
Acute Renal Failure complicating Acute Promeylocytic Leukemia(APL) in Pregnancy

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Case report: A 33-year old woman was admitted because of unprovoked antepartum hemorrhage at 30 weeks' gestation. Laboratory examination revealed hemoglobin 8g/dL, Platelet 12x 10^9/L and WBC 62 x 10^9/L with 91% abnormal promyelocytes. PT=15 sec, APTT=48.9 sec, creatinine 77 umol/L. ATRA(45mg/m2/day) and tranexamic acid were started immediately before delivery. Cesarean section was performed on the day of admission. Idarubicin(12mg/m2/day x 3 days) was started after delivery of baby. The baby was healthy and discharged subsequently. The patient developed acute renal failure on the next day with anuria, severe azotemia(creatinine 652 umol/L, urea 32.8 mmol/L) requiring hemofiltration. Ultrasound examination of kidneys showed no structural abnormalities and both renal veins were patent. Autoimmune markers were all negative. Uric acid was 0.43 mmol/L. She also experienced respiratory distress and the CT thorax showed patchy infiltration in both lower lobes and bilateral pleural effusions. Echocardiogram showed ejection fraction of 60% and no pericardial effusion.The differential diagnosis included RAS, fluid overload due to acute renal failure and sepsis. Tranexamic acid was stopped and high dose dexamethasone was started. The respiratory condition gradually improved with resolution of lung infiltrates. The steroid was tapered down gradually and the lung infiltrations reappeared. Thus ATRA was stopped and the lung infiltrations resolved again with a course of steroid. The renal function also improved gradually and hemodialysis was discontinued 4 weeks later while bone marrow aspiration confirmed APL in remission.
Discussion: This case illustrates the possible risk of severe thrombosis causing renal failure when tranexamic acid was administered together with ATRA. This case also illustrates that emergency delivery at > 28 weeks of gestation is feasible in APL despite coagulopathy.

P92
Bisphosphonate-induced Osteonecrosis of the Jaw: A New Complication and its Implications for the Treatment of Multiple Myeloma and Other Diseases

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Introduction: Osteonecrosis of the jaw is a rare condition that manifests as failure of the mandible or maxilla to heal after tooth extraction. Recently, bisphosphonates have been postulated as a cause for osteonecrosis of the jaw, especially in multiple myeloma and breast cancer patients.
Method: During clinic visits, patients on regular bisphosphonates at our centre were questioned about symptoms of jaw osteonecrosis and underwent a dental review if symptoms/oral examination were suggestive. We analysed available literature on incidence, treatment and prevention of jaw osteonecrosis.
Results: We detected four cases of bisphosphonate-induced osteonecrosis, three had multiple myeloma, one had breast cancer. Two involved the maxilla, the other two the mandible. All were reviewed by Dental Oncology, commenced on chlorhexidine mouthwash and antibiotics and their bisphosphonates ceased. All experienced improvements in pain over several months, although none had complete bone healing. Literature review reveals the precise incidence is unknown and probably under-reported. A dental review before commencing bisphosphonates, adopting strict dental hygiene and avoiding tooth extractions is recommended prophylaxis. Risk factors include female sex, prior chemotherapy, malnutrition and smoking. The mandible is most commonly affected (80% cases). Treatment involves penicillin-based antibiotics, chlorhexidine mouthwash and strict avoidance of surgical debridement. Hyperbaric oxygen is not beneficial. Intravenous nitrogen-containing bisphosphonates (e.g. Pamidronate, zoledronic acid) appear more likely to cause osteonecrosis than other biosphosphonates (e.g. clodronate). We found seven cases described in patients with osteoporosis without malignancy and others where osteonecrosis was spontaneous without preceding tooth extractions.

Conclusions: Bisphosphonate-induced osteonecrosis of the jaw is a rare, probably under-recognised complication. With appropriate dental prophylaxis, this might be avoided.

P93
Hickman Line-Related Infections in Non-Neutropenic Patients with Haematological Malignancies

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Introduction and Aim: Patients with advanced haematological malignancies commonly require central venous access devices such as Hickman catheters. With long-term placement, these devices are subject to a risk of infection. Whilst most infections have been reported as due to Gram-positive organisms, these studies have generally included patients with both solid and haematological malignancies who may be neutropenic or non-neutropenic. We aimed to define the incidence and microbiological profile of catheter-related infections (CRI) in patients with haematologic malignancies that occurred during non-neutropenic phases of their illness.
Method: Data was evaluated on 253 successive Hickman line insertions from January 2003 to December 2004. All patients had vancomycin prophylaxis prior to Hickman line insertions. CRI was defined as positive cultures of blood derived from the catheter with no other obvious clinical, radiological or microbiological focus of infection identified and no gut graft-versus-host disease. If simultaneously taken peripheral blood cultures were also positive, CRI were only considered if cultures from the catheter became positive at least 2 hours earlier. Neutropenia was defined as a neutrophil count of $<0.5x10^9$/L.
Results: There were 43 (23 male, 20 female) evaluable non-neutropenic patients who experienced 47 episodes of catheter-related bacteremia. Sixty four organisms were isolated of which the majority were Gram-negative organisms (73%), most commonly Stenotrophomonas maltophilia (19%), Klebsiella species (14%) and Acinetobacter (13%). The most common Gram-positive organism isolated was coagulase negative Staphylococcus (16%); Staphylococcus aureus represented 5% of isolates. The median time to infection from catheter insertion was 64 days (range 7-221 days). Seventeen episodes were directly related to Hickman catheter access. Thirty-three patients had their Hickman line removed because of infections; of 15 febrile ($T >38^0C$) at time of line removal, 9 became afebrile ($T \leq 37^0C$ with no further spikes to $>37.5^0C$) within 24 hours. The antibiotic regimens used at initiation of therapy were cefepime and vancomycin (n=18), cefepime alone (n=13), vancomycin alone (n=4) and others (n=12). Twenty-five patients required a change in antibiotics after sensitivity results were known; mainly due to Stenotrophomonas and Acinetobacter isolates.
Conclusions: The majority of Hickman-catheter related infections in non-neutropenic patients with haematological malignancies are due to Gram-negative organisms and initial antibiotic therapy should cover for these organisms until results of the culture are known.

P94
Strategy for Investigation of Patients with Red Cell Microcytosis and Hypochromia

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Red cell microcytosis and hypochromasia are frequently encountered in patients presenting to hospital, with iron deficiency (ID) and/or carrier status for thalassaemia/haemoglobinopathy (TH) being the two most common causes of this abnormality. The significance of these conditions often depends upon patient age, with TH having implications in patients of child-bearing age and ID precipitating a search for chronic blood loss especially in older patients. Since the advent of the automated haematology analyser, various

discrimination indices (DI) have been derived for distinguishing between these two conditions with variable utility depending upon instrumentation and the population under study.
We performed a retrospective study of DI in adult patients with confirmed iron deficiency (93) and thalassaemia/haemoglobinopathy (252) and derived our own index from this data set using logistic regression. Mean corpuscular haemoglobin, red cell count, red cell distribution width (RDW), and mean corpuscular volume x RDW were all significant parameters for distinction between ID and TH. The probability (p) of a patient having iron deficiency was given by the formula $p= e^x/(1+e^x)$, where x=22.8627-(0.6657 x MCH)-(3.2308 x RBC)-(1.8199 x RDW)+(0.0328 x MCV x RDW).
Receiver Operating Characteristic (ROC) analysis revealed our new index to be superior to Shine and Lal, Srivastava, Mentzer, and England and Fraser indices but exhibit similar performance characteristics to the RDW index (MCV x RDW/RBC) with a sensitivity and specificity for iron deficiency of approximately 91% and 90% respectively.
By adjusting the p cut-off or index discrimination value, the sensitivity of the DI for iron deficiency could be increased in older patients to 98% with only a modest drop in specificity (86%). Similarly, the sensitivity for TH could be increased to 95% in patients of child-bearing age with a drop in specificity to 79%. Further studies are required to validate this approach prospectively in various patient groups.

P95
Long Term Use of Hydroxy-urea in Young Patients with Essential Thrombocythaemia and High Risk Thrombotic Risk

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Aim: The optimal treatment of young patients with essential Thrombocythaemia (ET) has been controversial and Anagrelide has been advocated because of the concerns about the leukaemiageneic potential of Hydroxyurea. Storen et al [1] reported on a population of young patients followed for a median of 10.8 years and reported 20% thrombotic rate and 20% major bleeding incidence with the use of Anagrelide. We followed a cohort of 27 ET patients aged younger than 45 years (median age = 38 years) who commenced Hydroxyurea before January 1 2000 and who were previously untreated. The aim of the study was to compare the thrombotic risk and any complications from long term use of Hydroxyurea with previous young cohort studies.
Methods: Hydroxyurea was given for platelet counts over 1500 x 10^9/L or for the occurrence of vascular problems such as Myocardial infarction (2), ischaemic stroke (1), TIA's (2) or peripheral vascular ischemia (2). The median platelet count prior to initiation of therapy was 945 (range 760 x 10^9/L to 1600). The aim of therapy was to maintain a platelet count of between 400 and 6000x 10^9/L.
Results: After a median followup of 10 years (range 5 to 23 years) only one patient had to withdraw because of drug intolerance. No major thrombotic problems occurred. Excellent control of platelet counts was achieved (median level = 440 x 10^9/L). No cases of leukaemia occurred but one case of breast cancer occurred. Two cases of ET transformed to polycythaemia vera. No cases of \Myelofibrosis have occurred.
Conclusion: This indirect comparison of cohort studies suggests that Hydroxyurea is more effective than Anagrelide in preventing thrombosis in young patients at high risk. This is also confirmed by recent data from the PT1 study.[2]

1. Storen EC Tefferi A longterm use of Anagrelide in young patients with essential Thrombocytopenia. Blood. 2001. 97. 863-886.
2. Harrison et al . Hydroxyurea copared with anagrelide in High-Risk Essential Thrombocytopenia. WEJM 2005; 353 33-45

P96
Bisphosphonate-Associated Osteonecrosis of the Auditory Canal

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An association between bisphosphonate exposure and oral osteonecrosis has recently been described. More than 260 cases of maxillary or mandibular osteonecrosis in patients receiving bisphosphonates have now been reported, most of which have occurred in patients with systemic malignancies receiving potent intravenous bisphosphonates. Trauma and dental procedures are commonly reported precipitants. This has been thought to be a localised phenomenon, and has not previously been described at sites outside the oral cavity.
We present the first such case: a patient with multiple myeloma who developed osteonecrosis of the bony portion of the auricular canal after nine years of bisphosphonate use (initially with pamidronate, more recently with zoledronate). Routine examination of the ear revealed an area of mucosal breakdown, with exposed necrotic bone visible, at a site of the previous surgery. The lesion was not painful, and there was no clinical or radiological evidence of associated infection or myelomatous infiltration. The devitalised bone extended beyond and below the margins of mucosal ulceration. The patient had previously developed spontaneous maxillary osteonecrosis at two sites. All lesions responded to conservative management.
This case has significant implications for our understanding of the pathogenesis of bisphosphonate-associated osteonecrosis and the impact of long-term bisphosphonate exposure on bone homeostasis and healing. These agents are potent inhibitors of osteoclast mediated bone resorption, and also have local anti-angiogenic properties. This may reduce the ability of normal bone to respond to physiological demands in the presence of a bisphosphonate-induced reduction in remodelling and blood flow, a possibility which would explain the strong association between trauma at sites of existing stress (including the oral cavity and, in our patient, a previous surgical site in the ear) and the development of osteonecrosis.

P97
Is Tumour Lysis Syndrome and Herpes Zoster Infection Really That Uncommon after Bortezomib?

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Background: Bortezomib (Velcade), a proteasome inhibitor, has recognised side effects of peripheral neuropathy and myelosuppression. Although herpes zoster (HZV) reactivation (13% in 331 patients in recent Phase III APEX trial) and tumour lysis syndrome (TLS) have been reported, there is limited evidence on their incidence.
Method: Retrospective analysis of patients with relapsed or refractory multiple myeloma (MM) treated with bortezomib at a single institution between February-July 2005 as part of the Extended Access Program study.
Result: Total of 16 patients, median age 58 years, received a median of 3 cycles (range 1-6) of bortezomib (1.3mg/m^2 intravenously D1, 4, 8 and11 of 21 day cycle).
Four patients had reactivation of HZV, all with unilateral thoracic disease during the first 4 cycles. Three had suppressed normal gammaglobulins, the other was maintained on IVIG. None were taking dexamethasone but all had received this previously. All resolved after treatment with valaciclovir, with delay in treatment in only one patient and no dose reductions necessary.
Three patients developed significant TLS evidenced by raised LDH, urate and phosphate and low calcium after the first one to two doses of drug, 2 of which had predominantly light chain disease. Two patients, with no prior evidence of renal impairment, developed acute renal failure requiring inpatient management; one required several days of haemodialysis. Importantly, all three patients had major responses to treatment after the first 1-2 cycles and no further TLS with subsequent treatment.

Conclusion: Our experience of HZV reactivation (25%) in relapsed MM patients treated with single agent bortezomib warrants consideration of prophylactic valaciclovir. Clinicians should also be aware of the risk of early and potentially severe tumour lysis syndrome, an otherwise rare occurrence in MM.

P98
Hydroxyurea as a Cause of Cardiac Arrhythmia and Drug Fever

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Method: A case note review.
Results: A patient with no previous cardiac history was given hydroxyurea for polycythemia rubra vera. Within eight days he developed episodic irregular heart palpitations. He felt non-specifically unwell during this early period but then four weeks later developed a fever of 40.7 degrees centigrade leading to hospitalisation. Infective causes for the fever were excluded. He continued to have short episodes of palpitations during the admission although no cardiac arrhythmia was ever successfully captured on an electrocardiograph. The hydroxyurea was then stopped, giving prompt resolution of both fever and palpitations. Two weeks later he was electively admitted to hospital and rechallenged with 1 gram of hydroxyurea whilst being monitored by telemetry on a cardiology ward. The patient was afebrile prior to recommencing the hydroxyurea and an electrocardiogram confirmed sinus rhythm. Within six hours of receiving hydroxyurea, the patient developed atrial fibrillation (captured on a cardiac monitor and confirmed by an electrocardiogram) and a fever (38.5 degrees centigrade). Following withdrawal of hydroxyurea, his fever settled within 12 hours and he spontaneously reverted to sinus rhythm. Digoxin and metoprolol were required initially for rate control of the atrial fibrillation. Again no infective causes for his fever were found. The patient also had a normal echocardiogram and thyroid function tests to exclude an underlying cause for the atrial fibrillation. The patient has not had a further recurrence of his symptoms.
Conclusion: Although drug fever is rare (estimated to be <0.1%), it is a recognised complication of hydroxyurea. Cardiac arrhythmias have not previously been described as part of this allergic reaction. We review the literature and the incidence of allergic reactions to hydroxyurea in a cohort of patients over the last eighteen years.

P99
Review of Serial Bone Marrow Examination on Patients with Chronic Myeloid Leukaemia Treated with Imatinib Mesylate: Long Term Follow up

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There have been reports on the effects of Imatinib mesylate (Gleevec) in chronic myeloid leukaemia (CML) focusing on the clinical, cytogenetic and molecular findings. To our knowledge there has been no report of serial changes in bone marrow pathology with long term follow-up.
We examined morphological changes in the bone marrow and peripheral blood of 23 patients with CML (16 chronic phase (CP), 7 accelerated phase (AP)) at diagnosis, 3, 6, 9, 12, 18, 24 and 36 months after commencement of imatinib mesylate and correlated with cytogenetic and molecular results.
At 3 months, cellularity was reduced (median reduction CP 40% AP 62%), which was then sustained (median reduction at 24 months CP 55%, AP 63%). 13 of 16 CP patients and 7 of 7 AP patients had a decline in number of megakaryocytes, with an increase in morphologically normal megakaryocytes.

Changes were greatest at 12 months, and remained constant including in 6 CP patients examined at 36 months.
11 of 14 CP patients achieved cytogenetic CR at a median of 12.7 months. Of the 3 patients that failed to achieve cytogenetic remission, 2 had morphologic improvement. 5 AP patients achieved cytogenetic remission at a median of 10.2 months, all associated with morphologic improvement.
Molecular results were available for 13 of 16 patients in CP and 5 of 7 in AP. Only 1 CP patient attained molecular CR at 30 months. All patients demonstrated a initial reduction in BCR-ABL mRNA, which correlates with the morphological findings. However, in the patients (3 in CP and 3 in AP) who subsequently lost molecular response, there was no correlative change in bone marrow findings.
Imatinib mesylate resulted in reduction in bone marrow cellularity as well as the number of abnormal megakaryocytes in patients with CP and AP-CML. This response was most marked in the first 12 months, and remained stable whilst treatment was continued. The improvement was seen regardless of cytogenetic or molecular response.

P100
What the Peripheral Blood Smear Teaches about Megakaryocytic Maturation

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Aim: Knowledge about how megakaryocytes mature and platelets form has come chiefly from direct observations on bone marrow, or from studies on megakaryocytic cells grown in culture, and less from direct observations on the peripheral blood (PB). Circulating megakaryocytic cells, abundant in all phases of chronic myeloid leukemia (CML) in India, seem, however, to point to an alternative viewpoint. The purpose of this study was to evaluate how megakaryocytes mature and platelets form in the PB.
Method: Romanowsky-stained PB of 800 patients of CML in the 3 phases of the disease was evaluated to assess the type of morphologically identifiable Mk cells. Immunocytochemistry (APAAP) for megakaryocytes was done in selected cases.
Results/Observations: The most dramatic features are seen in the blastic and accelerated phases. There is a continuum of megakaryocytic maturation that begins with a megakaryoblast differentiating abnormally, and ends with a mature, functioning micromegakaryocyte. Blasts otherwise undifferentiated, reveal their lineage unequivocally by putting out into the circulation, dysplastic platelets / megakaryocytic cytoplasmic fragments that arise from a localized zone of the cell membrane. While the periphery continues to be engaged in abortive and tentative attempts at successful platelet formation, cytoplasmic granules appear, heralding shift towards normal maturation. The process culminates in a small mature micromegakaryocyte, which continues to form normal platelets.
Conclusion: 1. Megakaryoblasts are capable of platelet production without undergoing normal maturation. This unproductive effort, that yields dysplastic platelets, corrects itself as the cell matures further. 2. The familiar mature micromegakaryocyte is not a dyspoietic cell but one that actively contributes to platelet formation. 3. Large dysplastic platelet masses in the PB in CML arise largely from the PB megakaryocytic cells. 4. Study of PB Mk cells allows one to see megakaryocytic cells in a new perspective and opens vistas for further study.

P101
Production and Purification of IE1-pp65: Potential CMV Antigen Source for Adoptive Immunotherapy

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Aim: Human cytomegalovirus (HCMV) infection is mainly controlled by T cell mediated responses in the healthy host. In the immunocompromised host, HCMV infection can lead to life-threatening CMV disease. Adoptive immunotherapy involving the transfer of HCMV-specific T cells have been shown to protect stem cell transplant recipients from CMV disease. This study aimed to produce and purify the recombinant chimeric protein IE1-pp65 comprising two of the most immunodominant anti-HCMV T cell targets (IE1: 72 kDa, pp65: 65 kDa) for the generation of mutiple anti-HCMV T cells.
Methods: A Baculovirus vector was generated encoding a 6×His-tagged IE1-pp65 protein. Using up to 200 mL suspension cultures, Sf9 insect cells seeded at 1×10^6 cells/mL were infected with this recombinant baculovirus at MOI=2. Protein was harvested after 48-72 hr and purified by Ni-NTA affinity chromatography based on the His-tag. IE1-pp65 protein expression and purification were analysed by Coomassie staining and immunoblotting. Monocyte-derived dendritic cells were pulsed with a commercial CMV pp65 protein. After 7 days, irradiated pulsed-DCs were incubated with autologous T cells for 6 days. ^{3}H-Thymidine was added 18 hr prior to harvesting and proliferation measured as cpm.
Results: Soluble IE1-pp65 has been expressed in insect cells using the Baculovirus Expression System and then purified by affinity chromatography. An expected size band of approximately 130 kDa has been detected by Coomassie staining and immunoblotting using anti-penta-His and anti-pp65 mAbs. Interestingly, T cells demonstrated high proliferation in response to autologous pp65-pulsed DCs compared to minimal proliferation with non-pulsed DCs during *ex vivo* culture. It is expected that our protein will also cause significant T cell proliferation in the same manner.
Conclusions: IE1-pp65 can be successfully produced and purified. Donor monocyte-derived dendritic cells have been shown to process a commercial CMV pp65 protein and present antigenic peptides to donor T cells causing them to become activated. With further research the recombinant chimeric IE1-pp65 protein may also be able to stimulate donor T cells and be potentially useful for immunotherapy.

P102
Clinical Application of Allogeneic Mesenchymal Stem Cells

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Adult (postnatal) mesenchymal stem cells (MSCs), derived from mammalian bone marrow, normally differentiate into bone, cartilage, muscle, adipose or stromal tissue. They also appear to be able to differentiate into tissues outside the mesenchymal lineage, including neuronal and hepatic tissue. They are therefore candidates for a broad range of therapeutic applications in regenerative medicine. In a pig model of acute myocardial ischemia, porcine MSCs injected intravenously caused a reversal of reduced left ventricular ejection fraction, which was fatal in control animals. In a goat model of meniscal injury, caprine MSCs injected into the knee joint after meniscectomy produced neomeniscal tissue and appeared to slow or prevent subsequent osteoarthritis. MSCs are also non-specifically suppressive of T cell function and, when co-transplanted with HLA-identical sibling hematopoietic stem cells in a phase I clinical trial in patients with haematological malignancy, appeared to decrease the incidence of graft-versus-host disease and improve disease-free survival. Further exploration of their potential in organ transplantation and haematopoietic stem cell transplantation is merited.

P103
Evaluation of Transferrin Receptor/Ferritin Ratio in the Diagnosis of Iron Deficiency in Patients with other Medical Conditions – A Pilot Study

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Aim: The clinical diagnosis of iron deficiency is not always straightfoward. Classically, serum iron (FE), ferritin (FERR) and iron saturation (FESAT) have been used to evaluate iron status. These indices,

however, are greatly affected by presence of chronic medical disorders. Soluble transferring receptor (sTFR) and a sTFR/Log ferritin ratio (RATIO) have recently been suggested to have higher sensitivity and specificity in diagnosing iron deficiency.
In this pilot study, the usefulness of sTFR and RATIO in the prediction of bone marrow (BM) iron stores was examined.
Method: 250 people who had undergone diagnostic BM aspiration for a variety of medical conditions over the last three years at our Centre were studied retrospectively. Of these, 32 patients were selected as they had both BM iron examination and a panel of tests for iron status. These included sTFR, RATIO, FE, FESAT, FERR, haemoglobin (Hb), mean cell volume (MCV) and mean cell haemoglobin (MCH).
Results: Eight of out 33 patients (24%) had absent BM stainable iron. Our results showed the following sensitivity in predicting absence of BM iron stores: sTFR 100%, RATIO 100%, FE 100%, FESAT 88%, FERR 13%, Hb 50%, MCV 13%, MCH 25%. The specificities were: sTFR 44%, RATIO 83%, FE 32%, FESAT 52%, FERR 60%, Hb 48%, MCV 76%, MCH 76%. Elevation of sTFR in this group of patients was due to iron deficiency, haemoglobinopathy, blood loss, B12 deficiency, and lympho- and myelo-proliferative disorders.
Conclusion: sTFR is more sensitive than any other iron indices studied in identifying absence of BM iron in patients with other medical conditions but lacks specificity. The use of RATIO improved the specificity compared to sTFR. Low FERR or FESAT alone is specific but insensitive. Raised sTFR can also be seen in conditions with hyperproliferative erythropoiesis other than iron deficiency.

P104
FMC 7 versus CD20 Expression in B Cell Lymphoproliferative Disorders – Unravelling the Relationship

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Introduction: CD20 and FMC7 are routinely utilised in diagnostic immunophenotyping of suspected B cell lymphoproliferative disorders (B-LPDs). There is conflicting evidence regarding a correlation between FMC7 and CD20 expression in normal and malignant B cells. FMC7 binds to a particular conformation of the multimeric epitope of CD20 which is sensitive to the amount of membrane cholesterol. Cholesterol is unevenly distributed in lipid rafts in cell membranes and this is the putative explanation for variable FMC7 expression.
Aim: To compare the immunophenotypic fluorescence intensities of FMC7 and CD20 expression in B-LPDs and identify the correlation.
Methods: We performed a retrospective analysis of immunophenotypic data of B-LPDs from Jan 2004-July 2005. Diagnoses were confirmed with review of histological, molecular, and cytogenetic results. Flow cytometry was performed using a Becton Dickinson FACSCalibur. Mean fluorescence intensity (MFI) of FMC7 (BD FMC7 clone – FITC) and CD20 (BD L27 clone – P-CY5.5) marker was calculated and compared using regression analysis (MS Excel 2003).
Results: The median log MFI of CD20 and FMC7 for all B-LPDs analysed (n=51) was 23.8 (range 2.2-100.3) and 4.1 (range 0.8-33.9) respectively. The median log MFI of CD20 and FMC7 for CLL's analysed (n=22) was 9.8 (range 2.2-19.9) and 1.1 (range 0.8-2.1) respectively. The median log MFI of CD20 and FMC7 for non-CLL B-LPDs analysed (n=29) was 41.3 (range 8.8-100.3) and 7.6 (range 2.0-33.9) respectively. R^2 for log MFI of CD20 versus FMC7 for all B-LPDs, CLL's and for non-CLL B-LPDs were 0.58, 0.02 and 0.38 respectively.
Conclusion: Definitive correlation between FMC7 and CD20 expression on B-LPDs has not been demonstrated in our small patient cohort with the likely explanation relating to varying membrane cholesterol quantities within the CD20 epitope altering the conformation and binding of FMC7. The median log MFI of CD20 and FMC7 are reproducibly lower in the CLL cohort, confirming previous reports.

P105
Surveillance for Healthcare-Associated Bacteraemia in an Australian Haematology-Oncology Unit

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Aim: There are few Australian data on the incidence of healthcare-related bloodstream infection (BSI) in haematology-oncology patients. In response to a perceived increase in incidence of BSI coincident with the introduction of a new needle-free system, we reviewed rates of line-related bacteraemia in our unit.
Methods: We reviewed patient charts between 1 July 2004 and 30 June 2005 at our institution, abstracting clinical details and data on Hickman line insertion and removal. We noted infections and the duration of line days in patients in which the Clave CLC2000 connector system (Abbott Laboratories, IL, United States) or the Interlink (Baxter, Toongabbie, NSW) had been used. We defined BSI according to CDC guidelines.
Results: During the study period, 19 BSI were observed in 98 patients. There were 13130 line days; the incidence of BSI was 1.45 per 1000 line days. In patients where the Clave system had been used, the BSI incidence was 1.47 per 1000 line days compared to 1.44 per 1000 line days when Interlink connectors were used (RR=1.02, p=NS). Double lumen lines were associated with infection (5.29 vs 1.02 per 1000 line days, RR 5.2, p=0.001). There was no significant interaction between number of lumens and whether Clave or Interlink connectors were used.
Conclusion: There are reports of increasing healthcare-related BSI associated with the use of the Clave needle-free system in intensive care units. Our data suggest that the use of the Clave connectors was not associated with BSI in haematology-oncology patients. Double lumen lines were strongly associated with BSI. These data provide a baseline for surveillance of healthcare-associated BSI in haematology-oncology units.

P106
"Rainy day" Autologous Stem Cell Harvests in New South Wales

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There is a prevailing attitude that rainy day autologous stem cell harvests are inappropriate. Paradoxically stem cell storage tanks are near full capacity in NSW. While only ~210 autologous stem cell transplants are performed in NSW each year, >1800 autologous stem cell harvests are stored in nearly 5000 bags in 8 cryopreservation laboratories. This presents a critical storage problem.
Methods: Thirty-three NSW haematologists answered a web survey about rainy day harvest (RDH), attitudes and practices, in March 2005. Respondents were asked whether they would perform a rainy day stem cell harvest for each of five patients lacking a sibling donor.
Results:

Patient	RDH – storage permitting Yes (%),
52 y.o CML with 3log reduction in bcr-abl	72 - 85
44 y.o. DLBCL 8years prior. Now in CR1 after therapy for Follicular lymphoma.	39

35 y.o with Gd2 Stg3 Follicular lymphoma in CR1	48
58 y.o int. risk AML in CR1	58
39 y.o with Myeloma - VGPR to VADx3 - Store in 3 bags to facilitate both initial tandem transplant, and rainy day storage?	30

18 respondents listed several indications for routine RDH. Only one institution had a written policy re. RDH. Eight respondents had 1-5 patients for whom storage lack had prevented a RDH. 70% would be willing to cryopreserve stem cells for private stem cell storage.
Conclusion: RDH are occurring across NSW, but for some patients there is a gap between desired clinical practice and the resources to support it. There is a need to develop consensus on the diseases, and patients, for whom rainy day harvest may be appropriate. Currently being drafted within the BMT Network NSW, this consensus will require regular prospective review of utilization rates and available evidence to meet changing indications. It will add weight to ongoing requests for additional funding for stem cell storage and facilitate clinical trials in an area where evidence is lacking.

P107
Evaluation of Relative *BCR* Expression in Different Cell Lines Using DzyNA RT-qPCR

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Aim: Real-time reverse transcriptase quantitative PCR (RT-qPCR) is routinely used for detection of leukaemia specific fusion genes at diagnosis and to monitor response to therapy. *BCR* transcript levels are often used as internal controls to quantify *PML-RARA* transcripts in acute promyelocytic leukaemia and *BCR-ABL* transcripts in chronic myeloid leukaemia. Quantitative results are expressed as the ratio of disease specific transcripts to control transcripts (RDC). Therefore the expression level of *BCR* transcripts is critical to the calculation of the RDC. *BCR* quantitation can be determined using serial dilutions of plasmid calibrators of known concentration to create a standard calibration curve, and can then be expressed as an absolute copy number per reaction. Alternatively, serial dilutions of cell line RNA can be used to create a calibration curve and the *BCR* expression level can be expressed as cell line RNA equivalents. Several different cell lines are being used by various laboratories as sources of RNA for qPCR assays. We sought to document the expression level of *BCR* transcripts in different cell lines.
Method: We quantified *BCR* transcripts in six different cell lines (K562, BV173, MEG-01, A547, HeLa and THP-1) with a single tube DzyNA (or BD QZyme™) RT-qPCR method. BV173 RNA was used to create a standard curve. The *BCR* transcript level was determined using 100ng of cell line total RNA per reaction.
Result:
The figure shows mean expression levels (±SD) of *BCR* transcripts relative to BV173 as well as whether the cell lines are *BCR-ABL* positive. *BCR* expression in all cell lines was significantly different (by *t*-test, $p < 0.05$), except for the two comparisons indicated in the figure.
Conclusion: These results have implications for comparison of qPCR results between laboratories; specifically, where cell line RNA is used to construct *BCR* calibration standard curves. This work supports the need for universal standardization of RT-qPCR calibrators.

P108
Reduced Intensity Conditioning Allogeneic Stem Cell Transplantation Using Tacrolimus, Sirolimus and Methotrexate GVHD Prophylaxis in High Risk Recipients

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Reduced intensity conditioning (RIC) in Allogeneic Haematopoietic Stem Cell Transplantation (HSCT) has been increasingly used as a means to induce a graft versus leukaemia/lymphoma (GVL) effect. RIC allografting can be considered for patients previously not thought suitable for a myeloablative procedure due to excessive toxicity. The challenge however remains to adequately prevent and control GVHD in high risk recipients without negating the GVL effect.
We adopted the Dana Farber GVHD prophylaxis with dose modification to account for our centre's use of azole antifungal prophylaxis. Tacrolimus was administered at 0.02mg/kg daily, sirolimus 1mg daily and methotrexate 5 mg/m^2 (days 1,3,6 and 11). The RIC used included fludarabine 30mg/m^2 x5 and melphalan 140mg/m^2.
Twelve patients (8M:4F) have been transplanted with this RIC HSCT regimen. The median age was 56 (38-67) with 4 patients over 60. 7/12 were MUD transplants and 5/12 sibling, all using peripherally collected stem cells.
We have observed a relatively low rate of severe GVHD with grade I disease in 2/12, grade II in 4/12 and grade III in one patient when immunosuppression was withdrawn. There was no grade IV disease. 6 of the 7 patients who developed GVHD were MUD recipients. There was no transplant related mortality at 100 days. All engrafted. At a median follow up of 182 days (15-464) two patients had died of relapse (days 128 and 208). Another had cytogenetic relapse. The remainder maintain complete remission.
We conclude from these preliminary data that RIC with Flu/Mel combined with tacrolimus, sirolimus and methotrexate GVHD prophylaxis resulted in high engraftment and prevented severe GVHD with acceptable relapse rates and transplant related mortality in this high risk group of patients.

P109
An Audit of Myeloma at Fremantle Hospital

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Aim: In recent years there have been significant changes in the management of multiple myeloma, including the increased use of autologous peripheral blood stem cell transplantation (PBSCT) and introduction of thalidomide, bortezomib and arsenic. Our aim was to assess the influence these changes have had on the treatment and outcomes in patients with myeloma at our institution.
Method: We performed a retrospective case series analysis of consecutive patients with myeloma treated between January 2002 and June 2005. Patients were identified from the department's marrow biopsy and PBSCT databases. Demographic data, details of treatment, survival and complications were extracted from individual patient notes.
Results: Seventy-one patients were identified with a median follow up of 18 months. The median age at diagnosis was 66 years (range 32 to 93 years). Bisphosphonate therapy was administered to all patients. Multiagent intravenous chemotherapy was used as initial treatment in 45 patients, consisting of vincristine, doxorubicin and dexamethasone in 29 patients (64%). Most of these patients were under the age of 70 (n=38, 84%) and subsequently proceeded to high dose melphalan with PBSCT (n=29, 64%). There was no transplant-related mortality. Maintenance therapy consisted of steroids (n=8, 28%), bisphosphonates (n=12, 41%), interferon (n=4, 14%) or thalidomide combined with steroids (n=5, 17%). There have been 5 subsequent deaths after a median follow up of 36 months. The median survival has not been reached. Thalidomide therapy was used in 30 (42%) patients overall, mostly as second line therapy (n=20, 67%), and as initial therapy in 5 patients. Thomboembolic complications were experienced in 4 patients (13%). Thalidomide was stopped due to neuropathy in 8 patients (27%).
Conclusion: The overall survival and complication rate for patients with myeloma at our institution compares favourably with published data. Maintenance therapy post-PBSCT has become standard of care as has the use of bisphosphonates. The introduction of thalidomide represents the most significant change in our management of myeloma over the last five years. Most patients will receive this therapy at some point in their disease and there is a trend toward earlier use. Unfortunately, the side effects of thalidomide are problematic, resulting in cessation of the medication in many patients.

P110

Cefepime Monotherapy as Empiric Treatment for Febrile Neutropaenia in Patients with Haematological Malignancies

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Aim: Recent publications indicate beta-lactam monotherapy is as effective as beta-lactam-aminoglycoside combination therapy in the empiric treatment of febrile neutropaenic patients with haematological malignancy. Aminoglycosides may have adverse effects, such as nephrotoxicity and ototoxicity, particularly in elderly patients. Our aim was to establish whether single agent cefepime could be used safely and effectively in our institution.
Method: We performed a prospective case series analysis of patients with febrile neutropaenia treated with cefepime and gentamicin. Fifty consecutive episodes in 30 patients were identified between January 2003 and June 2005. All patients were treated with cefepime 2g b.d. with gentamicin 5mg/kg. Demographic data, details of underlying haematological malignancy, microbiological isolates and patient outcomes were extracted from individual patient notes.
Results: The median age was 58 years (range 21-77 years). The most common underlying haematological malignancies were acute myeloid leukaemia (22 of 50 episodes) and non-Hodgkins lymphoma (21 of 50 episodes). Positive blood cultures were obtained in 11 of 50 episodes. Ten patients had gram positive infections, most common were *staphylococcus epidermidis* and coagulase negative *staphylococci*, and 4 were gram negative (*pseudomonas aeruginosa, enterobacter cloacae, flavabacterium oryzihabitans, stenotrophamonas maltophilia*). Overall there were 4 deaths. Three of these patients died of sepsis which failed to respond to empiric therapy. One of these patients had *candida krus*ei and *candida albicans* in sputum cultures and oesophageal biopsy, as well as *scedosporium apiospernu*m in pleural fluid. A second patient had *candida krusei* isolated from blood cultures. None of the patients who died had gram negative isolates.
Conclusion: In this high risk group of patients, cefepime monotherapy would provide appropriate broad-spectrum cover for isolated organisms. Based on this evidence and published data, the protocol at our institution was changed to cefepime monotherapy 2g b.d. Gentamicin is added only in patients with signs of severe sepsis in whom gram negative infection is more likely.