ASTH NEWSLETTER
The Australasian Society of Thrombosis and Haemostasis

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Dear Fellow Clotter

SECRETARIAT NEWS

How time flies! It's hard to believe that I've been back from Ethiopia for well over a year now. Of course, this also means that I've been back in my role as the ASTH secretariat for the same time and seen the full annual cycle of events. This last quarter has probably been the busiest, with all the planning for the Scientific Workshop finally culminating in a productive and stimulating day, and the same can also be said for the HAA meeting and the AGM.

The Workshop was a great success – with positive feed back from delegates and sponsors alike. It's often a hard task to balance the needs of both these groups – one looking for instructive content and the other looking for promotional opportunities, however I think we managed to keep everybody happy and provided plenty of opportunity for networking too.

Council will be looking at Workshop feedback in more detail over the coming months and will try to incorporate suggestions in to the next Workshop in Adelaide. Nevertheless, one delegate comment stood out for me – that we should encourage more young people to attend. We tried to address this issue this year to some extent by offering one year's free membership with every non member Workshop registration. We found that this offer was often taken up by younger people working in the H&T field. But it'd be great to see even more 'younger' faces next year- perhaps you could start identifying possibilities now and encourage junior staff members to get involved.

Members attending the AGM were presented with an overview of the Societies activities and financial standing for the 2007-08 year. Of particular note was the Science and Education Trust fund which we are keen to use to

SECRETARIAT NEWS *continued*

encourage and support young researchers in their chosen career in the field of H&T. If you have any suggestions please let me know.

The ASTH will be closed from 1st-27th January, re-opening on Wednesday 28th. I hope you all had a pleasant festive season and are now refreshed to start 2009.

Megan Sarson

The ASTH would like to welcome the following members who have joined since the last newsletter

Michaela Walters
Chee Wee Tan
Victoria Potter
Lesley Schonegevel
Lisa Lincz
Deepak Singhal
Peter Tan
Sue Strutt
Amanda Campbell
Jeanene Lam
Tina Noutsos
Andre Samson
Liz Gardiner
Robert Andrews
Tracy Dixon
Celeste Bell
Nancy Darmadi

We would also like to welcome those new members who wish to keep their contact details private.

A CHANCE TO WIN WITH APACE CERTIFICATION

You will remember from the May 2008 newsletter that the Australian Professional Acknowledgement of Continuing Education (APACE) scheme is now available to ASTH members for a small administrative fee ($30). The APACE scheme is a voluntary program for medical laboratory scientists that recognizes continuing education, formal courses and a wide range of professional activities that contribute to your professional growth and provides a method by which your professional development activities may be recognised. A *Certificate of* APACE *Participation* will be issued to members who meet the requirements, a nice addition to your resume.

The APACE committee has recently approved a monthly prize ($50 Coles/Myer voucher) to be drawn from the applicants submitted each month starting January 2009. Presently AIMS receives about 150 applications per year, so the odds aren't too bad to pick up one of the monthly prizes. Members of the APACE committee are excluded from the prize draw.

If you'd like to know more about the progam check out the AIMS web site at *http://www.aims.org.au/c/index.php?page=apace*. To participate you will need to register with APACE and then start recording your continuing education/ professional activities. Registrants will be required to accumulate a minimum of 100 CEU credits within a maximum submission period of 2 years. The 3 year timeframe for rural applicants is being phased out as it is now easier to reach 100 credits without attending a conference. There are many opportunities to gain credit points by participating and completing online training, eg. Bloodsafe program or the CSL SVDK competency test and snakebite management quiz. Your documentation and fees can either be submitted on line directly to AIMS or as a hard copy to the ASTH Secretariat.

To our NZ members

APACE has been approved by the New Zealand Medical Laboratory Science Board as a recertification programme for New Zealand Medical Laboratory Scientists.

And, you can submit retrospectively, send in an application in the next few months for "activites" you have participated in over the last 2 years.

Emma Perrin
ASTH *representative on the* APACE *Committee*

HAA2008 REPORT – PERTH

The recent HAA meeting in Perth was held from 19 to 22 October. 900 delegates attended, drawn to undertake a long trip to unseasonally hot Perth by an outstanding conference programme. Gavin Cull and Ross Baker are to be congratulated on organising a memorable event.

The faculty of international and local speakers covered a great range and depth of topical issues, although for my money, the star of the show was ASTH invited speaker Prof Frits Rosendaal. Frits experience in venous thrombo-embolism is second to none, and his ability to blend information with entertainment is a highly effective way of communicating. He gave two memorable presentations on female hormones, and travel, relating to VTE. Insights into the manner of prophylaxis used by experts of various nationality undertaking long haul flights to the ISTH in Sydney in 2004 possibly revealed more about national character than evidence based practice (the French preference was for stockings).

Hatem Salem's presentation on warfarin reversal, based on his recent study confirmed earlier work done in Perth by Brad Auguston that Prothrombin Complex Concentrate (PCC) alone is efficient and safe for rapid warfarin reversal, despite the 2004 ASTH guideline recommending concurrent administration of FFP as a source of FVII. Surveys of current practice in warfarin reversal reveal that vitamin K, FFP and PCC are used in isolation or combinations and doses (and therefore presumably response) vary considerably. However, a revision of warfarin reversal guidelines is not anticipated in the immediate future.

Tim Brighton delivered an overview of current strategies for predicting recurrence of VTE and optimizing treatment duration. A number of recent studies have focussed on

HAA2008 REPORT – PERTH *continued*

D-dimer assay after cessation of warfarin therapy, and assessment of residual vein occlusion. The former approach involves potential resumption of warfarin therapy in the absence of a defined clinical event, which might be poorly accepted by patients. The latter approach relies on a poorly standardised assessment. No clear algorithm can be applied, and the art of individualised therapy based on risk stratification has not yet been supplanted.

Harry Gibbs faced a potentially tough gig with his talk on venous thrombosis at unusual sites at the end of the Sunday afternoon session. Harry delivered a highly entertaining and informative presentation, which has left him in danger of repeat scheduling to that time slot, safe in the knowledge that he can revive a fatiguing audience. Without wishing to hit too far below the belt, he kindled interest in thrombosis at a site that all men would find most incapacitating. Those of us who run labs offering jak-2 mutation testing are bracing ourselves for a surge in requests.

Alison Street gave the Carl de Gruchy Lecture, on behalf of the HSANZ, on the subject of Haemophilia, History and Hope. Alison charted the roller coaster history of haemophilia management, with particular reference to Dr Ron Sawer, after whom The Alfred Haemophilia Centre is named. Unfortunately, access to safe and effective management options in many less developed nations is currently limited. The World Haemophilia Federation is committed to raising the global standard of care to that currently offered in developed countries, where young patients have preservation of function and opportunity throughout life, while older patients can be treated in an effective and safe manner.

Rob Bird

ASTH SCIENTIFIC WORKSHOP 2008 PERTH

The 4th ASTH Scientific workshop was held recently on Saturday 18 October. The program was excellent and many made the long journey west for the day.

The program began with Erica Malan's (Monash MC) presentation about the current status of POC INR testing. She reviewed the devices in use, validation procedures, clinical efficacy of self management (including patient selection and training) and the role of the laboratory (including external QA). She finished with a reminder of the effect a strong lupus anticoagulant (high β2GP titre) can have on a coaguchekXS INR (falsely high). Next up Tom Exner filled us in on his work (Haematex Research) in developing a locally manufactured INR calibrant set for ISI/MNPT validation. In 2004 the SSC recommended the use of single manual testing with an IRP (international reference thromboplastin) to validate local INR testing systems. This recommended method is becoming increasing difficult as the need for manual testing diminishes. A set of INR reference plasmas was prepared by partially adsorbing pooled normal plasma (assigned INR via consensus INR >20 laboratories). An inter-laboratory validation exercise (4 labs) was then carried out (JTH 2004; 2;1946-53) to compare use of this calibrant set to manual testing with an IRP. Over 90% of results fell within acceptable limits but this outcome may have been due to unreliable results with the manual clotting tests using IRPs.

Our third speaker, Kate Maslan (Royal Perth) presented an excellent update on oral direct thrombin inhibitors. Dabigatran etexilate is still undergoing phase III trials in acute and secondary VTE and stroke prevention in patient with AF. Kate highlighted some considerations with the

Thanks to our workshop speakers

imminent arrival on the market of oral DTI's, there is no antidote (surgery and bleeding), monitoring is difficult (ecarin clotting time not readily available in many labs), compliance (difficult to assess if patients have missed dose) and cost. Our final speaker before morning tea was Tracy Dixon (Fremantle) who presented a case of inherited dysfibrinogenaemia. This case highlighted the mixed phenotypic expression of the γ275Arg→Cys mutation as described on the fibrinogen database (as of May 2008, 454 abnormalities on the database).

After the break, Roslyn Bonar (RCPA) spoke about the lower limit of assay sensitivity (LLS) for the diagnosis and classification of vWD. The RCPA results from the last 10 years (type 3 vWD) and the results from sample VW8-08b (acquired Type 2A-like VWD) were reviewed. The LLS tends to be around 5-10U/dL for FVIII:C, VWF:Ag, VWF:CB and VWF:Act, but 20U/dL or more for VWF:RCo. Automation does not provide better LLS performance.

The findings of this review reflect significant diagnostic limitations that may affect many vWD testing labs. Next Susan Rodgers (IMVS) gave us an excellent overview of lab tests for vWD (basic, specialised and mutation analysis). Susan mentioned the worth of performing both the RiCo and CBA in the basic test panel, as each assay is useful in identifying different patient groups. The more advanced tests may be required for differentiation of the 4 type 2 sub-types. Ristocetin-induced aggregation (RIPA) should be performed in all cases of suspected type 2 vWD, in order to diagnose type 2B. The FVIII binding assay is required to distinguish between haemophilia and type 2N vWD. Multimer analysis is required to distinguish between type 2A and 2M vWD. Mutation analysis of the vWF gene is helping to improve our understanding of vWD and is very useful for diagnosis of type 2B, 2N and Vicenza (treatment may need to be different). Following on from Susan we were treated to an unusual case of acquired von Willebrand syndrome (avWS) presented by Kent Chapman (John Hunter). Kent took us through his "journey" of this difficult case in a very entertaining talk. Joyce Low (St Vincent's) topped off a great session with her impressions on how a laboratory automated system (LAS) might work in an Australian coagulation laboratory.

After a descent break for lunch and a chat with the trade we were privileged to hear Professor David Lane (Imperial College, London) speak on ADAMTS13, vWF and TTP. This is the second year that we have "borrowed" one of the invited international speakers from the HAA conference to present at the workshop. This gives those participants who can only make it for the workshop a chance to hear a world renowned expert in the field of thrombosis and haemostasis. We then had Jim Thom (Royal Perth) present a review on the assessment of platelet function using flow cytometry, including some of the methodological issues. The markers of activated platelets can be detected by flow cytometry using a wide range of monoclonal antibodies. Flow cytometry is a powerful research tool that can be used to detect surface glycoproteins, platelet derived micro particles, granule content, activation markers, complexes with other cells (eg. platelet monocyte aggregates) and metabolic response to agonists. The final talk before afternoon tea was from Brian Dale (University SA) on educating medical scientists. Brian began his career in diagnostic labs in WA before moving to South Australia where he has been a lecturer for 5 years. Brian gave us a highly entertaining "lecture" with some surprising points.

The final session began with Murray Adams (University TAS) who presented a tidy summary of global assays of haemostasis. He gave us an overview of the history of the assays, the various types of systems, the advantages and potential limitations and the clinical utility. Murray concluded with his impressions of the future of global coagulation assays which should see a move to standardisation and identification of clear indications for there use. To cap off the scientific program we relaxed into the final presentation by Jill Smith (Royal Perth) who touched our emotional sides with her wonderful talk on her work (and her band of volunteers) to recycle and reuse not only lab equipment but any excess hospital "stock" to areas in the world (near and far) that are less fortunate than us.

Congratulations to Grace Gilmore and her team of local organisers on an excellent day. The ASTH wishes to acknowledge the important support of all the sponsors, with special mention of Siemans Medical Solutions for their additional support for the sundowner and Helena Laboratories for production and supply of the workshop CDs.

Emma Perrin

ASTH WORKSHOP SPONSORS

BARRY FIRKIN ORATION

The highlight of the ASTH program in Perth was the Barry Firkin Oration. It was very well attended by the wider haematology community in the main meeting auditorium. Alex provided insights from his vast experience of translating clinical trial research into practice and highlighting the challenges that lie ahead of us all.

It is difficult to now believe that study of the 1960s that described the efficacy of Heparin treatment to prevent death in pulmonary embolism was ground breaking. It only required around 20 patients to demonstrate the absolute benefit of treatment versus placebo. The end point was mortality. This was radically compared to the current trials in venous thrombosis which require thousands of patients utilising surrogate end points of venography or ultrasound to demonstrate equivalence in safety and efficacy of new antithrombotic medications.

Alex has demonstrated that clearly we have come a long way in managing patients with thrombotic problems and it is an exciting time to be investigating this area with the various new treatments that are available.

BARRY FIRKIN ORATION

President A/Professor Chris Ward proudly acknowledged Alex's contribution to the ASTH and Australian haematology. He presented him with the last uniquely-designed glass sculpture to commemorate the award.

The council will embark upon an expression of interest for the design for the next five years for the Firkin Award. It has been a tremendous boost to the Society's profile and the commemoration of Barry Firkin's influence and subsequent significant contribution by members subsequently over time in Australian haematology.

Ross Baker

Alex Gallus and Chris Ward

ASH 2008 REPORT

A cool but otherwise delightful San Francisco in the festive season was a big attraction for a record 22,000 participants at this year's 50th birthday celebration ASH meeting. The choice of sessions on offer means the ASH meeting experience can be unique for each attendee, with different presentations able to build on a theme. I have summarised my particular ASH 2008 themes under the following headings.

Haemostasis and tumour metastasis

Dr Varki from La Jolla reviewed data on the potential association between LMWH and metastatic disease. The current focus is inhibition of P- and L-selectin binding to their natural ligands, unrelated to the anticoagulant effect of LMWH. Dramatic reduction of metastatic potential by LMWH but not by warfarin in animal models supports this concept. The theory is that metastatic potential may be inhibited when pathological mucin ligands on tumour cells are blocked from binding to selectin receptors. Of interest, the synthetic pentasaccharide does not have this selectin-blocking effect at clinically relevant levels. This presents potential for a clinical trial, comparing LMWH with the pentasaccharide, administered in the perioperative period of newly diagnosed cancers, where both agents have anticoagulant activity, but only one has selectin-blocking activity. An oral presentation (396, Hu et al) assessed the association between hypercoaguability and tumour at the level of the cell cycle. They found that thrombin enhanced murine model prostate tumour growth by stimulating cell cycle regulators, causing tumour cells to leave G0 phase and progress to S phase. Platelets and thrombin often feature in these discussions. Animal models of metastasis suggest that GP 1b-IX contributes to tumorigenesis, indicated when a functional absence of GP 1b-IX correlates with a reduction in number of metastatic foci (Jerry Ware, program book pg 99). It is possible that the "thrombogenicity" of tumour cells, PARS expressed by cancer cells giving rise to thrombin-mediated signalling, allows the metastasing cell to stably adhere to distant vascular beds.

Syk signal transduction

Spleen tyrosine kinase (Syk) received attention in relation to very different pathologies. Jonathan Freidberg et al (plenary session, abstract 3) described Syk as essential to B cell viability: when the B cell receptor binds ligand, Syk is activated, and the cell is "rescued" from apoptosis. A subset of lymphomas exhibit constitutional over-activity of Syk, creating a malignant "tonic" B cell survival signal. They showed in a clinical intervention trial of a Syk inhibitor in cases of B cell tumour, that blocking this tonic B cell survival signal was safe and well tolerated, enhancing the disease-controlling effect of fludarabine. Suzanne Delaney et al (abstract 409) presented on the same theme but different disease.

Syk in platelets generates a kinase signal after ligand binding to GP VI and GP IIb-IIIa. Using a mouse model of arterial thrombosis, pharmacological targeting of Syk with a kinase inhibitor showed that Syk acts in arterial thrombosis via two mechanisms: conferring stability to platelet interactions downstream of GPIIb-IIIa, and by initiating thrombus formation on collagen surfaces. This dual activity makes it a preferred and theoretically safe target for inhibition of arterial thrombosis, as it does not compromise primary haemostasis.

The platelet lifecycle

This year the Scientific Committee session (program book pg 106) addressed genetic regulation of platelet-poiesis, regulators of platelet birth, and of platelet death. Understanding transcriptional control of thrombopoiesis favours the linguistly-inclined: Clever protein purification work has identified Runx-1 and Fli-1 as important binding partners in the differentiating stem cell, with this heterodimer forming a large complex with other transcription factors, to generate what is now referred to as a megakaryocyte-specific "enhancesome". Defects in some of the contributing proteins have been found to cause familial thrombocytopenias. Elisabeth Cramer from Paris referred to the work of Ian Morrison and colleagues from Dunedin New

Zealand in describing how a defect in cytochrome c can cause ectopic platelet release and enhanced apoptotic behaviour. A deficiency of megakaryotic culture research to date has been the absence of blood flow, or shear, in the model. Dr Cramer presented research that has incorporated shear equivalent to that in capillaries and small arteries, showing that shear effect is able to generate platelet formation 20-fold that seen in static conditions. The excellent work on platelet apoptosis conducted in Melbourne's Walter and Eliza Hall Institute of Medical Research was presented by Dr Benjamin Kyle (program book pg 107). The counterbalance between anti-apoptotic Bcl-xL and pro-apoptotic Bak and Bax was reviewed. The interplay between platelet activation via classic signalling pathways and apoptosis was described. Preliminary research hints that Bcl-2 proteins, which control apoptosis, may be required for platelet production.

Paediatric Thrombosis

We can test children for the usual range of known congenital prothrombotic markers, but should we? Following the usual reminder of poorly defined age-related reference ranges, the utility of testing was discussed for two scenarios: the child with an acute thrombosis, and the child without thrombosis with a family prothrombotic marker.

Regarding the first group, catheter-related thrombosis seems not to be significantly affected by congenital thrombophilic states, and in this group, testing is unhelpful. However, with spontaneous VTE in the otherwise well child, testing is relevant, with a higher "positive" result rate, therapeutic relevance for antithrombin or severe protein C deficiency (by protein replacement), and the indication that thrombosis relapse risk is higher in result-positive children. In the second class of child, well, with a family history of prothrombosis, testing may be helpful by providing the potential to modify lifestyle choices (BMI, activity, future contraceptive choices).

The timing of testing will depend on the problem, with benefit more likely during the adolescent years or later. Of note for the testing of well people, there is a recently passed genetic non-discrimination law in the US that gives protection to these individuals, including for the purposes of insurance cover. Finally for childhood thrombosis, there was review of what is known on use of new anticoagulants for the young. A paediatric study of the Xa inhibitor rivoraxaban is now planned, before the drug has been approved in adults, and this is seen as an appropriate recognition of the importance of characterising new drugs in the paediatric setting.

Coagulation cofactors and vWF

Reinhard Schneppenheim from Hamburg (abstract 589) gave a good presentation on modelling the vWF multimer's accessibility to ADAMTS13 cleavage. He showed a movie depicting the unravelling of the globular vWF multimer under shear, arrived at by computational computer analysis. This was something I had not seen before. Finally (an arbitrary and premature place to stop, but space is limited), there was an excellent presentation given by Mettine Bos (abstract 586), a collaboration between Philadelphia and Australia, on why Brown snake venom is so hugely procoagulant. The venom contains factor V, which is different to human FV in several important ways. The B domain is markedly shortened, with the heavy chain disulphide-linked to the light chain, a non-conserved feature apparently unique to the snake. FV from the Brown snake has a relatively high affinity for FX in the prothrombinase reaction, highly functional in solution, without the need to bind to the PS-rich platelet lipid membrane. With this detail in mind, I was relieved to walk past the Australian-bound plane at San Fran airport, and instead wind my way back to snake-free New Zealand.

Mark Smith

CONGRATULATIONS TO THE ASTH MEDAL RUNNERS-UP

Kate Burbury (Peter MacCallum Cancer Centre, Vic), B Snooks, D Jupe and D Westerman: "Warfarin reversal for elective surgical procedures, using low dose intravenous vitamin K: impact on vitamin K-dependant factor levels."

Claire McLintock (University of Auckland, NZ), Carl Eagleton, Lesley McCowan and Robyn North: "Pregnancy outcome in women with mechanical heart valves treated with enoxaparin."

AND THE HAA 2008 POSTERS WINNERS

Fiona Scorgie (Calvery Mater Newcastle Hospital, NSW), Simon Brown, Michael Seldon, Lisa Lincz and geoff Isbister: "Factor deficiencies associated with venom induced consumption coagulopathy in Australian snakebite."

Paul Ellery (Curtin University, WA)and Murray Adams: "Effect of lipoproteins on the release of tissue factor pathway inhibitor and the expression of tissue factor in endothelial cells."

ASTH 2008 TRAVEL GRANT WINNERS

Murray Adams

Kate Burbury

Lisa Lincz

Huy Tran

Deepak Singhal

Peter Tan

2008 ASTH MEDAL WINNING ABSTRACT

INCREASING SHEAR RATES CAUSE SHEDDING OF PLATELET GLYCOPROTEIN (GP)VI

Elizabeth Gardiner,[1] Jane Arthur,[1] Jing Jing,[1] Justin Hamilton,[2] Michael Berndt,[1] Robert Andrews.[1]

[1] Department of Immunology, Monash University, Melbourne, Australia;
[2] Australian Centre for Blood Diseases, Monash University, Melbourne, Australia

Glycoprotein (GP)VI, which binds collagen, and GPIb-IX-V, which binds von Willebrand factor (vWF) and other ligands, form a unique adhesion-signalling complex on human platelets. Following vascular damage or disease, engagement of GPVI/GPIb-IX-V leads to αIIbβ3-dependent thrombus formation. We previously showed ligand binding to GPVI leads to metalloproteinase-dependent ectodomain shedding, generating an ~55-kDa soluble GPVI fragment and an ~10-kDa remnant fragment that remained membrane-associated.

Aim – To determine whether shear force was sufficient to induce shedding of GPVI.

Methods – Human platelet-rich plasma or washed platelets were subjected to increasing shear rates in a cone-plate viscometer and then levels of intact and cleaved GPVI were examined by western blot using anti-GPVI antibodies raised against either the GPVI ectodomain (recognising intact and ~55-kDa soluble GPVI) or the GPVI cytoplasmic tail (recognising intact and ~10-kDa remnant GPVI).

Results – Increasing platelet aggregation was observed in platelet suspensions subjected to shear rates from 300 s^{-1} up to 3000 s^{-1} for 5 minutes and >90% aggregation was achieved using a shear rate of 10,000 s^{-1}. Aggregation was blocked by inclusion of 10 µg/ml function blocking anti-αIIbβ3 (CRC64). Increasing shear rates also induced a loss of full length GPVI and the appearance of the ~55-kDa soluble GPVI ectodomain and increasing levels of the ~10-kDa GPVI remnant on platelets, and 5 to 7-fold increase in soluble GPVI in plasma by ELISA. Proteolysis of GPVI was blocked by the metalloproteinase inhibitor, GM6001, implying that shearing of platelets was sufficient to cause activation of platelet metalloproteinases, in the absence of GPVI ligands. Preliminary data further suggested that blockade of αIIbβ3, GPIbα or vWF minimally affects shear-induced shedding of GPVI.

Conclusions – Together, these results suggest GPVI shedding is triggered in shear-activated platelets, with potential implications for the stability of a forming thrombus at arterial shear rates. No conflict of interest to disclose.

Congratulations to Elizabeth Gardiner

OBITUARY – PRABHA SESHADRI

Prabha Seshadri was one of the most gifted haematologists I have ever met. She represented the truly integrated physician – able to deliver care to the individual patient using the diagnostic resources of the clinician and the laboratory in an elegant fashion. Her laboratory skills, particularly morphology, were legendary. Her specific contributions came from the exquisite use of the laboratory to solve clinical problems. She was a generous and stimulating teacher.

Her life was lived with remarkable grace. She bore her illness with dignity and courage. All those privileged to have known her have been deeply affected by her passing.

Douglas Coghlan

The comments below were written by laboratory staff/colleagues from the Repatriation Hospital and presented at the Memorial Service

Clearly it would be impossible to define Prabha, but 'mentor' is a word that many would use. 'My Best friend and mentor' was a description given by someone very privileged.

'Inspirational' – she carried herself with grace and dignity and always with style. 'A perfect lady', someone told me, and she had an understated elegance.

'A fabulous tennis player. She always beat me – even with one lung!' another person gleefully told me. But I am sure that no-one would ever dare to call her handicapped.

'She is a flower, serene but brilliant, dearly loved.'

'She took the time to know my name.'

In truth, we were shown only what she would permit us to see – a very private person. Would we even really know her age? Certainly no one would guess correctly. Not a single grey hair and never a hair out of place.

Her father had once changed her official birth date to allow this talented young woman an early entry to medical school. Of course she passed with flying colours from the medical school in Bangalore. She worked as a haematology fellow at McMaster University Medical Centre in Ontario, Canada with her husband Ram, where she delivered their first child, Tara, in 1975. She worked with Jack Hirsch who considered her among the most brilliant students he ever taught. A lifetime friendship followed. Fortunately for us, Prabha came to work at Flinders Medical Centre where she became the first Senior Haematology Registrar before delivering their second child Neil in 1979.

Prabha distinguished herself by being unconstrained by any set path. She worked in private and public laboratories, known to her colleagues for her integrity, unquestionable knowledge and skills. Known to her patients for her compassion and understanding. 'She had great integrity as a human being'.

Her work at the Repatriation General Hospital is today once again being acknowledged. Clearly, she was responsible for shaping both laboratory practices and clinical services in Oncology in ways that had eluded any predecessors. Dr Ann Read and Prabha changed the focus of the pathology department creating clinical research projects for the staff and educating colleagues through Grand rounds.

Likewise, she along with Dr Ed Chandraratnam was responsible for establishing a haematology department at Clinipath laboratories. Her energy and enthusiasm obviously matched her intelligence.

'So very professional and conscientious' was another comment given to me. I would personally say 'driven by an unseen force'. I know of no one else who could have along resection, be on an exercise bike within days of surgery, playing tennis within weeks and back at work in just 6 short weeks. She would not be beaten. And she never was. We listened at her farewell dinner as she told us 'I have grown from these malignancies. They have made me a better person and doctor'.

She dies as she lived – to her own beat, in her own way, determined, courageous, uncomplaining, generous, unfathomable. Many people have told me they liked the piece we put in the paper. Particularly the last part. She was truly an excellent teacher, patient advocate, physician, morphologist and mentor. But simply – she *was* never wrong! And we miss her dearly.

UPCOMING MEETINGS IN 2009

MEETING	WHERE/DATES	CONTACT
The 3rd International Symposium on Women's Health Issues in Thrombosis and Haemostasis	Prague 6-8 February 2009	
XXII International Symposium on Technological Innovations in Laboratory Hematology	Las Vegas 11-14 May 2009	*http://www.islh.org* Abstract Submission Deadline: 15 February 2009
XXII Congress ISTH with 55th Annual SSC Meeting	Boston 11-16 July 2009	*http://www.isth*2009*.com/*
2009 BSHT/UKHCDO Annual Meeting	Newcastle Upon Tyne 7-9 October 2009	*www.bsht.org.uk/*
AIMS 2009 National Scientific Meeting	Adelaide 12-16 October 2009	*www.aims.org.au*
ASTH Scientific Workshop 2008	Adelaide 17 October 2009	ASTH@*bigpond.com*
HAA2009 Joint Annual Scientific Meeting HSANZ/ANZBT/ASTH	Adelaide 18-21 October 2009	*www.fcconventions.com.au*/HAA2009/ Abstract Submission Deadline: 13 July 2009
APSTH-JSTH Joint Symposium	Osaka, Japan 20-22 November 2009	*http://www.jsth.org/apsth/information/*0008*.html*
The American Society of Haematology 51st Annual Meeting	New Orleans 5-8 December 2009	*www.hematology.org*