News Letter
July - Sept 2005
Pakistan Society of Haematology

From the desk of President PSH

The new executive committee of PSH took over the office after the first quarter of 2005. The delay in change of hands was due to many reasons. PSH is still in infancy; with the passage of time, these processes will be refined and regularized. I hope Dr. Nadir Ali, secretary PSH and Editor of the Newsletter will keep you posted with events & news in the field of Haematology. Recently I came across a news item, which was related to Thalassaemia. There are suggestions that a law may be passed, which will require marrying couples to undergo blood tests for the screening of Thalassaemia. A "clean bill of health" should be available before the Nikkah and the couple may be asked to produce this certificate if an officer of law demands it. I had written a letter to the Editor of Dawn newspaper and had opposed this thought process. This is likely to open floodgates for corruption and should not be done. We need to support the idea of setting up of screening laboratories for thalassaemia. The government can make the test affordable by waving off duties and taxes on instruments and consumables, and fixing realistic charge for such tests. Couples at risk should be encouraged to attend counseling centers for appropriate advice. We need to reduce the burden of thalassaemia care. This should, however, be done rationally and respectfully. Members are welcome to give their views on this subject.

The executive committee has constituted a scientific committee, which will organize scientific events at regular interval in various cities. We hope our younger colleagues will find these useful. Please contribute to the newsletter and give your comments about its contents.

Dr. Khalid Zafar Hashmi.
President
Pakistan Society of Haematology.

Consensus Report from the NHL Course 2005, Karachi

Bismillah Taqee Institute of Health Sciences & Blood Diseases Centre organized a two day course on non-Hodgkin's lymphoma on 14-15 January 2005. This course was designed to cover the standard of care for common and some uncommon but important types of lymphomas. It was organized for 40 haem / oncology delegates but 56 people eventually attended. 10 speakers from various cancer centers in Pakistan and one speaker from King Faisal Specialist Hospital and Research Centre, Saudi Arabia took part in it. Bismillah Taqee Institute of Health Sciences & Blood Diseases Centre sponsored the stay and registration fee of 16 senior postgraduate residents in haematology / oncology. Delegates took keen interest in case discussion session (tumour board) on both days. Four cases of exceptional educational value were discussed daily.

At the end of NHL course following points came out from the presentations and discussion among the participants:

1. NHL is among the first 5 most common tumours in Pakistan.
2. Its incidence has risen in the last 22 years (Pattern of tumours reported in 1982 from JPMC, Karachi by Professors Manzoor Zaidi and Naeem Jaffary showed that it was not among first 10 common tumours).
3. Currently, WHO classification is the gold standard to classify NHL.
4. Diffuse large B-cell lymphoma (DLBCL) is the most common type of lymphoma in Pakistan. It accounts for 74% of all B-cell NHL as compared to the Western data where it is reported to be 31%.
5. T-cell NHL accounts for 20% all NHL as compared to 9% in the West.
6. Follicular lymphoma, Mantle cell lymphoma and Maltoma account for less than 5% cases.
7. bcl-2 and p53 mutations occur in over 50% of DLBCL each. Both of them are associated with poor outcome. In contrast, they are found in 25-30% cases reported in the West.
8. bcl-6 mutation occur in 30% cases of DLBCL as compared to 52% in the West. Its presence confers improved outcome.
9. Micro array analysis of gene expression profile in NHL is currently being used as a research technique to categorize the prognostic groups within NHL. It is going to revolutionize the practice of oncology.

10. CT scan with contrast should be carried out for staging and then after 4 courses and then at the completion of treatment. This seems expensive at the outset but in the end it saves hundreds of thousands of rupees if salvage therapy for relapses can be avoided when proper staging has been done and NHL is managed accordingly.
11. PET scan has begun to influence the practice of oncology in general and lymphoma in particular. Baseline PET scan could replace CT while during the treatment, PET scan findings could reduce the number of chemotherapycycles.
12. Rituximab-CHOP has become the standard of care as frontline therapy for DLBCL in advanced stage disease in all age groups.
13. In relapse setting, Rituximab is currently being evaluated for in-vivo purging with salvage therapy and for maintenance post autologous peripheral blood stem cell transplantation.
14. Randomized trial data (Intergroup SWOG, USA) did not show any benefit of Rituximab when given with frontline chemotherapy and then as maintenance.
15. Autologous peripheral blood stem cell transplantation should be offered to all relapsed patients under 60 years of age who have chemosensitive relapse or have attained second complete remission.
16. Autologous peripheral blood stem cell transplantation has disappointing results in primary refractory or chemo-resistant NHL.
17. Autologous peripheral blood stem cell transplantation is not found to have any advantage as frontline therapy as compared to frontline chemotherapy.
18. Allogeneic stem cell transplantation (full dose or reduced intensity conditioning) is currently not considered the standard of care because of high treatment related mortality and little of evidence of graft versus lymphoma effect.
19. Maltoma (mucosa associated lymphoma) is a low grade B-cell malignancy associated with H. pylori, is rare in Pakistan. This can be effectively treated with anti-H. Pylori treatment.
20. Chronic Lymphocytic leukaemia / small lymphocytic lymphoma (CLL / SLL) is one disease, slowly progressing in nature. Less common in Pakistan. The cells express CD5, CD23, CD20 antigens on their surface. Expression of CD38 and ZAP-70 carries a poor outcome. ZAP-70 work up has become part of the work up of this disorder and is highly recommended. Based on its expression, early treatment can be offered to them if it is expressed.
21. Fludarabine alone and in combination with cyclophosphamide is showing promising results in CLL / SLL and follicular lymphoma as first line therapy.
22. Although most patients who are ZAP-70 negative and have indolent disease may not require any treatment at all or may benefit from chlorambucil.
23. ZAP-70 positive CLL / SLL should be offered Fludarabine based therapy.
24. In resistant cases, anti-CD52 antibody (CAMPATH-1H) should be considered.
25. Burkitt's lymphoma / leukaemia is another uncommon B-cell disorder. It is associated with Epstein Barr virus at least in endemic areas. It is rapidly progressive and fatal if not treated. Current therapeutic approaches using aggressive combination chemotherapy can cure a significant number of patients.
26. Radiation therapy has an important role to play in localized disease (stage I and II) as part of combined modality treatment. Advanced stage (III & IV) disease requires systemic therapy.
27. For CNS disease, systemic therapy containing high dose methotrexate / cytosine arabinoside should be given.
28. Paediatric lymphomas are almost always are aggressive and are B-Cell.
29. There classification is simple and have a high cure rate (>90% cure rates in the West while 65% overall survival has been reached in Pakistan in specialized paediatric cancer centres).
30. Paediatric lymphomas are not treated with CHOP chemotherapy, they require aggressive protocols.
31. Major cause of death in paediatric lymphoma in Pakistan is not relapse but infection during treatment period (Febrile neutropenia).

From the minutes of PSH executive committee meeting

(Held on 14 June 2005 at LNH Karachi)

Dr. Shaheen Kouser resigned from the appointment of secretary PSH, resignation was accepted and Dr. Nadir Ali was elected as new secretary for the remaining term of 2005-2006.

Scientific sub committee was elected as follow:

1. Dr. Tahir Shamsi, Dr. Ghulam Nabi Kakipoto, and Dr. Saba Jamal for Karachi.
2. Brig Khalilullah and Dr. Atifa Shoaib for Rawalpindi / Isalamabad.
3. Dr. Fazal -e- Razik for Peshawar
4. Dr. Nisar for Lahore
5. Dr. Luqman Butt for Quetta.

News Letter July-Sept 2005
Pakistan Society of Haematology

Hemophilia Society Office inaugurated in PIMS

The office of federal Chapter of Hemophilia Welfare Society, Pakistan was inaugurated on July 4, 2005. Speaking on the occasion, Dr. Tahira Zafar, Consultant Haematologist and Chairperson of the Society said that the establishment of the society office will streamline the maintenance of medical record of the hemophilia patients who are treated in the PIMS Hemophilia clinic. The treatment of hemophilia is very costly and out of reach of the majority of the patients. The hemophilia society provides free of cost expensive factor concentrate injections which are the mainstay of hemophilia treatment, Dr Tahira added. The society is also registered with World Hemophilia Federation, and receives technical support for the improvement in diagnostic and treatment standards of the Hemophilia patients in Pakistan. PIMS, a declared *"Hemophilia Friendly Hospital"* is the only tertiary care center in the country which offers free medicines and specialized consultation for hemophilia which is one of the commonest inherited bleeding disorders. However in Pakistan, due to lack of awareness and facilities, only 5-10% of these patients are ever diagnosed. Most of these patients live in rural areas and die before their disease is diagnosed. Due to lack of awareness and proper treatment facilities, most of the hemophilia patients suffer crippling joint problems and hepatitis C infection. The hemophilia clinic is supported by the diagnostic workup performed under the supervision of Prof. Khalid Hasan, Head of the hematology department. The blood transfusion needs of the patients are the responsibility of Dr. Hassan Abbas Zaheer who is in charge of the PIMS blood transfusion services. Dr. Anjum Javed, Director, Children Hospital provides the crucial administrative support necessary for the quality service to the patients.

Quality assurance of viral marker testing in blood banks

Contributed by:
Dr. Nuzhat Salamat. FCPS (hematology) CTM (transfusion medicine) UK. Consultant Hematologist CMH Multan

In order to perform the donor testing for viral markers and preserve the recipient safety it is mandatory for any blood bank or transfusion service to know and implement some mandatory quality control procedures for these testing. It is also important to document the test performance with standard procedures for each run so that damage control is instituted as early as possible. The fractionation of blood enhances the number of patients at risk because components from one whole blood gets transfused to at least three to four recipients. Although achieving zero transmission rate of TTI is not possible even with latest of technologies like NAT(nucleic acid testing) but for our country maximizing the implementation of few basic scientific and recommended practices will be great step and will reduce the preventable errors and rates of TTI. There is a long list of measures that should be taken, most important are:

1. **Selection of viral Screening assay(Kits):**
   Commercially marketed kits make it difficult for pathologist to make optimum choice. Since there is no centralized national system in place yet that can offer proper kit evaluation and make the results public so individuals or institutions have to make their own evaluations. This in most cases lacks objectivity and proper evidence. Kit evaluation is mandatory health technology assessment. Which should ideally be done by laboratories having the necessary infrastructure and also should publish results in wider national interest. The objective way to do it includes following steps:

   a. ***Provision of background information of the principal source, distributors and products:*** This should include company, distributor profile/ technical details of products, type of antigens, and specificity of antibodies that are detected. Status of the products with reference to registration with regulatory/registration/evaluating agencies. e.g WHO, FDA, European Council, ICCB, HTA institutes, any national body e.g NIH etc.

   b. ***Evaluation of different parameters:*** The parameters that need to be evaluated should include sensitivity, specificity, predictive value, confidence limits, between run precision, linearity, detection limits, low level ranges, performance on seroconversion series, and potentially cross reacting samples. These parameters can be evaluated if appropriate and standard material is made available samples either purchased commercially or developed by institutions that are not component of the test kit. These are used for surveillance of test performance. These are tested the same way as donor sample to alert about the possibility of an increasing risk of error. The non reactive results will be invalidated on the basis of external controls, but will not be used to invalidate reactive results if test is done according to manufacturer's instructions and internal controls are performing as expected.

c. Invalidation of test results: The viral marker tests will be invalidated if the performance did not meet the requirements of manufacturer's instructions or if the control results do not meet the acceptance criteria already designed. In such cases all the results including reactive and non reactive will be declared invalid and all specimen should be treated in new run.

d. External quality assurance schemes: Participation in external quality assurance schemes which are extended by different countries helps to know what is the individual blood bank performance and quality of screening tests and compared among regional blood banks. This is one of the best ways to do document the performance of test system and to some extent quality of assay. These are usually expensive but the cost can be shared if blood banks can pool their resources. Unfortunately no national body has undertaken the responsibility to chalk out national external quality control assessment schemes and the collaboration with other countries remains individual initiative. Whenever resources permit this should be undertaken.

e. Donor population data: Unexpectedly increased reactive rate of donor population data with a test run may cause non reactive result to be considered invalid. The next assay performed on a single aliquot from affected specimens become initial test of record. Reactive results on the donor data may not be invalidated.

f. Disease surveillance data: Follow up of recipients of screened blood products for development of TTI and their incidence directly reflects upon the safety of blood transfusion and performance of test systems being used. The surveillance data is most vital for decisions like which TTI should be screened in our population and what are strategies that best suit our circumstances. The legislations should be only based on such technology assessments and not on what is currently practiced in developed countries. . For example law should be preceded after answering questions like what is the rate of transmission of malaria through transfusion and whether antibody based test are useful in endemic areas like ours.

In this limited space allowed I have not touched the details of other issues that has direct impact on quality of viral screening e.g equipment, operator proficiency, documentation etc. There are many more issues but this aspect of safety of blood needs urgent attention of government and professional authorities.

Dear Friends

1. PSH requests you to contribute in news letter by sending your comments, short communications, case reports, issues of national interest, new developments in your departments, and scientific activities in your institutes. Your contribution is the back bone of this society. Please post your comments and valuable writing material on the following address:
   Dr. Khalid Zafar Hashmi, Depatement of Haematology Liaquat National Hospital, Stadium Road, Karachi. Phone:021-4939612 Ext 2371. Please do not forget to send one electronic copy on floppy disk in addition to paper copy. It is further requested that report/write up should be brief and concise.
2. Many of the addresses and phone numbers with us are changed. We are in process of updating the address for better communication. If your address has been changed after membership please send us your present mailing address e. mail and phone contact.