news LETTER
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President's Column


Maj Gen Suhaib Ahmed

The winter of Rawalpindi awaits your participation at the 15th annual PSH conference. We will try our best to compensate the chilly weather by a warm welcome and of course a good scientific programme. Don't forget that we also plan to take you to the Murree hills to give you a real touch of the icy winter! This time the conference would be jointly held with the annual PAP conference. In fact it was due to the PSH's initiative that ultimately materialized in the first ever joint conference of the societies of Pathology. I once again take this opportunity to warmly welcome you to this mega event. I urge everyone, especially the young trainees in Haematology, to come forward and share with us your valuable research.

With warm regards,
Maj Gen Suhaib Ahmed

15th PSH conference (1st Joint PAP conference)

Dear PSH members we request you to join us at 15th PSH conference (joint event). Your participation is extremely important for the success of this event. Following is some information about layout of conference. You can also download brochure, current information, registration forms, abstract submission form, information about hotels from conference website www.36papconference.com or email to info@36papconference.com.

Please note that last date for abstract submission is 30th October 2012

Lay out of 1st joint conference

Senior Advisory Committee Haematology sessions
Dr Mohsin Anvery
Lt ® Gen Muhammad Saleem
Professor Abdul Hayee
Dr Moinuddin
Professor Muhammad Khurshid
Dr Khalid Zafar Hashmi
Maj ® Gen Masood Anwar
Professor Khalid Hassan
Maj Gen Suhaib Ahmed
Maj Gen Muhammad Ayyub

PSH Election Committee
Dr Tahira Zafar
Dr Muhammad Javed Asif
Brig Jalil Anwar
Dr Lubna Naseem
Col Choudary Altaf Hussain
Col Saqib Qayyum
Col Qamar Ul Nisa Choudary

Organizing Committee Haematology Sessions
Brig Parvez Ahmed
Dr Salman Naseem Adil
Brig Saleem Ahmed Khan
Brig Tariq Mehmood Satti
Dr Saba Jamal
Dr Syed Muhammad Irfan
Col Maqbool Alam
Dr Muhammad Nadeem

Secretary of conference: Brig Nadir Ali

PSH Scientific Committee
Brig Farhat Abbas Bhatti
Col (R) Lubna Zafar
Dr Mobina Ahsan Dodhy
Dr Samina Amanat
Brig Saadat Parveen
Dr Nadeem Ikram
Col Nasira Shaheen

Layout and schedule of conference

6.12.2012 900-1200 hours Pre-conference Workshop 1
Workshop: Molecular haematology. Venue: Genetics Resource Centre, House 14 Street 16 Race Course Road Westridge, Rawalpindi".
Maj Gen Suhaib Ahmed, Lt Col Hamid Iqbal, Maj Mehreen Ali Khan

6.12.2012 1500-1800 hours Pre-conference Workshop 2
Workshop: Transfusion Medicine venue: AFIT Rawalpindi
Brig Saleem Ahmed Khan, Brig Farhat Abbas Bhatti
Col Nuzhat Mushahid, Maj Nighat Shahbaz

7.12.2012 900-1200 hours Pre-conference Workshop 3
Workshop: General haematology and case discussions. Venue AFIP dept of haematology
Dr Khalid Hassan, Maj Gen Muhammad Ayyub
Brig Parvez Ahmed, Brig Nadir Ali
7.12.2012 1500 hours till dinner (inclusive)
Venue: convention center Islamabad

1500-1600 hours: PAP executive committee meeting

1730-1830 hours: Inauguration ceremony and Razi Lecture
2000 hours: dinner

8.12.2012 Venue: convention center Islamabad

900-1030 hours : Plenary lecture session common with PAP including Ibne-Sina Lecture haematology) of 30 min during joint session
Topic: Bone Marrow Transplant in Thalassaemia. By Dr. Lawrence Faulkner

1100-1300 hours Haematology update symposium
Chairperson: Professor Muhammad Khurshid AKUH

Co Chair: Dr Nisar Ahmed
Moderator: Dr Atifa Shuaib
Guest of honor: Professor Moinuddin
Speakers: (Complete title of topics will follow)
Dr Fazal e Razik: Thalassaemia prevention
Dr Tahir Sultan Shamsi: Thalassaemia management strategies
Dr Bushra Moiz: G6PD deficiency
Maj Gen Muhammad Ayyub: Haemostasis
Professor Samina Naeem: Acute leukemia
Brig Saleem Ahmed Khan : NAT in Transfusion medicine

1500-1700 hours Free papers
Chairperson: Professor Khalid Zafar Hashmi
Co Chairperson: Professor Luqman Butt
Moderator: Dr Faiza Fahim
Guest of honor: Maj Gen Masood Anwar and Maj Gen Suhaib Ahmed

1730 hours PSH General body meeting and elections

2000 hours: PSH executive committee meeting
2030 hours: Banquet dinner and entertainment/ cultural show joint with PAP

9.12.2012 Venue: Barian Murree Hills (100% Pick and drop facility)

800 hours: Breakfast session at AFIP

Pick facility 900 hours at Islamabad convention center

900-1100 hours traveling time

1100-1500 hours: Plenary session, closing ceremony, and lunch

1500-1700 hours traveling back to Islamabad/Rawalpindi

Controversy of the use of Haemoglobin F augmenting agent (Hydroxyurea) in the Management of beta thalassaemia.

Tahir Shamsi, Saqib Ansari
Department of haematology, NIBD & BMT, Karachi

Beta thalassaemia major is characterized by transfusion dependent anaemia resulting from absent / reduced synthesis of beta globin chains. The mainstay is blood transfusion and iron

chelation therapy. The only curative treatment is bone marrow transplant from an HLA identical donor. Recently, there is a lot of interest in finding a medical treatment which could obviate the need of blood. The observation that Hydroxyurea can cause a rise in HBF in sickle cell disease led many investigators around the globe to exploit its potential in other haemoglobinopthies. The hydroxyure has been shown to produce conflicting responses in beta thalassaemia major and intermedia. Earlier studies from Thailand and Italy showed a minimal clinical benefit of raising HB level 0.5-1.0 gm above the baseline. While reports from India and Iran showed independence from blood transfusion in many patients Skepticism has been shown on the use of Hydroxyurea by many clinicians and many concerns have been raised. Here we would like to elaborate on each concern point by point: Skepticism: 1- Numerous case reports and trials on Hydroxyurea in hemoglobinopathies did not show any benefit; its efficacy was only noted in sickle cell disease. Except in cases of homozygosity or compound heterozygosity of hemoglo0bin Lepore where the necessity of transfusion was eliminated. Clarification: Let us review few recently published series (beside our own Ansari SH et al, J Pediatr Hematol Oncol. 2011 Jul;33(5):339-43). Zamani F et al from Tehran, Iran. (Arch Iran Med. 2009 May;12(3):295-7.) Forty-nine beta-thalassemic patients enrolled in the study. The mean follow-up time was 60 months. The mean dose of hydroxyurea was 10 mg/kg per day (8-15 mg/kg). The mean packed red cell transfusions requirement fell from 22.75 units to 6.02 units after treatment ($P<0.01$). They reported a substantial and persistent increase in hemoglobin level and a significant decrease in blood transfusion. Hydroxyurea treatment was well-tolerated and it did not cause any hematopoietic suppression except in one patient who developed transient thrombocytopenia which resolved after short period of hydroxyurea cessation. The authors did not encounter any malignancies including leukemia in the five-year follow-up. Yavarian M et al reported in Haematologica. 2004 Oct;89(10):1172-8 response of HU in 133 transfusion dependent beta-thalassemia. Transfusion independence with a Hb >10gm/ dl was reported in 61% patients. A moderate response was seen patients in 23% who remained transfusion dependent but at longer intervals (6 months or more). XmnI polymorphism, the T-allele, in linkage to the haplotype I (+----) and to the internal betaglobin gene framework 2, was the most significant modulating factors involved. Another study from India (Italia KY et al Clin Chim Acta. 2009 Sep;407(1-2):10-5) reported 79 patients-[38-beta thalassemia intermedia-(group I), 41-beta thalassemia major-(group II)] on hydroxyurea therapy were followed-up for 20-24months. 58% in group I became transfusion independent and 16% showed a 50% reduction in transfusions after therapy which correlated with a higher mean fold increase in HbF and gamma mRNA expression levels. Forty-one percent of patients in group I had associated alphathalassemia and 72.7% were XmnI (+/+). Thirty-two percent of group II patients showed a 50% reduction in their transfusion requirements after therapy which also correlated with a higher mean fold increase in HbF and gamma mRNA expression levels. There is published data from Italy, Greece and Thailand which do not show such beneficial effect as reported from Pakistan, Iran and India. But mind you, all ethnic groups have different genetic mutations causing beta thalassemia major. This may be the cause of conflicting reports. We have to review all these studies carefully because of differences in population, selection of patients, dose of hyroxyurea, inclusion criteria and definition of responses and outcome measures. Skepticism: 2- The increment of hemoglobin in these trial was marginal ranging from 0.5 to 1.5gm and we all know that 0.5 to 1.0 gm variation in Hb is noted in many conditions including diurnal variation. In most of these trials the main focus was on Hb increment without considering the side effects which include nausea, vomiting and life threatening neutropenia. On the same note, as these patients were deprived of blood transfusions so they must have developed extra medullary hematopoiesis which lead to hepatosplenomegaly and skeletal abnormalities which is missing in the clinical findings of these trials. Clarification: In most trials, the dose of hydroxyurea used was 8-20 mg/kg per day in contrast to its dose used in CML (30-35 mg/kg/day). With smaller dose, although there is a potential to develop neutropenia but grade 4 neutropenia is not reported in any of the trial. One

important observation reported by most studies is the improved qualitym of life / well being reported by the patients. None of the trial reported any signs of extramedullary hematopoiesis (worsening of hepato-splenomegaly or skeletal abnormalities. Our group (Ansari SH et al) consistently published in the J Pediatr Hematol Oncol. 2011 Jul;33(5): 339-43 the size of spleen / liver in 152 patients at baseline and at different timelines suggesting "extramedullary haematopoiesis" does not develop in these subjects. Reason is two-fold; one is effective erythropoiesis due to a reduction in alpha : non-alpha chain imbalance, second is cytoreductive effect of the hydroxyurea. Skepticism: 3- Hydroxyurea carries mutagenic potential although its safety is established in sickle cell disease; what will happen to beta thassaemia major patients after thirty or forty years of exposure to this potentially mutagenic compound? In animal models, Hydroxyurea has the mutagenic potential. But in in long term follow up of over 20 years in sickle cell disease, no increased risk of malignancy has been reported. Nzouakou R et al developed a statistical model to study the clinical and biological benefits and safety of Hydroxyurea over 654 patient-year exposure (Acta Haematol. 2011;125(3): 145-52) in 123 patients during a total follow-up of 654 patient-years and total hydroxyurea exposure of 549 patient-years. Adverse events could arise at any time and were usually reversible. No malignancy was observed. Steinberg MH et al (Am J Hematol. 2010 Jun;85(6):403-8) reported the risks and benefits of 17.5 year follow-up of the use of hydroxyurea in sickle cell. The authors concluded that long-term use of hydroxyurea is safe and might decrease mortality. There was no increased incidence of malignancy during this period. We all know sickle cell disease is a "benign" disorder of haemoglobinopathy group of disorder. By the way use of hydroxyurea is an approved indication in sickle cell disease. Skepticism: 4-In the latest edition of Williams Hematology text book, it is written that Hydroxyurea is not beneficial in beta thalassaemia. How can we justify using it? Clarification: We agree with the comment of the "latest edition of Williams Hematology" that hat the results of HU trials are disappointing (this represent the case series/trials reviewed by the author of the chapter). We already referenced the large series reported from India, Iran and Pakistan which showed a beneficial effect. Certainly the routine use of hydroxyurea can not be justified outside a clinical trial setting. With a clear pattern of response of hydroxyurea in different type of mutations in beta globin gene, published papers have pointed out that its inadvertent use can not be justified. Presence of XMN-1 polymorphism is the classic example of good responder along with few other genetic modifiers like Hb lepore and sickle cell disease, Hb-E/beta thalassemia, Cap+1 and alpha thalassemia co-inheritence. It produces a dismal response in a third of patient especially in patients with homozygous 619 bp deletion, Fr 41-42, Cd 15, CD5. Patients who have IVS1-1, Fr 8-9, XMN-1 and Cap+1 showed a good response (Ansari SH et al, J Pediatr Hematol Oncol. 2011 Jul;33(5):339-4) Research is done to find an answer. A negative result also has a very important message as well. Research and evidence base medicine also mean critical appraisal of the data without any prejudice and subjectivity. We can expect better and safer HB-F augmenting agents in recent future which will pave way to current therapeutic options.

PSH elections

PSH elections for office bearers 2013-2014 will be held tentatively on 1st Dec 2012 during PSH annual conference. All junior members and regular members are suggested to clear dues by 30th Sept 2012. Junior members are required to pay Rs 300/year and regular members Rs 600/year. All regular members are suggested to become life member by paying Rs 6000.00 as life membership fees. The eligibility to participate in elections is as follow:

Election Related Clauses of Constitution

Clause-4:

a. Members (regular/ordinary and life members) of good standing are eligible to vote as well as to contest for an office.
b. Associate members of good standing are eligible to vote but not to contest for an office.
c. Junior members of good standing are eligible to vote but not to contest for an office.
d. Senior members, Honorary members and Corporate members are neither eligible to vote nor to contest for an office.

Clause-5:

President: No member will hold the office of the president for more than two terms.

President Elect: A person who has attained the age of 60 years will not be eligible to contest the office of the President Elect. A person elected as president elect will not be eligible for re-election to the same office for a minimum period of six years.

Secretary/Treasurer: A member can be re-elected as Secretary/treasurer for another, even consecutive term but will not be eligible for election to this office thereafter.

Elected members of the Executive Committee: A member can be elected as the member of the Executive Committee for any number of terms but will not be allowed to contest for more than two consecutive terms.

Clause-10:

All members (4-a) of at least three years standing who have cleared their dues in time before the date of election will be eligible for election to all offices.

About PSH and PSH conference

Pakistan society of Haematology (PSH) was officially registered in August 1998, and first haematology annual conference was also held same year at Hotel PC Rawalpindi, arranged by Rawalpindi Chapter. It was decided that annual conference will be held regularly, and will be hosted by all chapters turn by turn. Today we are preparing to host 15th PSH conference arranged by Rawalpindi chapter. Those who witnessed the 1st conference know how great and encouraging the event was. From first conference to date the enthusiasm, unity, friendship, and co-operation among the haematologist has grown tremendously. I am sure many of us are not aware how it was achieved. I assume it was not possible without tolerance, sacrifice and devotion of our founders. Following are few milestones through our organization passed:

1. 1991, 22nd November: First meeting of proposed PSH was held at Hotel PC, Lahore

attended by Dr Muhammad Khurshid , Brig (now Lt Gen Retd) Muhammad Saleem, Dr Khalid Zafar Hashmi, Dr Naseem Siddiqui, and Dr Abdul Hayee. Meeting was held in presence of Dr A V Hoffbrand of Royel Free Hospital, UK

2. Initially society was named as Pakistan Society of Haematology/Blood Transfusion later on Pakistan Society of Haematology/oncology/Blood Transfusion and finally Pakistan Society of Haematolgy (PSH)

3. 1996: general body meeting at Peshawar: Elections
   a. President: Lt Gen Muhammad Saleem
   b. VP: Professor Muhammad Khurshid
   c. Secretary: Dr Khalid Hassan
   d. Coordinator: Col(now Maj Gen retd) Masood Anwar

4. 1998 April: Affiliation of PSH with International Society of haematology

5. 1998 Aug: PSH registration with Govt of Pakistan

6. 1998 October: 1st PSH conference

7. Presently the society comprises of 217 members, held 14 annual conferences and > 70 workshops/technical sessions

Pakistan Society of Hematology (PSH) is a non-political, non – sectarian Govt registered organization consisting of hematologists of Pakistan. PSH promotes the advancement of hematology including transfusion medicine, through encouragement of research, improvement of teaching & technical methods, organization of scientific meetings, publication of scientific material, and is affiliated with other National & International organizations. PSH also provides forum for the persons practicing hematology and transfusion medicine to discuss problems and to formulate agreed viewpoints at National and International forum. Membership (1). Members: MBBS or equivalent plus post graduate qualification in hematology/transfusion medicine and show evidence of active work in hematology during the last three years including the period spent in training for post graduate examination in hematology/transfusion medicine. (2). Associate members: Those who possess the prescribed for a member but not completed three years of active work in hematology (3). Junior members: Registered students of postgraduate training in hematology/transfusion medicine for at least one year. (4). Corporate members: Those with MBBS qualification and have keen interest in hematology, and become members on payment of Rs 5000 per annum. They will not be eligible for vote or contest of any office.

Dear friends

We request you to join us in newsletter 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 newsletter. It is requested that report/write up should be brief and concise. For information, suggestions, and correspondences please e-mail to: dr.nadir.ali@gmail.com

In case you are a member and you are not receiving mails from us please update your postal and e address urgently

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Your views and news

Dear Colleagues: Your contributions to PSH newsletter are backbone to its success. Please send short communications, case reports, scientific activities and developments in your departments and issues of common interest. Photographs of scientific events/meetings are also welcome. Members are requested to visit PSH website and post in their contributions.

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