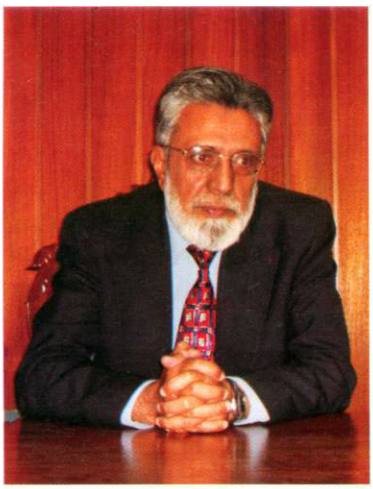
Vol. 2 No 1 April- June 2007

Newsletter

Pakistan Society of Haematology

PRESIDENT's COLUMN



My dear colleagues:
First of all I must thank you for the trust which you expressed in electing me unanimously President of your society. I pray to Allah The Almighty to give me courage and strength to honour this obligation. I am also lucky for having Professor Khalid Hassan as President Elect with me. I as convener and he as first Secretary of the Society were entrusted with the long overdue task of establishing Pakistan Society of Haematology. With his untiring efforts this task was completed successfully and today, Masha-Allah we have a well established organization that is being acknowledged at all forums. Our new Secretary, Brig Parvez Ahmed has always been instrumental in furthering the cause of Haematologists in Pakistan and objectives of the Society. He is a long standing associate of mine. I am confident that this team, together with your cooperation, will achieve all the set targets.

Our first and the most important target is to net all present and future haematologists in the Society. Let us all strive for that. Our web site www.psh.org.pk will be soon updated and activated. You will find the membership form on the web site that can be down loaded. Start an intensive campaign of membership of all categories so that we reach our target within six months.

Our second target is establishment of local chapters at as many places as possible. The criteria for establishing a local chapter is given in the Constitution of the Society which is also available on the web site. These chapters should meet once in a month over scientific agenda. This will help in bringing us together and in improving our professional knowledge and skills.

Our third target is an extensive continuing education programme. I suggest that all local chapters must organize one major event (a seminar or a workshop) of one to two days duration. We are planning to start a programme of monthly workshops, primarily for our Pathologist and Clinical Colleagues. These workshops are to be conducted in smaller places and preferably should be of half day or so to ensure maximum participation. I request you to volunteer for conducting such workshops. Those of you who volunteer are requested to send me their names with brief CV, subject of their liking and area in which they can be easily available.

My dear friends the strength of every organization lies in its unity. Let us remain united in furthering the objectives of our Society. Whatever activity, pertaining to haematology we organize must display the emblem of PSH along with the Institution to which we belong. If we have any differences we should discuss and resolve at our own forum. Let all know that at least there is one community in Medical Profession that is always seen united. This will give your Society strength and negotiating power for promoting its noble objectives. One may gain a little fame by solo flying but you all know that it is the solo flyer who is more prone to fatal accidents.

I think I have said enough for the first column and should leave some thing for the future as well. I request you all to strengthen our hands and also pray for us to meet our obligations to you with honour.

Maj. Gen. (Retd) Masood Anwar

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NEW EXECUTIVE COMMITTEE

New executive committee was elected during 9th Annual Conference Pakistan Society of Haematology held at Lahore from 9-11th March 2007. Following are the office bearers of executive committee:

PRESIDENT	PRESIDENT ELECT	SECRETARY/TREASURER
Maj. Gen. (Retd) Masood Anwar	Professor Khalid Hassan	Brig. Parvez Ahmed

MEMBERS

ARMED FORCES	PUNJAB	SIND	NWFP	FEDERAL AREAS
Brig. Muhammad Ayyub Brig. Khalil Ullah	Dr. Nisar Ahmed Dr. Samina Naeem Dr. Atifa Shuaib	Dr. Tahir Shamsi Dr. Salman Adil	Dr. Fazal-e-Razik	Dr. M. Tahir Khan

ABOUT PSH

Pakistan Society of Haematology was formed in 1996 with the aim of promoting advancement of haematology and transfusion medicine in the country. Presently it has more than 150 members and we all should make efforts to enroll every haematologist in the country. We request all our members to take special interest in extending the membership to all those haematologist around you who have not yet become members. PSH website was launched long ago but became non-functional due to certain reasons. We are trying to rejuvenate the website. This would be interactive website http://www.psh.org.pk .The website would be interactive and provide on line forum for sharing views with other Haematologist and case discussion with the experts. Other features will be facility to download online membership form, news letter, list and addresses of the members. Hopefully the website will be operational within this month Inshallah.

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HIGHLIGHTS OF CONFERENCES, MEETINGS AND SYMPOSIA

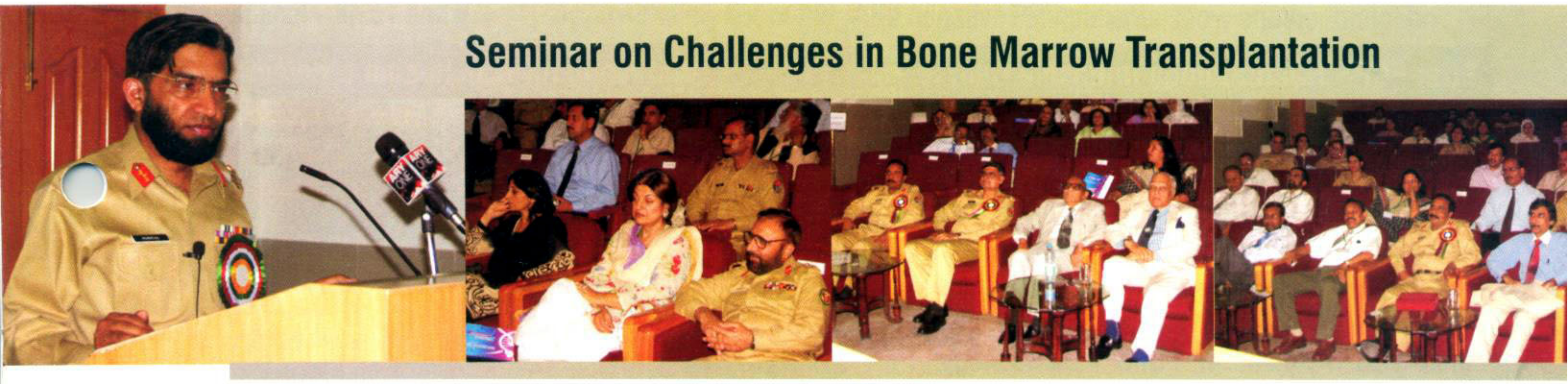
The 9th National Conference Pakistan Society of Haematology

The 9th National conference of Pakistan Society of Haematology was held on 9-11 March 2007 at Shaikh Zayed Medical Complex, Lahore . Prof Shahida A R Shah was the chief organizer and she was assisted by Dr Muhammad Javed Asif and Dr Mona Aziz. Lt Gen (Retd) Muhammad Saleem was the Patron and played crucial role in organizing the confrerence. Prof Anwaar A Khan Chairman Shaikh Zayed Medical Complex, Lahore had a pivotal role in the arrangements and logistics. Their guidance was vital and unabated, throughout. The conference was a huge success with 292 registered participants. The inaugural session was graced by Federal Health Minister Muhammad Naseer Khan and was attended by many dignitaries, senior professors and eminent haematologists from all over the country and abroad There were three symposia; "Judicious use of blood and blood products", "Haematological challenges in Liver disease" and "Updates in diagnosis and management of ALL". They were all well attended. The banquet and musical show was arranged at Aiwan-e-iqbal. The chief guest was the cabinet secretary Mr Kamran Rasool and it attracted a huge gathering. The delegates were shown the important places in Lahore including shopping at Liberty Market and dinner at Food Street. A sumptuous lunch and picnic at a farmhouse in the suburbs of Lahore was one of the salient features of this conference.

Organizing committee of 9th PSH Conferecne

Prof Shahida A R Shah giving welcome address in Inauguration ceremony at 9th PSH conference Lahore

Seminar on Challenges in Bone Marrow Transplantation



Lt Gen Mushtaq Ahmed Baig, Surgeon General giving the inaugural address at Seminar on Stem Cell Transplantation held at AFBMTC on 14 Apr. 2007 & a view of audience at Seminar on Stem Cell Transplantation

A one day seminar on challenges in Bone Marrow Transplantation was held on 14 April 2007 at Armed Forces Bone Marrow Transplant Centre Rawalpindi. The seminar was inaugurated by Lt Gen Mushtaq Ahmed Baig Surgeon General Pakistan Army. It was widely participated. Experts in stem cell transplantation and other fields delivered state of the art lectures. Main focus of the seminar was peculiar problems in stem cell transplantation recipients in Pakistan. State of the art lecture on stem cell transplantation was delivered by Dr Salman Naseem Adil. Other speakers included Dr Tahir Shamsi, Dr Muhammad Irfan, Dr Muhammad Usman Sheikh, Dr Tasneem Farzana, Brig Suhaib Ahmed, Brig Muhammad Ayyub, Brig Tahir Aziz, Brig Khalil Ullah, Brig Parvez Ahmed, Col Tariq Mehmood Satti, Lt Col Nadir Ali, Lt Col Shahid Raza , Lt Col Chauhdry Altaf Hussain, Lt Col Amir Ejaz, and Lt Col Qamar-un-Nisa Chaudhry.

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PSH Rawalpindi-Islamabad Chapter Meeting

PSH Rawalpindi-Islamabad Chapter meeting was held on 25 May 2007 at Department of Haematology Armed Forces Institute of Pathology Rawalpindi. 34 Haematologist/residents attended the meeting. The programme included scientific presentation by Brig Suhaib Ahmed and business agenda. It was unanimously decided that 10th PSH conference should be held at Pakistan Institute of Medical Sciences Islamabad during February 2008. The meeting was followed by dinner. The scientific presentation on *JAK2* mutation was greatly applauded and has been included in this news letter.

Brig Suhaib Ahmed giving scientific presentation to the Participant at PSH Rawalpindi-Islamabad Chapter meeting on 25 May 2007

Forthcoming Events

First FCPS Haematology Intensive Course

Department of Paediatric Haematology and Transfusion medicine, Children's Hospital and the Institute of Child Health Lahore has organized 6 days intensive course in Haematology from 25 June 2007 to 30 June 2007. The course will be especially useful for final year resident in FCPS Haematology. Eminent Haematologist and experts in various fields will conduct the course thus enabling the participants to have an extensive review of the subject. The programme will consist of lectures followed by practicals and case discussion with experts. For registration and further details please contact Dr Nisar Ahmed the chief organizer of the course at Children's Hospital Lahore.

Workshop on Transfusion Medicine

Armed Forces Institute of Transfusion in collaboration with PSH has organized a two days workshop on transfusion medicine from 8-9 August 2007. The workshop programme will be extensive and cover all the important aspects of transfusion medicine including crossmatch, antibody detection, blood component preparation and difficult clinical problem solving. For further details please contact Brig Muhammad Ayyub Commandant AFIT at telephone number 051-56134188.

10TH Annual Conference Pakistan Society of Haematology

10th Annual Conference of Pakistan Society of Haematology will be held form 16-18 February 2008 at Pakistan Institute of Medical Sciences Islamabad (PIMS). Further details and schedule of the conference will be announced by organizers in due course of time. For further details please contact Professor Khalid Hassan at mobile number 0333-5178210.

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JAK2 mutation in Myeloproliferative Disorders (MPD)

Brig Suhaib Ahmed
MBBS; MCPS; FCPS; PhD (London), Head Department of Haematology, Armed Forces Institute of Pathology, Rawalpindi

Myeloproliferative Disorders (MPD) are clonal disorders of haematopoiesis that lead to an increase in the number of one or more mature blood cell progeny. Polycythemia vera rubra (PRV) is characterized by an increased hematocrit, a hypercellular marrow with increased numbers of erythroid, megakaryocytic, and granulocytic precursor cells; and a variable increase in the number of reticulin fibers. Essential thrombocythemia (ET) is characterized by an increase in the number of platelets in the peripheral blood and an increased number of megakaryocytes in the marrow, which tend to cluster together and have hyperlobated nuclei. Idiopathic myelofibrosis (IMF) is characterized by the presence of leukoerythroblastic blood film "teardrop" red cells, disordered cellular architecture in marrow, dysplastic megakaryocytes, formation of collagen fibers and new bone formation in the marrow [1].

Between March and April 2005 four independent groups reported a G-T point mutation (V617F) in exon 14 of JAK2 gene on chromosome 9 in a large number of PRV patients [2]. The normal (wild type) JAK2 protein is bound to the erythropoietin receptor on erythroid cells as an inactive dimmer. On activation of the receptor by erythropoietin the JAK2 protein is phosphorylated and acts like a tyrosine kinase that is involved in signal transduction (STAT-signaling) pathway. The mutant JAK2 protein has the same action in the cell except that it remains active even in the absence of erythropoietin. The normal as well as the mutant JAK2 proteins are also bound to the cell surface receptors for thrombopoietin and G-CSF on cells of megakaryocytic and myeloid lineage. The mutant JAK2 protein, therefore, has a much wider phenotypic expression involving multiple cell lineages [3].

Several studies have reported the exon 14 JAK2 mutation (V617F) in 95% of patients with PRV and 50-60% each of the patients with ET and IMF [1]. Approximately 5% of the JAK2 negative PRV patients show another mutation in the exon 12 of the JAK2 gene [4]. The JAK2 mutation has also been reported in the lymphoid lineages of some patients of PRV [5] and a very small proportion of apparently healthy elderly individuals [6].

Until recently, robust tools for the diagnosis of the MPD have been lacking. Criteria for the diagnosis of PRV are mostly modifications of 20-year-old standards from the Polycythemia Vera Study Group. The available tests are expensive, not universally available, and lack in sensitivity and specificity. Testing for the JAK2 V617F mutation is now widely available and promises to simplify the diagnostic workup. Allele-specific polymerase-chain-reaction (PCR) assay, pyrosequencing, restriction-enzyme digestion, and real-time PCR are all sufficiently sensitive to detect the presence of a heterozygous mutation in as few as 5 to 10% of cells. These assays have low rates of false positive results, making them useful diagnostic tools [1].

Proposed diagnostic criteria for V617F-positive myeloproliferative disorders is outlined in Table-1. The presence of the JAK2 mutation in a patient with polycythaemia (PCV >0.52 L/L in men and >0.48 L/L in females) is sufficient for the diagnosis of PRV. In patients with the JAK2 mutation, analysis of the red-cell mass and erythropoietin levels are likely to become obsolete. Similarly cytogenetics in patients with the JAK2 mutation generally does not add useful diagnostic or prognostic information [1].

Table-1 [1]

JAK2-positive Polycythemia (diagnosis requires the presence of both criteria)

A1. High hematocrit (>0.52 L/L in men or >0.48 L/L in women) or an increased red-cell mass (> 25 %

above predicted value).
A2. Mutation in JAK2

JAK2-positive Thrombocythemia (diagnosis requires the presence of all three criteria)

AI. Platelet count > $450x10^9$/liter
A2. Mutation in *JAK2*
A3. No other myeloid cancer especially *JAK2*-positive polycythemia, myelofibrosis, or myelodysplasia

JAK2-positive Myelofibrosis (Diagnosis requires the presence of A1, A2 and any of the two B criteria)

A1. Reticulin grade 3 or higher (on or 0-4 scale)
A2. Mutation in *JAK2*
B1. Palpable splenomegaly
B2. Otherwise unexplained anemia (hemoglobin <11.5g/dL for men; <10.0g/dL for women)
B3. Teardrop red cells on peripheral blood film
B4. Leukoerythroblastic blood film (presence of at least 2 nucleated red cells or immature myeloid cells in peripheral blood film)
B5. Systemic symptoms (drenching night sweats, weight loss >10% over 6 months, or diffuse bone pain)
B6. Histologic evidence of extramedullary hematopoiesis

Clinical applications:

JAK2 mutation testing may be helpful in the following clinical settings [7]:

- Abdominal vein thrombosis
- Aquagenic pruritis
- Unexplained splenomegaly
- Thrombocytosis
- Granulocytosis
- Leuko-erythroblastosis
- Myelofibrosis
- Extramedullary haematopoiesis

The Pakistani perspective [S. Ahmed unpublished observations]

Recently *JAK2* mutation was studied at AFIP in 37 Pakistani patients of MPDs diagnosed between 2004-2007 by conventional methods. Archival bone marrow slides were used for DNA analysis. The results (Table-2) showed an overall positivity in 26 (70%) patients. Eight out of the nine (89%) patients of PRV had the mutation. The only negative patient was a high altitude dweller with Hb 24 g/dL and no palpable splenomegaly. JAK2 positivity was seen in 7/10 (70%) ET, and 9/12 (75%) patients of IMF.

Test facility for JAK2 testing at AFIP

Test for JAK2 mutation is now routinely available at AFIP. Please refer the patients with all clinical and haematological findings and 2 ml blood in EDTA. The cost of testing for non-entitled patients is Rs. 2000 and the average reporting time is three days.

Table-2 *JAK2* positivity in 37 Pakistani patients of various MPDs.

Disorder	*JAK2* mutation
PRV	8/9 (89%)
ET	7/10 (70%)
IMF	9/12 (75%)
Mixed MPD	2/4
MPD/MDS	0/2
Total	26/37 (70%)

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A TRIBUTE TO OUR PREDECESSORS

It is said that history is made up of significant events, which shape our future and outstanding leaders who influence our destiny. We must pay tribute to our seniors whose vision and efforts lead to the formation of Pakistan Society of Haematology in March 1996. Their contributions towards haematology in general and PSH in particular place them in inimitable position. PSH will remain a living tribute to their vision. We acknowledge the efforts put in by preceding executive committee specially past President Dr Khalid Zafar Hashmi and Secretary Lt Col Nadir Ali. In their short tenure they were able to significantly increase PSH membership and most importantly were instrumental in giving a new outlook and regularity to PSH Newsletter. Indeed by regularly issuing the newsletter they have given us the daunting task of keeping up the standards.

YOUR VIEWS AND NEWS

Dear Colleagues

Your contributions to PSH newsletter are backbone to its success. In fact our ultimate aim should be to publish "Pakistan Journal of Haematology" at least on quarterly basis. Please send short communications, case reports, scientific activities and developments in your departments and issues of common interest. Easiest way to send these contributions is by email. In case a hard copy is sent please also enclose one electronic copy on CD. Photographs of scientific events/meetings are also welcome.

UPDATING ADDRESS

We strive hard to communicate to all our members. Please update your addresses in case there is any change in your address. All members are requested to email us their mobile/phone contact and email address.

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