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# President's Column


Prof. Dr. Samina Naeem

Dear Colleagues Assalam o Alaikum !

It is amazing how quickly time goes by! It seems like yesterday that I was writing my first President's column and now I am winding down my association with this forum as a president. Let me begin by saying how privileged I feel to have had the opportunity to serve as the president of this outstanding society and to follow in the footsteps of so many great chairs who have served before me.

My primary goal as the president of PSH was to provide a forum for networking and collegial support, to create educational opportunities in order to promote the highest standards of hematological practices and facilitate the careers of young interns. I have endeavored to maintain an administrative structure and philosophy that is responsive to the changing needs of its members; in this regard my last effort as the president was get PSH accreditation for CME by PM&DC. My job would have been much more arduous if it were not for the support, advice, and work of PSH members and office bearers. I would specially like to mention Dr Humera Rafiq who provided me with the most able assistance and her contribution in numerous spheres has been substantive for the progress of the society.

The infelicitous attack on the school in Peshawar left our hearts bleeding. No words can express the ignominy of such a heinous act. But it could not waver our resolve and determination. Despite bereaved hearts we move forward with even more adamant desire for the amelioration of our beloved homeland. By the time this issue reaches you the scenic city of Rawalpindi situated in the backdrop of magnificent Margala hills would have hosted the mega event of the 17th annual conference of PSH. I am confident that the untiring efforts put into this event will make it a colossal success.

A very challenging and illuminating experience of mine as president PSH is coming to an end, one that I will treasure for the rest of my life. In closing, let me echo an anonymous wordsmith in saying that "the finish line is just the beginning of a whole new race". It is most reassuring that an eminent colleague, General Ayyub, is taking over the responsibility. He has held positions of high responsibility and has an impressive academic background of which we are proud. I am sure that he is going to carry high the banner of PSH. I close my letter with these words for my aspiring hematologists: 'the best way to predict future is to create it.' I wish you all great success in your future deliberations.

With warm regards,

**Prof.Dr.Samina Naeem**

# ACADEMICS

## Lab Diagnosis of Thalassaemia

**Maj Gen (R) Suhaib Ahmed, HI (M) ,MBBS, FCPS (Pak), PhD (London)**

Hypochromia and microcytosis are the hallmark of thalassaemia. Once iron deficiency is excluded thalassaemia is the next most common cause of hypochromia and microcytosisin Pakistan. Since thalassaemia is an inherited disorder it uniformly affects all red cells whereas in iron deficiency the red cells of varying ages are affected differently. Another important distinguishing feature of thalassaemia is basophilic stippling that lacks in iron deficiency.

### Typical β-thalassaemia trait

Most people with typical βo-thalassaemia trait have haemoglobin in the low normal range, raised TRBC, low MCV (usually < 75 fl) and low MCH (usually < 25 pg) (Table 1). RDW is lower in thalassaemia (usually < 41fl) than in iron deficiency (usually > 41fl). Diagnosis of β-thalassaemia trait is confirmed by Hb-A2 level that typically ranges between 3.5-7.0%. Hb-A2 levels between 3.0 and 3.4.0% are considered borderline and may be seen in normal people or β-thalassaemiacarriers with coexisting iron deficiency or α-thalassaemia trait.

### Atypical β-thalassaemia trait

People who have β-thalassaemia mutation but whose phenotype is masked by a variety of mechanisms are categorized as atypical β-thalassaemia carriers. Their identification is often difficult. It is important to identify them because their marriage to an individual with β-thalassaemia trait can produce a child with thalassaemia major.

### β+-thalassaemia

Mild β+-thalassaemia trait is relatively uncommon in Pakistan. Most people are due to Cap+1 (A-C) mutation that is seen in about 2.5% of β-thalassaemiacarriers. They have almost normal haematological parameters including Hb-A2 level (Table 1).Most Cap+1 carriers have MCH in the lower normal range (around 26pg). Because of the silent nature the carrier status of Cap+1 carriersis usually discovered when they give birth to a child with thalassaemia major. The confirmation of Cap+1 mutation is possible only by PCR.

### Co-existing iron deficiency

Since iron deficiency is very common in Pakistan it is also common to see it co-exist with β-thalassaemia trait. Such individuals are more anaemic and have low serum ferritin but their Hb-A2 levels are usually high. Approximately 10% of people with β-thalassaemia trait and co-existing iron deficiency have normal Hb-A2 levels. In such patients Hb-electrophoresis may be repeated after correction of iron deficiency or PCR may be done to resolve the ambiguity.

### Co-existing α-thalassaemiaand β-thalassaemia trait

Co-inheritance of α-thalassaemiaand β-thalassaemiatrait is not uncommon in Pakistan. It results in masking of the haematological features of typical thalassaemia trait. One gene deletion α-thalassaemia(-α/αα) does not affect the features of typical β-thalassaemia. People with co-existing β-thalassaemiatrait and two gene deletion α-thalassaemia (-α/-α or --/αα) tend to have "normalized" red cell indices (usually around the lower normal range). However, their Hb-A2 level isusually >4.0%. In doubtful cases PCR may be required to show the co-existence of β- and α-thalassaemia mutations.

**Hb-D/βo-thalassaemia**

It is not uncommon to see individuals having co-inheritance of βo-thalassaemiaandHb-D trait. They have hypochromic microcytic red cell indices. Hb electrophoresis shows raised Hb-A2and single band in the region of Hb-D. They do not have Hb-A because of the presence of Hb-D mutation on one chromosome and βo-thalassaemiamutation on the other. Since no Hb-A is formed they show only Hb-D and Hb-A2. The diagnosis may be confirmed by parent's study (one having β-thalassaemia trait and the other Hb-D trait) or by PCR. It is important to distinguishHb-D/βo-thalassaemia from homozygous Hb-D because the former when married to a βo-thalassaemia carrier can result in the birth of a child with thalassaemia major.

**Table 1.Comparison of haematological parameters in β-thalassaemia trait and normal individuals from Pakistan (Ahmed 1998).P in 126 samples including 1 sample that was negative for MP on light microscopy (Table-2, Figure-6).**

| Parameter | Normal | $\beta^{o}$-thalassaemia trait | $\beta^{+}$-thalassaemia trait |
|---|---|---|---|
| **Hb**<br>Male<br>Female<br>Female (Pregnant) | <br>13.6 ± 1.7<br>11.6 ± 1.7<br>11.3 ± 1.5 | <br>12.6 ± 1.2<br>10.5 ± 1.1<br>9.6 ± 1.5 | 12.1 ± 1.8 |
| **TRBC**<br>Male<br>Female<br>Female (Pregnant) | <br>5.34 ± 0.80<br>4.81 ± 0.66<br>4.05 ± 0.41 | <br>6.23 ± 0.62<br>5.39 ± 0.62<br>4.81 ± 0.70 | 4.46 ± 0.69 |
| **MCV** | 4.7 ± 7.8 | 63.0 ± 5.6 | 82.4 ± 3.8 |
| **MCH** | 28.1 ± 3.3 | 19.9 ± 1.68 | 26.0 ± 1.92 |
| **Hb-$A_2$** | 2.5-3.5% | 4.0-7.0% | 2.8-3.2% |

**β-thalassaemia major**

The blood picture of typical β-thalassaemia major shows moderate to severe hypochromic, microcytic anaemia, marked aniso-poikilocytosis, and numerous nucleated red cells (Fig. 1). The white cell count is usually raised due to the presence of numerous nucleated red cells that are counted as white cells by the electronic counters. The actual white cell count may be obtained by correcting for the number of nucleated red cells seen on the blood smear.

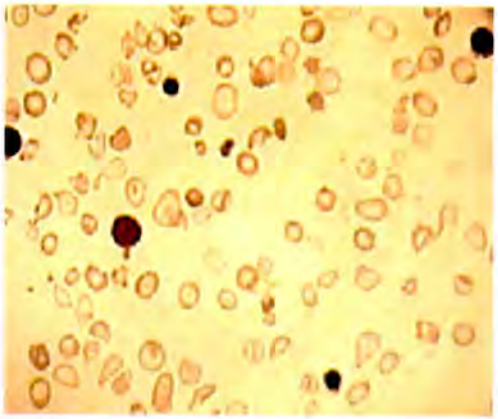


**Fig.1.Peripheral blood film in patient of -thalassaemia major**

The diagnosis of β-thalassaemia major is confirmed by finding markedly raised fetal haemoglobin (Hb-F) that ranges from 30% to over 95% (Table 2). In an un-transfused

patient the presence of Hb-A indicates β+-thalassaemia whereas its absence indicates βo-thalassaemia.

**Diagnosis of β-thalassaemia major in previously transfused patients**

Recent blood transfusion(s) can create considerable confusion in the diagnosis -thalassaemia major. The typical picture is modified. Depending on the amount and the frequency of blood transfusions the red cell morphology becomes dimorphic (Fig 2) while all of the red cell parameters are also normalized. The Hb-F is reduced due to an immediate effect of haemodilution and a late acting suppression of endogenous erythropoiesis. The Hb-F may fall to <1% in patients who are on chronic blood transfusions. Table 2 gives a comparison of the haematological parameters in patients of β-thalassaemia major with and without blood transfusions.

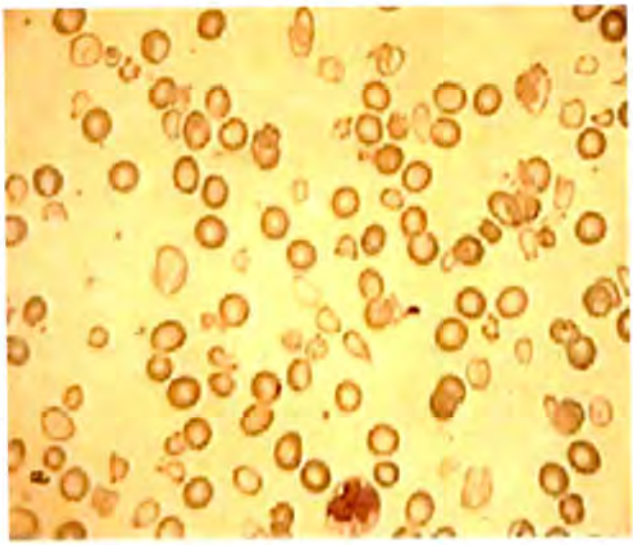


**Fig. 2.Peripheral blood film in patient of β-thalassaemia major who has received recent blood transfusions. A mixture of hypochrmic microcytic red cells and the recently transfused normochromic normocytic red cells is seen.**

It is common practice to withhold blood transfusions in the multiply transfused patients of β-thalassaemia major in the hope that the haematological picture would become clearer. This may be useful in patients who have received only few blood transfusions. But it is of no use in patients who have received multiple blood transfusions because erythropoiesis in such patients usually remains suppressed for a long period. The diagnosis in the multiply transfused patients can be established by demonstrating -thalassaemia trait in the parents or by PCR for the -thalassaemia mutations.

**Table 2.Comparison of the haematological parameters in patients of -thalassaemia major with and without blood transfusions (Ahmed et al, 2003).**

| Haematological Parameters | Untransfused (n=171) | | Transfused (n=109) | | *p* value |
|---|---|---|---|---|---|
| | Mean | Range | Mean | Range | |
| Hb (g/dl) | 6.3 | 1.9-9.0 | 6.2 | 2.3-11.2 | 0.20 |
| MCV (fl) | 70 | 57-83 | 74 | 58-98 | 0.014 |
| MCH (pg) | 21 | 15-29 | 24 | 16-31 | 0.015 |
| Hb-F (%) | 95 | 30-97 | 31 | 0.5-97 | <0.001 |

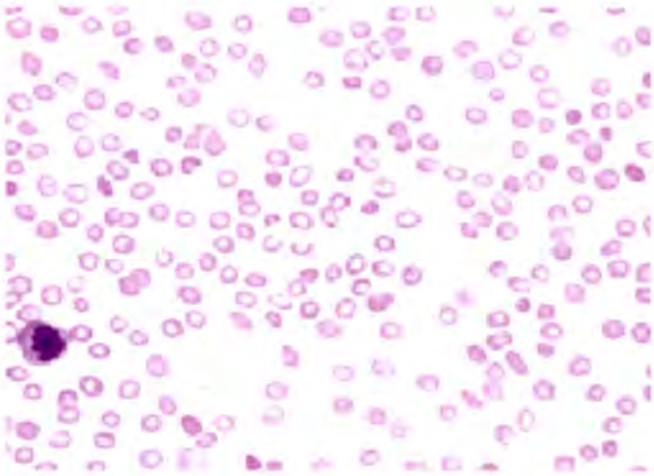
**References:**

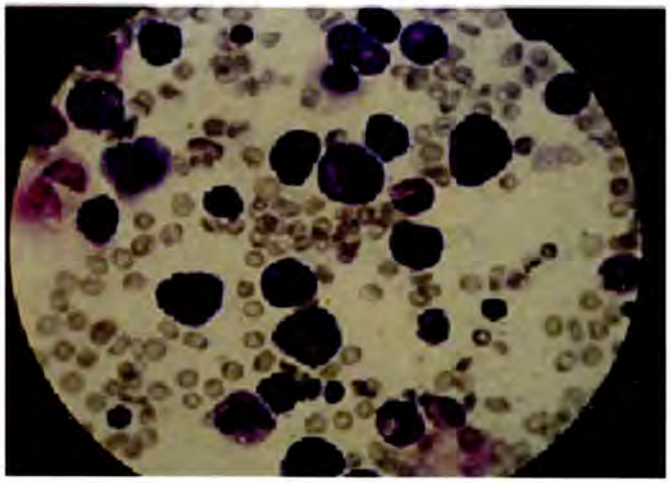
1. Suhaib Ahmed (1998) Approach for prevention of thalassaemia in Pakistan. PhD Thesis, University of London.
2. Suhaib Ahmed; Zahurur Rehman; Karamat A. Karamat (2003) Diagnosis of -thalassaemia major in previously transfused patients. JCPSP 13: 19-20.

# A CASE OF CONGENITAL AMEGAKARYOCYTIC THROMBOCYTOPENIA

Dr Rafeeda Maab, Dr Romaisa Naeem, Dr Sara Ikram, Dr Huma Sheikh.

A 9-month-old infant was referred to Hematology section KEMU, with provisional diagnosis of immune thrombocytopenic purpura, because of recurrent petechia and ecchymoses on his body since 1 month of age and persistently low paletelet count. There was a delay in achieving milestones. The antenatal and postnatal history was nugatory. No history of sepsis, infection or DIC at birth and no consanguinity between parents was recorded. Physical examination revealed widespread petechiae ,ecchymoses and another noteworthy finding was limb and truncalhypotonia. His complete blood count revealed mild hypochromic microcytic anemia, Hbwas 10.6 g/dl, WBC count 4.3 × 109 /l, and reduced platelet count of 21 × 109 /l.The size of platelet was normal and no platelet clumping was observed on smear examination. No mature or immature megakaryocytes could be seen in bone marrow aspiration smears, but myeloid and erythroid cells and bone marrow cellularity were normal.





The blood count results of the parents and two siblings were normal. A complete skeletal survey was done which showed no abnormalities.The diagnosis of **CONGENITAL AMEGAKARYOCYTIC THROMBOCYTOPENIA (CAMT)** was reached based on presentation of patient in early life, clinical signs, on the evidence by blood tests of thrombocytopenia with a normal mean platelet volume, normal skeletal survey and on the observation in a bone marrow aspirate of absent megakaryocytes. A CT scan was done due to presence of neurological signs.It exhibited cerebellar hypoplasia which has an association with CAMT .Fanconi anemia, thrombocytopenia-absent radius syndrome and Wiscott-Aldrich syndrome are the differentials which were ruled out.

Congenital amegakaryocytic thrombocytopenia (CAMT) is a rare autosomal recessive bone marrow failure syndrome characterized by an isolated and severe decrease in the number of platelets and megakaryocytes during the first years of life that develops into bone marrow failure with pancytopenia later in childhood. . The cause for this disorder appears to be a mutation in the gene for the thrombopoeitin (TPO) receptor, c-Mpl, despite high levels of serumTPO.

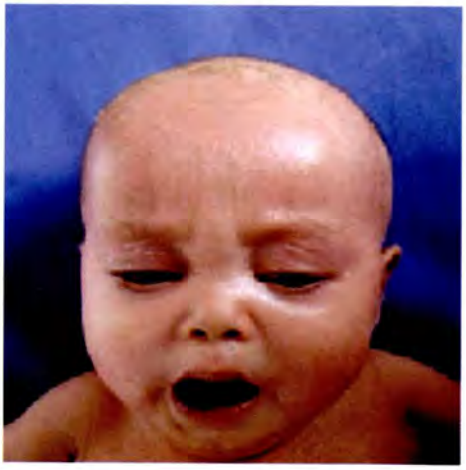
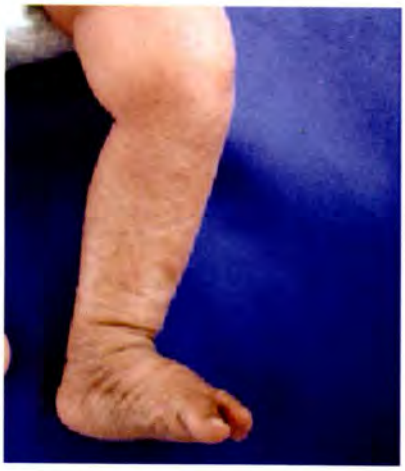
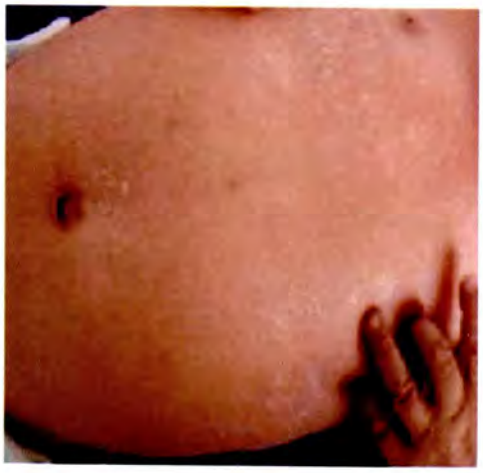
The exact prevalence is unknown and less than 100 cases have been reported in the literature. In addition, the incidence may be underestimated due to difficult and inconsistent diagnosis of the disease.The management is supportive, mainly consisting of multiple platelet transfusions. At present, hematopoietic stem cell transplantation (HSCT) is the only curative therapy.

Prognosis of CAMT is poor and with supportive therapy, progression to full marrow failure occurs during the first years of life. 30% of patients with CAMT die due to bleeding complications before the HSCT and 20% due to the HSCT.

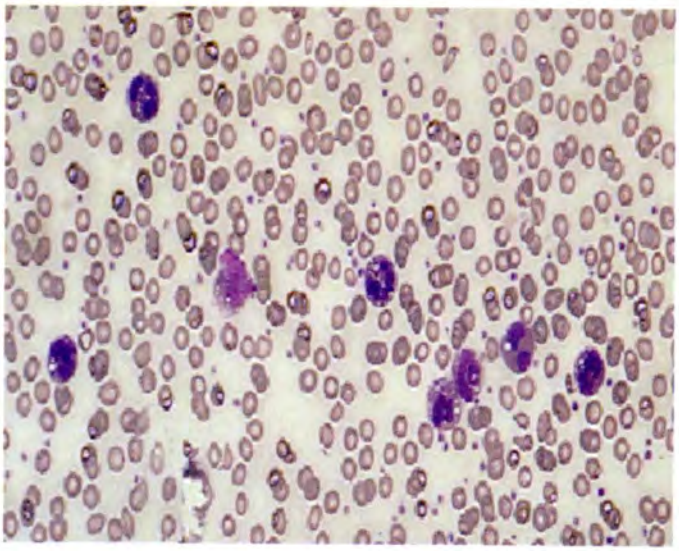
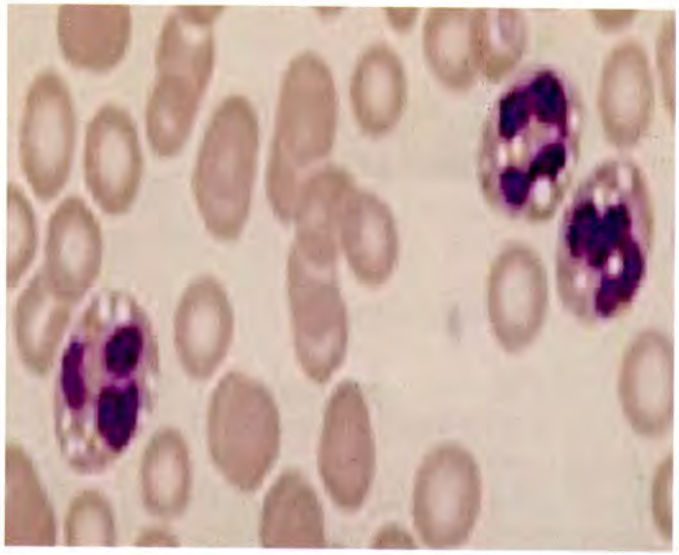
# A CASE OF DORFMAN CHANARIN SYNDROME

Dr Umera Saleem, Dr Hajrah Syndeed, Dr Sidra Aslam,
Dr Ammarah Sharif, Dr Arsala Rashid

A 14 months old child presented with complaints of generalized redness and scaling of skin affecting face, trunk and limbs since 2nd week of life, abdominal distension and watery diarrhea since 4 months. No associated fever, sore throat, neck stiffness or involuntary movements. The child was born prematurely and his developmental milestones were delayed. The skin was normal at birth. No H/O drug intake by the mother and no medications in the past except for ORS and I/V fluids for diarrhea. Parents were first cousins. On GPE, dysmorphic features such as depressed nasal bridge, increased intercanthal distance, upturned nostrils and long philtrum were seen. Generalized erythema and redness were seen. No bullous lesions were present. Ectropion and mild yellow tinge in sclera was evident.
On systemic examination, Liver was palpable 3 fingers below the right costal margin. Rest of the examination was unremarkable.

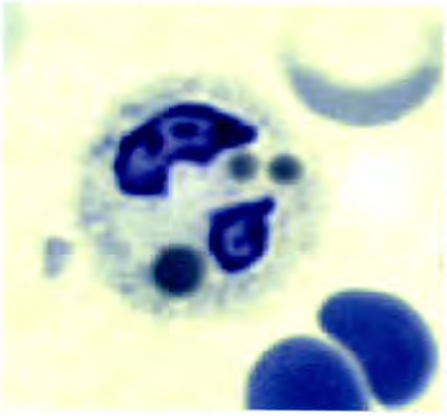
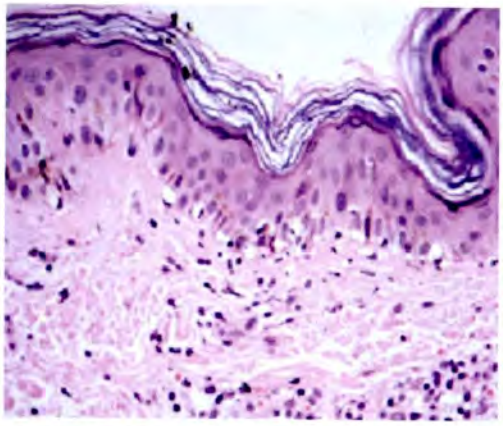
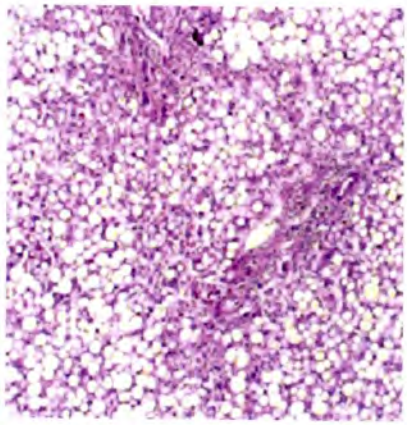




CBC was unremarkable while peripheral film showed multiple vacuoles1-2μm in cytoplasm of all neutrophils and eosinophils. No other reactive changes or atypical cells were present

Ruling out the possibility of sepsis by blood culture, CRP and CXR, storage artefact by a freshly made film,

apoptosis by carefully examining for other features supportive of apoptosis and autophagocytosis by ruling out exposure to antibiotics and radiation, a diagnosis of DorfmanChananrin Syndrome was made. It was supported by Sudan Black B stain positivity in vacuoles, deranged LFTs, deranged Fasting Lipid Profile, skin histopathology showing epidermal basal layer vacoulation and liver biopsy showing micronodular cirrhosis with macrovesicular staeatosis.

## ACADEMIC ACTIVITIES AND EVENTS OF PSH FORUM:

Keeping alive the tradition of monthly local chapter meetings of PSH,various institutes of Lahore namely KEMU, SMDC,Chughtai Lahore Lab and FMH have been graciously hosting the haematology community from September to December 2014 for sharing their experiences regarding interesting cases and diagnostic conundrums haematology experiences registering cases haematology and diagnostic conundrums

The 8th FCPS Haematology intensive course was held at Children's Hospital & institute of Child health, Lahore on 5-8 November 2014. Eminent Consultants from all over Pakistan participated to enlighten the residents on various aspects of success in examination.


*8th FCPS Intensive Course 2014* *PSH LOCAL CHAPTER MEETING KEMU*

A Mock examination was organized in the month of September for residents appearing in FCPS II examination.Prof. Samina Naeem, Prof. Tahir Shamsi Prof. Mona Aziz and Dr Humera Rafiq discussed and answered the queries of the residents.

# Dear Colleagues

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: humerarafiqsheikh@hotmail.com In case you are a member and you are not receiving mails from us please update your postal and e address urgently. You can find us at www.psh.org.pk

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