66TH ANNUAL CONFERENCE OF INDIAN SOCIETY OF HAEMATOLOGY & BLOOD TRANSFUSION

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UTTAR PRADESH HEMATOLOGY GROUP
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Haematocon 2025

Conference News Bulletin

DAY 2

LUCKNOW

6TH - 9TH NOVEMBER, 2025

INNOVATIONS IN HEMATOLOGY: SHAPING THE FUTURE OF DIAGNOSIS AND TREATMENT

HOLIDAY INN LUCKNOW AIRPORT, AN IHG HOTEL, UTTAR PRADESH, INDIA

DY CM COMMITS TO OPEN NEW HEMATOLOGY UNITS

The Deputy CM and Medical Education Minister inaugurates Haematocon-2025, praises hematologists for their service

THE Uttar Pradesh Government on Friday assured to consider opening of new haematological departments based on the recommendations emerging from deliberations from Haematocon-2025 being held in Lucknow.

Inaugurating the event, Mr Brajesh Pathak, Deputy Chief Minister and Minister of Medical Education of Uttar Pradesh, said the health infrastructures have grown vastly with the state having 81 medical colleges.

"There are some regions where medical colleges could not be opened. Efforts are being made to cover those regions. Without doctors, we cannot provide treatment to patients. Our focus is on opening medical colleges. In addition to that institutions imparting training on paramedics and nurses are also being opened. Uttar Pradesh has one Swasthya Arogya Mandir (primary health sub centre) for every 5,500 population, 3,300 primary health centres and 950 community health centres," said Mr Pathak

Besides, the state has 200 super specialty hospitals and 85 district level hospitals where free treatment is extended, he said.

"Through the conferences the government will get to know about new developments in health sector. The government is committed to study the outcome of the conference and take a decision to open new departments," Mr. Pathak assured. Speaking on the occasion, Padma Shri Prof Soniya Nityanand, Vice Chancellor of King George's Medical University and a hematologist herself, said Lucknow has emerged as a hub of hematology. "Starting from Sanjay Gandhi Postgraduate Institute of Medical Sciences to comprehensive departments of hematology, laboratory hematology and bone marrow transplantation in other medical colleges. Ram Manohar Lohia Institute of Medical Sciences has been able get funds from Uttar Pradesh Government for setting up a transplant centre with a new concept," said Prof Nityanand.

She said in KGMU, there has already been a hematology department which has got fund from Adiya Birla Capital Foundation to establish state-of-the-art BMT centre which will be inaugurated next month. Sharing information on the Haematocon-2025, ISHBT Secretary Prof Tuphan Kanti Dolai said the conference was attended by 350 national faculties and 30 international faculties while there was participation of 15 countries.

CONTINUED ON PG - 7

ISHBT to intensify country-specific partnerships

INDIAN Society of Haematology and Blood Transfusion (ISHBT) will now aggressively scout for association with hematological societies across the world. The Executive Committee which met during Haematocon-2025 here, on November 7 unanimously resolved to explore partnerships with hematological societies of Japan, Singapore, South Korea, Australia and European countries like Italy and Netherland.

"The country specific collaborations mooted will be in addition to current engagement with European Hematology Association and American Society of Hematology," said ISHBT Secretary Prof Tuphan Kanti Dolai.

President elect Prof Tathagata Chatterjee, who chaired meeting, approved the ISHBT's aspiration to go global through different collaborative programmes such as joint symposiums and exchange of scientific papers by renowned hematologists.

A host of administrative issues came up for discussions in EC meeting. Prof RK Jena, EC member, proposed to send a delegation of ISHBT to Charity Commissioner, Mumbai to apprise about bottlenecks being faced by the society in getting administrative procedural and structural issues streamlined.

The EC congratulated Prof SP Verma, Organising Secretary of conference, for the successful organising of the Haematocon-2025 that marked by wider participation and the smooth communication with delegates. Prof Verma suggested no major conference of hematology should be allowed three to four weeks prior to Haematocon so that the annual event gets maximum registrations. Dr. Amit Khurana briefed about the preparation of Haematocon-2026 slated to be held in Ahmedabad.

EC members hailed the efforts to update ISHBT's membership data. Currently, ISHBT has updated the list of 2,343 members. It is hoped that information about 1,000 more members would be updated in couple of years. ISHBT members were encouraged to provide data about hematologists working in their areas. The EC hailed Dr Rakhee Kar of smooth publishing of Indian Journal of Hematology and Blood Transfusion. Moreover, the ISHBT's financial account was tabled before all EC members.

COMPLEXITIES OF ITP: A PERSPECTIVE FROM TAIWAN

DR Chia Jen Liu, Chair of the Myeloma Working Group of the Taiwan Hematology Society, Taipei, delivered an insightful lecture on the complexities of Immune Thrombocytopenia (ITP), addressing the first-ever joint ISHBT-Asian Joint Symposium at Haematocon-2025 on a virtual platform on November 7.

Dwelling on 'Beyond platelet counts: Evolving paradigms in the treatment of immune thrombocytopenia' Dr Liu highlighted key research questions that continue to shape the understanding of ITP, including why antiplatelet antibodies develop, why the disease becomes more difficult to treat over time, and why most childhood ITP resolves while adult ITP tends to become chronic.

He also emphasized the need to explore the signaling pathways and cellular transcriptomic profiles that define different ITP subtypes and to investigate whether plasma cells play a role in treatment-refractory cases.

Outlining treatment strategies, Dr Liu stressed the importance of assessing bleeding risk, platelet levels, and comorbidities before initiating therapy.

Management, he said, must be individualized based on symptoms, lifestyle, and patient preferences, with continuous monitoring of platelet counts and bleeding symptoms. Corticosteroids remain the first-line therapy but are poorly tolerated and non-curative; prolonged use should be avoided.

For second-line and advanced stages, thrombopoietin receptor agonists (TPO-RAs) are now preferred over rituximab due to their long-term efficacy and positive impact on quality of life.

While splenectomy remains an effective option, it should be deferred for at least 12 months. Emerging agents such as fostamatinib, rilzabrutinib, efgartigimod, rozanolixizumab, sutimlimab, and daratumumab show promise in refractory ITP.

Dr Liu underscored evolving concepts favouring early initiation of TPO-RAs to prevent chronicity and aiming for durable remission rather than temporary platelet rise. He concluded that while current therapies enhance response rates, no curative strategy exists highlighting the need to focus on remission induction and immunologic restoration guided by patient values and quality of life.

Tuphan Kanti Dolai, ISHBT Secretary, and Prof RK Jena, Secretary Indian College of Hematology Secretary moderated the session. Prof Jena said the Asian camaraderie on addressing hematological challenges would continue in all annual Haematocons.

CONFERENCE GLIMPSES

The Indian approach to diagnosis, treatment and management of ITP

COL (DR) KUNDAN MISHRA
Prof (Med) & Head Dept of Clinical Hematology & BMT Command Hospital, Lucknow

IMMUNE thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by accelerated platelet destruction and impaired platelet production and often presents with cutaneous bleed and rarely with life-threatening bleeding. While its pathophysiology and treatment principles are well established globally, the Indian scenario presents distinctive epidemiological, diagnostic, and management challenges shaped by resource constraints, infection burden, and socio-economic diversity.

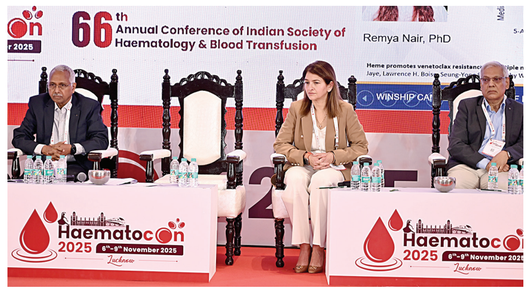
Understanding ITP through an Indian lens highlights both remarkable progress and persisting gaps in research, access, and awareness. In India, ITP occurs across all age groups, with pediatric cases commonly following viral infections and adult cases often presenting as chronic immune-mediated disorders. However, precise national incidence data remain limited due to the absence of centralized registries.

> Understanding ITP through an Indian lens highlights both remarkable progress and persisting gaps in research, access, and awareness. In India, ITP occurs across all age groups

The diagnostic process in Indian centers often remains simplified, relying heavily on platelet count rather than structured bleeding assessment or advanced tests such as anti-platelet antibody assays, flow cytometry, or thrombopoietin measurement. In tertiary hospitals, platelet function evaluation through viscoelastic tests such as Sonoclot analysis has revealed that bleeding severity in ITP often correlates poorly with platelet count, emphasizing qualitative dysfunction as an important determinant—a finding validated in recent Indian studies. Yet, such functional assays are largely unavailable outside academic institutions.

Treatment practices in India exhibit wide heterogeneity. Corticosteroids remain the mainstay first-line therapy, but the choice, dosing, and tapering regimens differ across physicians. High-dose dexamethasone, short courses of methylprednisolone, and oral prednisolone tapers are used variably, with limited adherence to uniform protocols. Intravenous immunoglobulin and anti-D immunoglobulin are restricted to critical cases due to cost. Second-line options such as rituximab and thrombopoietin receptor agonists (eltrombopag, romiplostim) are increasingly available, particularly in metropolitan and military tertiary centers, but high cost and limited reimbursement impede equitable access. Dapsone and azathioprine continue to be popular, inexpensive steroid-sparing alternatives in India, despite variable efficacy data. Splenectomy, once a common definitive option, has seen declining preference due to infection risks and availability of medical alternatives.

The Indian perspective of ITP is one of contrastsbetween tertiary excellence and peripheral limitations, modern therapeutics and financial inaccessibility, global guidelines and local realities. Moving forward, national registries, standardized treatment algorithms, and cost-effective monitoring strategies are essential.



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DR JG PAREKH ORATION

Role of morphology in diagnosing MPNs

DR TEJINDER SINGH
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MYELOPROLIFERATIVE neoplasms (MPNs) are clonal proliferations arising from a single mutated stem cell that produces clonal hematopoietic stem cells. The mutations initiating this proliferation- JAK2, CAL-R, and MPL- are termed driver mutations. These mutations trigger disease initiation but do not affect myeloid cell maturation. As a result, mature red cell production causes Polycythemia Vera (PV); white cell proliferation causes Primary Myelofibrosis (PMF); and platelet proliferation results in Essential Thrombocythemia (ET).

> WHO 2017 and 2022 have outlined the diagnostic criteria for various MPNs, emphasizing megakaryocyte morphology and reticulin assessment

The distribution of mutations varies: JAK2 mutation is present in nearly all PV cases, whereas CAL-R and MPL mutations are absent. Conversely, JAK2, CAL-R, and MPL mutations are found in PMF and ET. A single JAK2 mutation may give rise to PV, ET, or PMF, the latter having the worst prognosis and ET the best. Additional mutations such as TET2, IDH1/2, TP53, and ASXL1 contribute to disease progression to myelofibrosis or a blastic phase (AML). Thus, MPNs are now considered multi-mutation diseases.

Phenotype of the disease whether ET/PV or PMF will manifest depends upon the allele burden and homozygous/heterozygous mutations e.g., if JAK2 mutations are predominantly homozygous and allele burden is high, then phenotype is PMF and if the JAK2 mutation is predominantly-heterozygous with low allele burden then the phenotype is ET.

In such a situation, it is very important to diagnose a MPN and accordingly treatment is to be instituted. The diagnosis is made out on the basis of morphology of peripheram smear, bone marrow aspirate and bone marrow biopsy morphology.

WHO 2017 and 2022 have outlined the diagnostic criteria for various MPNs, emphasizing megakaryocyte morphology and reticulin assessment. In ET, bone marrow cellularity is normal or mildly hypercellular, with normal myelopoiesis and erythropoiesis. Megakaryocytes appear in loose clusters, giant in size with staghorn nuclei. In PV, marrow is hypercellular with panmyelosis and pleomorphic megakaryocytes. Erythroid hyperplasia is marked, and some cases progress to post-polycythemic myelofibrosis or AML. PMF shows progressive stages- prefibrotic, fibrotic, osteomyelosclerosis, accelerated, and blastic phases - and must be differentiated from secondary marrow fibrosis, post-PV MF, and MDS.

Since PMF carries the worst prognosis, accurate morphological diagnosis is essential. Despite molecular advances, morphology remains the backbone of MPN diagnosis.

DEALING WITH ARTERIAL THROMBOSIS IN INDIA

BRIG (DR) SANJEEVAN SHARMA
Head, Dept of Clinical Hematology, Army Hospital Research & Referral

ARTERIAL thrombosis, is a significant cause of morbidity and mortality worldwide. While commonly associated with older adults and atherosclerosis, arterial thrombosis in young adults (<45 years) poses unique challenges. It often arises from diverse causes beyond traditional cardiovascular risk factors, demanding a focused diagnostic and management approach.

Young adults with arterial thrombosis may present with acute ischemic events such as stroke, myocardial infarction, or limb ischemia. Unlike older populations, many lack typical risk factors like hypertension or diabetes. Instead, "unconventional" causes such as inherited or acquired hypercoagulable states, autoimmune conditions (e.g., antiphospholipid syndrome), vasculitis, or paradoxical embolism through cardiac defects often predominate.

Diagnosis begins with clinical evaluation and imaging to localize and quantify arterial obstruction. A comprehensive procoagulant workup is vital in young patients with unexplained arterial thrombosis. This includes screening for inherited thrombophilias (Factor V Leiden, prothrombin gene mutation), acquired conditions (antiphospholipid antibodies, lupus anticoagulant), deficiencies of anticoagulant proteins (protein C, protein S, antithrombin), paroxysmal nocturnal hemoglobinuria, and myeloproliferative neoplasms. Cardiac evaluation for sources of embolism and vascular imaging for vasculitis are also essential.

Management targets both the acute event and underlying cause. Acute arterial thrombosis often requires emergent revascularization via thrombolysis or surgical intervention. Long-term therapy is guided by etiology. Antiplatelet agents form the backbone of treatment for atherosclerotic thrombosis, while anticoagulation is preferred in thrombophilia or embolic situations. Immunosuppressants may be necessary in vasculitis or autoimmune diseases.

Lifestyle modification addressing modifiable risk factors such as smoking remains important even in young adults. Multidisciplinary care optimizing secondary prevention and managing complications is crucial to improve outcomes.

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ADVANCES IN CELL THERAPY: POTENTIAL APPLICATIONS

DR NEENA KAPOOR
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IMMUNE deficiency state can be congenital due to one or more elements of immune system missing or secondary to iatrogenic causes such as chemo and or radiation therapy for the treatment of cancer, autoimmune diseases and infections. Immune deficiency can also be seen in individuals of extreme age such as neonates or elderly individuals. Fatality in any of these patient population are either due to infections, cancer or hyper-immune reactive disease.

In 1968 the 1st successful allogenic bone marrow transplant (HSCT) from a histo-compatible donor in a SCID baby proved that this procedure is a curative therapy for severe combined immune deficiency. Since then, HSCT has been successfully applied for the treatment of many malignant and non-malignant diseases. Today potentially every individual who is a candidate for the transplant, has a donor.

The field of stem cell transplantation is at the state of maturity that now it is not how to do the procedure of transplantation, but how to do it safely and effectively. To accomplish that, the disease must be defined at cellular, molecular and genomic level. On basis of type and the status of the disease, conditioning regimen are being tailored. Myeloablation is still standard conditioning but with modification to have reduced toxicity. Pharma-kinetics guidance of each one of the agent is being used, provides safety and efficacy of conditioning regimen for transplantation. Modification of the graft, whether T depletion from PBSC/ bone marrow or enhancing the cell dose of the cord blood by having product expanded in vitro does affect engraftment, graft versus host disease, immunological and hematological recovery.

Advances in the supportive care has allowed us to prevent or effectively treat complications like sinusoidal obstructive syndrome. Availability of various antimicrobial agents has spared us from acute morbidity and mortality associated with infections. Being able to give specific antibody products to provide passive immunity like Pemivibart for pre exposure COVID prophylaxis in peri transplant period.

From standard stem cell transplant, cell therapy has embarked on gene therapy and gene editing. In last three decades the gene therapy had its own challenges. However now with the use of self-inactivating lente virus vector, has made the procedure safer with promising results. Still longer follow up is needed to determine the persistence of corrected gene and insertional mutagenesis.

Frontline treatment options in adult high-risk MDS in 2025

DR AURO VISWABANDYA
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MYELODYSPLASTIC syndromes (MDS) are a heterogeneous group of clonal myeloid disorders characterized by ineffective hematopoiesis, cytopenias, and a risk of progression to acute myeloid leukemia (AML). Patients are stratified into prognostic risk groups to guide therapy. High-risk MDS generally refers to cases with a higher likelihood of leukemic transformation and shorter survival. Accurate risk stratification is critical in identifying high-risk MDS patients. The Revised International Prognostic Scoring System (IPSS-R) is commonly used. The newer molecular IPSS (IPSS-M) incorporates somatic mutations into risk stratification, further refining prognosis.

The DNA hypomethylating agents are the cornerstone of frontline therapy for high-risk MDS. Azacitidine and decitabine are widely used and are the only non-transplant therapies approved for high-risk disease. Azacitidine has demonstrated a significant survival benefit in high-risk MDS (median overall survival ~24 vs 15 months compared to conventional care). Decitabine is an alternative HMA that produces comparable response rates; trial showed a survival benefit in high-risk patients (12.0 vs 6.8 months vs supportive care). Allogeneic hematopoietic stem cell transplantation (HSCT) is currently the standard-of-care for high-risk MDS patients eligible for the procedure and the only curative treatment.

AML-like induction chemotherapy (e.g. cytarabine plus anthracycline) is not routine for MDS but may be used selectively in high-risk patients with higher blast counts (close to 20%) who are transplant candidates. In younger, fit patients without adverse molecular features, induction can cytoreduce disease prior to HSCT. However, response rates to intensive chemotherapy in MDS are lower.

Supportive care is essential throughout therapy. Transfusion support, infection prophylaxis, and careful use of growth factors sustain quality of life. Iron chelation is considered in transfusion-dependent, transplant-eligible patients, while thrombopoietin agonists have shown no benefit in this group.

As of 2025, frontline management of high-risk MDS centers on HMA therapy and timely transplant consideration. While outcomes remain modest, emerging molecular and immune-based therapies offer renewed hope for durable disease control and future cure

Emerging therapies continue to evolve. Combinations of HMAs with agents such as venetoclax, magrolimab, or sabatolimab show promise but have not yet surpassed single-agent HMA efficacy. The 2025 VERONA trial reported no overall survival benefit for azacitidine plus venetoclax over azacitidine alone. Targeted therapies such as IDH inhibitors (ivosidenib, enasidenib) and p53 modulators like eprenetapopt are under active study.

As of 2025, frontline management of high-risk MDS centers on HMA therapy and timely transplant consideration. While outcomes remain modest, emerging molecular and immune-based therapies offer renewed hope for durable disease control and future cure.

Challenges in diagnosing and treating difficult MPNs in Indian conditions

COL (DR) ASHOK MESHRAM
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MYELOPROLIFERATIVE neoplasms (MPNs) represent a group of clonal hematopoietic stem cell disorders characterized by the excessive production of one or more blood cell lines—red blood cells, white blood cells, and/or platelets—in the bone marrow. These disorders disrupt normal hematopoiesis, leading to blood hypercellularity, altered blood viscosity, and clinical complications such as thrombosis or bleeding.

Despite advances, MPNs pose diagnostic and therapeutic challenges due to disease heterogeneity and potential progression to acute leukemia

The classical MPNs include polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF), along with chronic myeloid leukemia (CML), which is distinguished by the BCR-ABL1 fusion gene. Additional rare forms include chronic neutrophilic leukemia and chronic eosinophilic leukemia. The 2025 WHO diagnostic criteria emphasize integrating clinical features, comprehensive blood counts, bone marrow morphology, and molecular testing for mutations in JAK2, CALR, and MPL genes which are pivotal in pathogenesis.

Clinically, MPNs commonly present with symptoms related to hyperviscosity and splenomegaly such as fatigue, night sweats, weight loss, pruritus, and thrombosis. Laboratory evaluation involves complete blood count, peripheral smear examination, serum erythropoietin levels, and bone marrow biopsy with reticulin staining to assess fibrosis. Molecular testing by PCR or next-generation sequencing helps identify driver mutations, which inform diagnosis, prognosis, and therapeutic decisions.

Treatment strategies are tailored to the subtype, symptom burden, and risk factors. PV and ET are often managed with phlebotomy, low-dose aspirin, and cytoreductive agents to control cell counts and reduce thrombotic risk. PMF requires a more nuanced approach, including JAK inhibitors such as ruxolitinib to manage symptoms and splenomegaly, with allogeneic stem cell transplantation as a potential curative option for eligible patients. CML management is dominated by tyrosine kinase inhibitors targeting BCR-ABL1, revolutionizing patient outcomes.

Recent advances highlight the importance of molecular profiling in refining classification and prognosis, aiding personalized medicine approaches. Despite advances, MPNs pose diagnostic and therapeutic challenges due to disease heterogeneity and potential progression to acute leukemia.

Ceremony

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MDS Diagnosis: Morphology continues to remains the cornerstone of evaluation

DR DEBDATTA BASU
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MYELODYSPLASTIC syndromes (MDSs) are myeloid neoplasms characterized by morphologically abnormal and ineffective maturing haematopoiesis, resulting in peripheral blood cytopenias. The diagnosis of MDS is often challenging because of the diverse non-neoplastic causes of cytopenia, the distinction between MDS and other cytopenic clonal proliferations, and the border between MDS and acute myeloid leukemia (AML).

According to V edition of WHO classification of MDS (WHO5), the entity is now known as Myelodysplastic Neoplasm, with the abbreviation kept as MDS. The current MDS classification schemes incorporate morphologic features (bone marrow and blood blast percentage- <20%,degree of dysplasia>10% in one to three lineage, ring sider oblasts, bone marrow fibrosis, and hypocellularity) and also recognize three entities defined by genetics: isolated del(5q) cytogenetic abnormality, SF3B1 mutation, and TP53mutation. Accurate diagnosis requires the integration of clinical features with bone marrow and peripheral blood morphology, karyotyping, immunophenotyping, and genetic testing.

In spite of molecular and genetic advancements in the pathophysiology of MDS, morphology remains the cornerstone of MDS diagnosis. Patients generally present with cytopenias. Hemoglobin is < 10gm/dl, red cells are usually macrocytic with MCV >100 fl. Absolute Neutrophil Count of <1800/cmm and Platelet count of <1,00,000/cmm.
The dysplastic changes are as follows-

In the peripheral blood:

- Red cells – Macrocytosis, anisopoikilocytosis, nucleated red blood cells showing dyserythropoiesis, increased Pappenheimer bodies
- White blood cells – Neutropenia, Hypolobated neutrophils (Pseudo Pelger Huet cells), Hypogranularity, Ring neutrophils, abnormal lobe morphology and nuclear budding, Auer rod, occasional blast

Platelets – Large and giant forms and abnormal granulations
In the bone marrow – generally hypercellular for age:

- Erythropoiesis – megaloblastic maturation, dissociation between nuclear and cytoplasmic maturation, nuclear budding and binucleation, ring sideroblasts (with SF3B1 mutation)
- Myelopoiesis – Blast may be increased – depending on blast percentage, MDS is divided as MDS – low blasts (<5%) or MDS – increased blasts (>5% to 19%), Abnormal lobes, giant metamyelocytes, maturation arrest. On a trephine biopsy, and when stained with CD 34, abnormal localisation of immature precursors (ALIP) is seen.
- Megakaryopoiesis –Abnormal clustering, Micromegakaryocytes, monolobed megakaryocytes (5q deletion-MDS), lobe separation (Pawn ball shape).

MEETINGS TO BEDSIDE: TAKING LEARNINGS TO PATIENTS

DR NALINI PATI
Consultant Haematologist, The Canberra Hospital, Australia

IN 2025 to manage complex patients would need understanding of the available options in the local low middle income country (LMIC) setting which can be possible through networking and available local data. To sight one of the many examples, managing a relapsed refractory lymphoma patient, it may not be easy but would be possible with developing a basic understanding and then apply the knowledge to respective patient cohort. It starts with stratifying the cases with precise diagnosis, prognosticate, evaluate the best treatment strategy available in local setting.

The care in lymphoma patients, starting from diagnosis to overall management is no more one professional's job rather a job that should include intricate care in a multidisciplinary approach. As a result we have seen the significant improvement in the outcome of these patients with a survival improving all the time, even in some of the aggressive ones. The treatment has seen the influx of several novel, targeted therapy, helping clinicians in staying away from using chemotherapy, limiting the amount of side effect the patients would be experiencing to better results overall.

Recently with the advent of newer modality of therapy in the space of haemophilia care, such as extended half-life products and monoclonal antibody treatment such as emicizumab; it is important to understand the change in the laboratory testings, so that the clinicians can interpret the results more accurately with introduction of this new therapy. Furthermore, different viscoelastic tests such as Thromboelastographic studies and ROTEM test, point of care testing would help identify the deficiencies on the blood as a cause for bleeding manifestation and help better manage bleeding complications. This has helped in better utilisation of resources including blood products more accurately to achieve good haemostasis, such as in cardiovascular surgeries, massive transfusions. Similarly better understanding of laboratory testing in various complications such as in patients with haemophilia with inhibitors, would aid better treatment and monitoring.

In summary, having a better understanding of the basic sciences, laboratory findings, their interpretation and applying these findings in the day to day patient care would lead to help fine-tune the management of the patients, management of their complications, and better monitoring in the future.

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REACHING CLOSER TO THE FINISH LINE: CLASSIC HL

DR RANJANA ADVANI
Saul A Rosenberg Professor of Lymphoma, Stanford University, USA

CURRENTLY classic Hodgkin Lymphoma (cHL) is a highly curable disease, and only 15- 20% of patients experience progression or relapse after standard frontline regimens. The typical Hodgkin and Reed Sternberg (HRS) tumor cells represent less than 5% of the involved tumor tissue and is surrounded by a complex tumor microenvironment (TME). HRS malignant cells display a characteristic immunophenotype with CD30 positivity and release several cytokines, which all contribute to TME modulation and immune evasion. HRS cells achieve immune evasion by multiple mechanisms including enhanced expression of programmed cell death protein-1 receptor (PD-1) and ligands (PD-L1/PD-L2)

In the last decade, with the increasing understanding of cHL biology and TME role in disease course, novel molecules have been introduced in clinical practice. The anti-CD30 antibody-drug conjugated brentuximab vedotin (BV) and PD-1/PD-L1 checkpoint inhibitors (CPI) have led to paradigm shifts in management and are now used both in front line and relapsed/refractory setting with significantly improved outcomes. Results of the SWOG 1826 US Intergroup trial and the GHSG HD21 trial have established Nivolumab-AVD (N-AVD) and BV, etoposide, doxorubicin, cyclophosphamide, dacarbazine, and dexamethasone (BrECADD) respectively as new standards of care for advanced stage cHL in the front line setting with 2-4 y progression free survival (PFS) >92%.

CPI combinations also represent an important advance in salvage therapy and appear to offer a specific PFS benefit. In addition to direct immune-mediated effects, CPI may also sensitize patients to subsequent chemotherapy. Currently, immunotherapy combinations represent a preferred strategy pre-ASCT, and several regimens have demonstrated excellent efficacy. For select patients with low volume disease, sequential regimens starting with a single novel agent may provide a chemotherapy-free route to transplant.

Given high response rates with CPI-based salvage, current studies are exploring the option of omitting ASCT in select patients in favor of CPI maintenance. With the high efficacy and limited toxicity of BV and PD-1 inhibitors, the combination of these compounds represents a valid alternative to conventional chemotherapy for patients ineligible for standard therapy due to age or comorbidities and several trials support this concept.

In summary there has been major progress over the last 3 decades with cure rates now in excess of 90% bringing us closer to the finish line.

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Decoding & managing heparin-induced thrombocytopenia

COL (DR) JASDEEP SINGH
Senior Advisor (Path) & Hematopathologist, DGAFMS

HEPARIN-Induced thrombocytopenia (HIT) is a serious, immune-mediated adverse reaction to heparin therapy characterized by a significant drop in platelet count and a paradoxical increased risk for thrombosis. Diagnosing HIT promptly is critical to prevent life- and limb-threatening complications.

Clinically, HIT typically occurs five to 10 days after starting heparin and manifests as a platelet count drop of at least 30-50% from baseline, often accompanied by new arterial or venous thrombosis. HIT type II (immune-mediated) is distinguished from the benign HIT type I (non-immune); only type II necessitates urgent intervention.

Diagnostic evaluation begins with clinical risk assessment using the 4Ts score, encompassing thrombocytopenia magnitude, Timing of platelet fall, presence of Thrombosis, and exclusion of other causes. A high or intermediate 4Ts score warrants laboratory testing.

Laboratory diagnosis involves immunoassays (antigen tests) like ELISA which detect antibodies against platelet factor 4 (PF4)/heparin complexes and have high sensitivity (80–100%) but lower specificity, as false positives occur due to non-pathogenic antibodies or other clinical factors, necessitating confirmatory testing. Functional assays detect platelet activation induced by HIT antibodies, confirming their pathogenicity.

The gold standard is the serotonin release assay (SRA), boasting approximately 95% sensitivity and specificity, though technical complexity limits availability. Other tests include heparin-induced platelet activation (HIPA) and flow cytometry-based assays.

No single test fully confirms HIT; diagnosis relies on combining clinical probability with laboratory evidence. Negative immunoassays generally exclude HIT, while positive tests require functional assays for confirmation.

Management includes immediate discontinuation of all heparin products and initiation of non-heparin anticoagulants to mitigate thrombosis risk. Warfarin is contraindicated in acute HIT due to limb gangrene risk until platelet recovery.

Management of Philadelphia positive ALL in 2025

DR RAJAT KUMAR
Professor of Medicine, University of Toronto, Canada

PHILADELPHIA positive (Ph+) acute lymphoblastic leukemia (ALL) is defined by the t(9;22) translocation, creating the BCR-ABL fusion gene, which drives leukemogenesis and uncontrolled proliferation. Although rare in children, it accounts for up to 30% of adult ALL cases. Historically, Ph+ ALL had a poor prognosis, and allogeneic hematopoietic cell transplantation (allo-HCT) was the only curative option, though limited by transplant-related mortality and graft-versus-host disease. With the advent of tyrosine kinase inhibitors (TKIs) and monoclonal antibodies, outcomes have improved dramatically, allowing non-transplant approaches to become feasible.

TKIs form the backbone of frontline therapy. Imatinib, the first-generation TKI, has largely been replaced by dasatinib and ponatinib, which offer high potency

TKIs form the backbone of frontline therapy. Imatinib, the first-generation TKI, has largely been replaced by dasatinib and ponatinib, which offer higher potency and CNS penetration. In studies, dasatinib combined with chemotherapy achieved 94% complete remission (CR) and 93% molecular response, though relapses often carried the T315I mutation. Ponatinib, active against T315I, showed superior results, with complete molecular remission (CMR) rates of 79% and three-year overall survival (OS) of 79%, outperforming earlier TKIs.

Blinatumomab, a bispecific T-cell engager (BiTE) targeting CD19 and CD3, has emerged as a game changer. Combined with TKIs, it induces deep molecular remissions with low toxicity, even in elderly patients. In the D-ALBA trial, sequential dasatinib plus blinatumomab achieved 98% CR, 93% CMR, and 81% OS at four years. Similarly, ponatinib plus blinatumomab demonstrated durable responses with fewer relapses. However, higher CNS relapse rates have prompted recommendations for increased intrathecal chemotherapy and incorporation of high-dose methotrexate or cytarabine in consolidation.

For elderly patients, low-intensity regimens combining TKIs, blinatumomab, and minimal chemotherapy offer effective disease control with far fewer side effects than traditional chemotherapy.

Allo-HCT remains an option for patients with persistent or recurrent minimal residual disease (MRD) or high-risk mutations. Those achieving deep MRD negativity may safely defer transplant. Long-term discontinuation of TKIs, as in CML, may be possible for select patients with sustained CMR exceeding 48 months, though prospective data are awaited.

In 2025, Ph+ ALL represents a success story of targeted therapy — transforming a once-fatal disease into a manageable, potentially curable condition without transplantation.

CONFERENCE GLIMPSES

Metabolic Rewiring: A key driver of disease progression, therapeutic resistance in MM

DR MALA SHANMUGAM
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CANCER cells possess enormous metabolic flexibility that allows them to evade programmed cell death, escape immune surveillance, and adapt to changing environments during invasion and metastasis. Our long-term objective is to investigate cancer metabolism to identify targetable metabolic vulnerabilities and predictors of therapy response to develop metabolism-informed precision therapeutic strategies.

In the case of Multiple Myeloma (MM), tumor cells exhibit context-specific metabolism influenced by both genetic mutations and micro-environmental factors. Extrinsic metabolites and intrinsic tumor metabolism have profound implications on therapy sensitivity and resistance. We have previously established glutamine metabolism regulates MM cell survival, sensitivity to BH3 mimetics and drug resistance.

Our earlier research established the critical role of glutamine metabolism in regulating MM cell survival, sensitivity to BH3 mimetics, and resistance mechanisms. Expanding on this, we demonstrated that reduced electron transport chain activity and low oxidative phosphorylation are linked with increased sensitivity to venetoclax, a BCL-2 inhibitor.

In the case of Multiple Myeloma (MM), tumor cells exhibit context-specific metabolism influenced by both genetic mutations and micro-environmental factors

In our recent Blood (2025) publication, we found supplementation of venetoclax-sensitive/BCL-2 dependent MM cells with heme promoted resistance to venetoclax that was reversed by heme chelation with hemopexin. Heme biosynthesis was found to be suppressed in venetoclax sensitive MM and targeting heme biosynthesis sensitizes resistant MM to venetoclax. Examination of the heme-activated kinome, identifies heme activation of the MAPK axis. Our cellular energetics and steady state metabolomics revealed heme to activate de novo purine biosynthesis.

Targeting MEK or de novo purine biosynthesis restores sensitivity to venetoclax in heme-exposed MM. Elevation in purine biosynthesis correlates with poor PFS and OS in MM and noted in the CD1 vs CD2 subgroup of MM. We have also investigated the effects of heme on immune cells and identified ex vivo heme supplementation to reduce dysfunction-related triplet-expressing phenotypes (PD1+/LAG3+/TIM3+) and increase enrichment of effector memory cells (CD62L-CD45RA-) in both CD4+ and CD8+ subsets isolated from normal human donor PBMC, MM patient bone marrow-derived T cells and patient-derived CAR T cells.

We are continuing to investigate the implications of both extrinsic and intrinsic heme on MM therapy sensitivity.

RELAPSED REFRACTORY AML TARGETS & OUTCOMES

PROF MB AGARWAL
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ALTHOUGH outcomes for newly diagnosed acute myeloid leukaemia (ND-AML) have been incrementally improved over the last decades, management of relapsed and refractory (R/R) AML remains a medical challenge. A curative intent for R/R AML usually involves chemotherapy (with or without targeted therapy) with subsequent consolidation, including allogeneic haematopoietic stem cell transplantation. Despite this, long-term survival rates of R/R AML only reach approximately 10% in adults and 40% in children.

Somatic mutations, gene expression, and functional drug testing are important for the selection of small molecule inhibitors of oncogenic signaling pathways (e.g., FLT3), menin inhibitors that disrupt leukemogenic programmes, inhibitors of isocitrate dehydrogenases (IDH) to restore oncometabolic homoeostasis, and proapoptotic Bcl-2 homology 3 (BH3) mimetics, such as venetoclax. Targeting the recently identified resistance factor SAMHD1 promises to overcome resistance to cytarabine and fludarabine. Given the growing number of potential combinatorial drug regimens and the genetic heterogeneity of AML, real-time ex vivo drug response profiling to guide individualized treatment decisions will become an important complement.

We argue that better outcomes for R/R AML critically depend on being guided by precision oncology to define the best combination of chemotherapy, targeted therapy, and immunological therapy informed by phenotypic and genotypic patient- and disease-specific parameters.

Dy CM commits...

CONTINUED FROM PG - 1

As many as 118 oral papers and 363 posters were presented amidst participation of 1,500 delegates, he said. Sunita Sharma, Director General of Health Services, Uttar Pradesh, said hematolgoy stands at a critical juncture with new innovations and diagnostic technics. She called upon hematologists to dwell upon emerging technologies and bring into practices for greater benefit of patients.

Guests were effusive of organising capability of Professor SP Verma, organising secretary, and Prof Rashmi Kuswaha, co-organising secretary, for successfully conducting the Haematocon-2025. The spirit of Vijai Tilak, president of organising committe was also appreciated.

Tarun Kumar Datta, former professor of hematology, was conferred ISHBT Lifetime Achievement award on the occasion. ISHBT abstracts and other publications were released during the inaugural ceremony.

ISHBT President Sarmila Chandra, president elect Brigadier Tathagat Chatterjee and past president PK Sasihadharan also graced the occasion.

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FOOD AS MEDICINE FOR SICKLE CELL DISEASE PATIENTS

EARLY screening and curative therapies including gene therapy are major advances in improving lives of those living with sickle cell disease (SCD). However, in resource limited environments the majority of individuals remain in a nutritionally deprived state.

Additionally, individuals with SCD may suffer from disease-related malnutrition as a result of increased demands for absorbed nutrients, caused by multiple factors including a higher metabolic rate. Deficiency of vitamins, zinc, magnesium, and anti-inflammatory fatty acids, among others, have been well-documented in SCD.

Nutritional deficiencies may begin during gestation because of inadequate parental diet affecting the health of the offsprings. Recent studies suggest that improvement in nutritional demands of SCD leads to improved survival and reduced pain. In diverse populations with cultural and geographical heterogeneity, fulfilling the dietary requirement can be a major challenge. Many food supplements (nutraceuticals) can address the nutritional demand while also offering disease modifying benefits as well as reduction in pain. Palmitoylethanolamide (PEA) is a notable example; PEA is a paracannabinoid lipid mediator with marked anti-inflammatory and analgesic effects in SCD. PEA is present in foods, such as eggs and legumes, and novel formulations for direct supplementation are becoming more available. Additionally, clinical studies suggest that PEA may have analgesic efficacy in various human pain conditions, without the intoxicating effects associated with cannabinoids. Sailin-HbS is another nutraceutical example, comprising black pepper seeds, Vijaysar/Indian kino stem, clove fruit, leaves of jowar/Egyptian millet, and turmeric stem, which has been formulated based on the principles described in Ayurvedic literature for the use of natural plants with medicinal properties.

Sailin-HbS has demonstrated the potential to alleviate sickling and some of its comorbid features in early investigations . An increasingly popular nutraceutical, curcumin has gained attention because of its natural antioxidant and anti-inflammatory and antisickling properties. However, its limited absorption and bioavailability have been barriers in its medicinal use. A novel transdermal curcumin formulation circumvents many of these limitations; it is rapidly absorbed through the skin requiring lower doses to achieve similar levels of absorption from oral consumption.

Thus, clinical trials for food supplements and other integrative approaches are needed to improve outcomes for SCD in India.

Ceremony

CONFERENCE GLIMPSES

Medico-legal issues in hematology practice

PROF ATUL MEHTA
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THE National Health Service in the UK spends around £3 billion (2% of its total budget) on settling litigation claims; the amount has been rising by 10-12% each year for the past 5 years. Around 40% of the budget is spent on high value maternity-related events; and the average compensation payout is £200,000. Almost 60% of litigation claims are successful; and 85% or so are settled out of court.

A central legal principle is the Bolam criterion, which defines the standard of clinical care expected of a doctor. It holds that a medical professional is not in breach of their duty to the patient if their actions were in line with a responsible body of medical opinion, even if other practitioners hold a different view. This "peer review" standard requires that only a specialist in the same field as the accused can advise on breach of duty. Refinements stipulate that the actions of the doctor must withstand logical analysis; and the patient must have given informed consent to the treatment.

Adherence to peer reviewed practice requires written protocols and guidelines. This is a key role for specialist societies such as the Indian Society for Haematology and Blood Transfusion; guidelines formulated by international societies can only be adopted after careful consideration. Formulating and disseminating good practice guidelines is an integral part of modern medicine and is central to the international imperative of the need to raise standards of care.

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Thrombosis and cancer are together the biggest causes of death. Failure to observe good practice in preventing, diagnosing and treating blood clots (for example, in surgical practice) leads to negative consequences; and haematologists will need to advise on causation. For example, was a specific dose of thromboembolism prophylaxis responsible, on the balance of probabilities, for a post operative pulmonary embolism? Or was it a significant contributory factor in causing post operative bleeding?

Thrombosis is the biggest cause of maternal mortality and haematologists and transfusion specialists are intimately involved in the prevention and treatment of pregnancy related coagulation problems. Delays in diagnosis of haematologic cancers are much more likely to be due to deficient care by general practitioners or physicians; but it is haematologists who assess the precise extent to which poor practice led to suboptimal outcome.