



PATHWEL *times*

BIMONTHLY NEWSLETTER 2026 | Jul - Aug | Vol 3.4

Dr Jamal Nasir

Vice President, Pakistan Thalassaemia Welfare Society



A Proud Moment for PATHWEL

We are pleased to share that Dr. Jamal Nasir, Vice President of PATHWEL, has been appointed as a Member of the Syndicate of the University of Health Sciences (UHS), Lahore. This prestigious appointment reflects his extensive experience, leadership, and longstanding commitment to healthcare and public service.

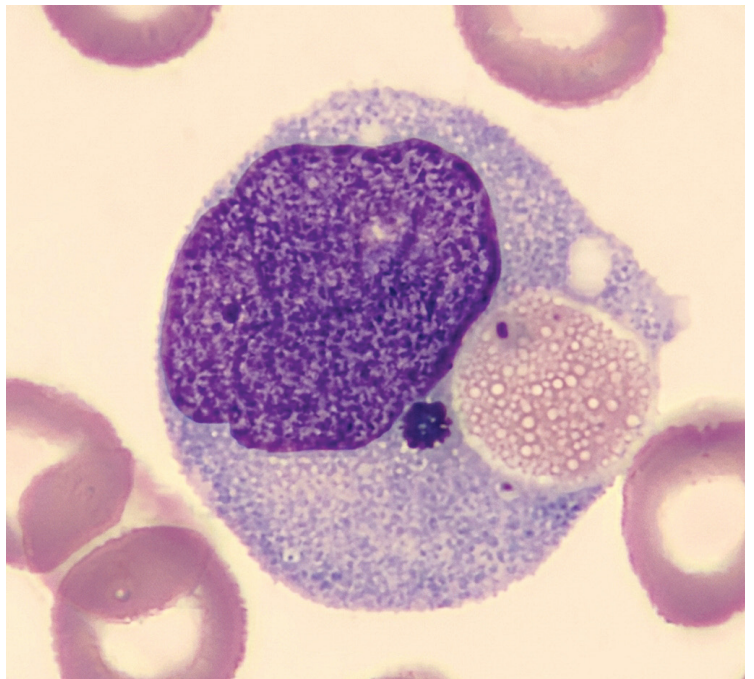
Dr. Jamal Nasir, former Health Minister of Punjab, has remained actively involved in social welfare, philanthropy, and initiatives focused on improving healthcare and supporting communities. Throughout his career, he has demonstrated a strong dedication to serving the people and contributing to the development of the healthcare sector.

His appointment to the UHS Syndicate is a significant recognition of his valuable experience and contributions to healthcare, education, and public service. It is also a moment of great pride for PATHWEL Center of Hematology & Bone Marrow Transplant. We extend our heartfelt congratulations to Dr. Jamal Nasir and wish him continued success in this important role.

Picture Quiz

Given below is a picture of peripheral blood smear showing a circulating monocyte actively phagocytosing an erythrocyte. What is the diagnosis?

(Answer on page 6)



Strengthening Molecular Diagnostics at PATHWEL
A refurbished and upgraded molecular lab brings advanced testing closer to our patients.

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From Editor's Desk

Why a Good Laboratory Is the Heart of Modern Hematology

In hematology, the laboratory is not simply a place where samples are tested and reports generated. It is an integral part of clinical care—a place where clues to a patient's illness are transformed into information that guides treatment.

Modern hematology has made this role increasingly important. Diagnosis may require morphology, flow cytometry, immunophenotyping, molecular studies, cytogenetics or other specialized investigations. Yet sophisticated technology is only as valuable as its interpretation. The most meaningful results emerge when different sources of information are brought together.

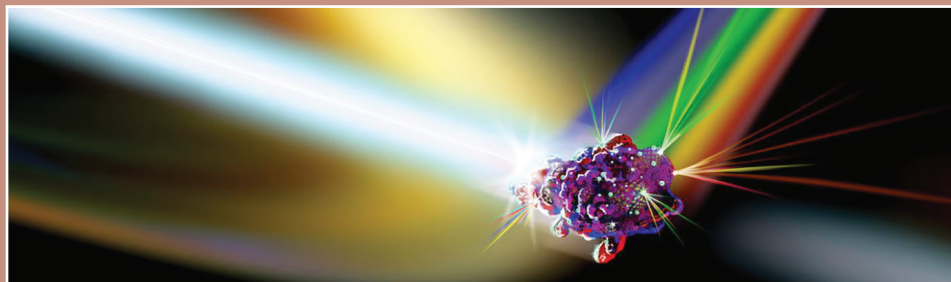
Flow cytometry provides a good example. Its findings can be significantly enhanced when interpreted alongside cell morphology, blood counts, bone marrow findings and the clinical scenario. A laboratory result should never be viewed in isolation. Integrating all available information allows the laboratory team to provide a more accurate and clinically meaningful interpretation.

At PATHWEL, this integration is one of our greatest strengths. Our laboratory and clinical services function as one closely connected network. Laboratory doctors and technologists work hand in hand with hematologists and clinicians, discussing difficult cases, reviewing results and correlating laboratory findings with the clinical picture. This interaction helps ensure that investigations are relevant, results are correctly interpreted and clinical decisions can be made without unnecessary delay.

Speed is another important advantage. Because the laboratory is integrated within the hospital, many investigations can be performed and reported within a very short time. In hematology, where patients may be critically ill or treatment decisions need to be made urgently, rapid access to reliable results can be as important as the sophistication of the test itself.

This close partnership is particularly valuable for patients receiving chemotherapy, undergoing transplantation or requiring intensive supportive care. Continuous communication allows important changes in blood counts, infection markers, transfusion requirements, MRD and other parameters to be recognized and acted upon promptly.

As PATHWEL continues to strengthen its molecular, flow cytometry and other advanced diagnostic capabilities, our goal is not simply to build a more sophisticated laboratory, but a better-connected one. Because ultimately, the best laboratory is the one that stands beside the clinician—and closer to the patient.



A Major Leap Forward in Patient Care at PATHWEL

PATHWEL has acquired an advanced Flow Cytometer—bringing a new era of diagnostic precision and MRD assessment to our patients.

This important addition to our diagnostic services will significantly strengthen the diagnosis, classification, and monitoring of hematological malignancies, particularly acute leukemias. Most importantly, it will enable timely and sensitive Minimal Residual Disease (MRD) assessment, an essential tool for evaluating treatment response, guiding further therapy, and improving risk assessment.

For patients undergoing high-dose chemotherapy and Bone Marrow Transplantation, access to reliable MRD testing can make a meaningful difference in clinical



decision-making and long-term outcomes. This advancement will reduce dependence on external testing and bring sophisticated diagnostic capability closer to our patients. Another milestone in PATHWEL's journey—from compassionate care to advanced, evidence-based hematology.

A Moment of Honour at the Mega Azadi Show

On August 12, 2026, Maj Gen (R) Prof Dr Parvez Ahmed, Medical Director of PATHWEL Center of Hematology & Bone Marrow Transplant, was honoured at the Mega Azadi Show for his distinguished contributions to medicine, healthcare, and humanitarian service. He received a commemorative souvenir from His Excellency Khazar Farhadov, Ambassador of Azerbaijan to Pakistan, and Mr Saeed Ahmed Shaikh, Director General, Pakistan Broadcasting Corporation. The event was graced by Mr Attaullah Tarar, Federal Minister for Information & Broadcasting, as Chief Guest. The recognition reflects Dr Parvez Ahmed's enduring commitment to serving humanity



and remains a source of pride and inspiration for the entire PATHWEL family.

Growing Together: Welcoming Our New Colleagues



We are delighted to welcome Dr Iqra Zeb Qureshi to the PATHWEL family. Having successfully completed her fellowship training in Hematology, she now joins our laboratory team as Registrar, bringing valuable knowledge, skills, and dedication to our expanding group of healthcare professionals.

We are confident that Dr Iqra's expertise will strengthen our laboratory services and contribute meaningfully to patient care. We wish her a rewarding, successful, and fulfilling journey with PATHWEL. Welcome aboard!

PATHWEL is pleased to welcome Dr Anam Humayun, who is joining us to begin her fellowship training in Clinical Hematology.

We are excited to have her embark on this important journey with our team and hope her time at PATHWEL will be filled with learning, growth and meaningful experiences in the care of patients with blood disorders.

Welcome to PATHWEL, Dr Anam! We wish you every success in your fellowship journey.



Blood Camps' Diary

Every blood donation is an act of kindness that becomes a lifeline for someone waiting for a transfusion. For children living with thalassemia, regular blood transfusions are not an occasional need—they are an essential part of life. Behind every unit donated is a person who chose to give a little of themselves so that another person could continue to live, grow and dream.



PATHWEL is deeply grateful to every voluntary donor, institution, organization and community partner who supported our blood donation camps during May and June. From universities and workplaces to public spaces and community organizations, each venue became a place where compassion was transformed into action. We are especially thankful to those who gave their time, encouraged others to donate and helped spread awareness about thalassemia prevention.

To every donor: your generosity gives more than blood—it gives hope, strength and another tomorrow.

NUTECH University, Islamabad | 13 May 2026

PATHWEL launched its May–June blood camp series at the National University of Technology (NUTECH), Islamabad, on 13 May 2026. The drive included an awareness session on voluntary blood donation and thalassemia prevention, led by Dr Syed Kamran Mahmood. Students and university community members participated in discussions emphasizing the importance of safe and regular blood donations. NUTECH's strong partnership with PATHWEL continues to support awareness activities and blood drives. The camp highlighted the vital role educational institutions play in encouraging youth participation and fostering a culture of voluntary blood donation nationwide.



Allama Iqbal Park, Rawalpindi | 6 June 2026

With educational institutions closed for summer, PATHWEL organized a community blood donation camp at Allama Iqbal Park, Rawalpindi, on 6 June 2026. The Parks and Horticulture Authority (PHA) provided valuable support, helping PATHWEL reach donors for children with thalassemia. The park setting allowed direct public engagement and emphasized that voluntary blood donation can sustain patients requiring regular transfusions. The initiative reflected PATHWEL's commitment to expanding donation opportunities beyond institutions and making them accessible across wider community spaces.



Centaurus Mall, Islamabad | 8–9 June 2026

PATHWEL held a two-day blood donation drive at Centaurus Mall, Islamabad, on 8 and 9 June 2026. The camp received generous support from Sardar Yasir Ilyas Khan, who had earlier pledged assistance for children with thalassemia. The mall's busy public setting enabled PATHWEL to engage diverse community members and encourage voluntary blood donation. The initiative underscored the importance of partnerships and showed how organized action, public awareness, and community goodwill can support patients who depend on regular transfusions.



Evacuee Trust Complex, Islamabad | 15 June 2026

PATHWEL organized a blood donation camp at the Evacuee Trust Complex, Islamabad, on 15 June 2026, strengthening institutional support for thalassemia patients. Chairman Evacuee Trust, Mr. Qamar Uz Zaman, and PATHWEL Medical Director, Maj Gen (R) Prof Dr Parvez Ahmed, discussed future collaboration and measures to improve patient assistance. Mr. Bilal, Deputy Administrator, ETPB Islamabad, coordinated and supported the initiative. The camp underscored how institutional partnerships can expand voluntary blood donation opportunities and build a dependable support network for children requiring regular blood transfusions throughout their lives.



Green Trust Tower, Blue Area, Islamabad | 17 June 2026

Following the successful collaboration at the Evacuee Trust Complex, PATHWEL organized another blood donation camp on 17 June 2026 at Green Trust Tower in Islamabad's Blue Area. The initiative was made possible through the continued cooperation of the Chairman Evacuee Trust and the close coordination of Mr. Bilal, Deputy Administrator, ETPB. Their support enabled PATHWEL to extend the blood donation campaign to another workplace and community setting. The camp demonstrated how one successful partnership can open the door to further opportunities for helping thalassemia patients. By bringing blood donation closer to people at their places of work, PATHWEL continues to encourage a culture of voluntary donation and collective responsibility for patients who require regular transfusions.

**Committee Chowk, Dhoke Khabba, Rawalpindi | 24 June 2026**

On 24 June, PATHWEL conducted a community blood drive at Committee Chowk, Dhoke Khabba, Rawalpindi, in collaboration with Saqi Kausar Medical Foundation. The initiative was supported by Mr. Muhammad Naseer Khan, who personally obtained approval from the Deputy Commissioner, Rawalpindi, to organize the drive. His wife and daughter also joined the PATHWEL team, offering wholehearted support throughout the day despite the intense summer heat. Their dedication reflected a strong spirit of community service and commitment to thalassemia patients. Held in a busy roadside location, the camp encouraged the public to donate blood and support this vital cause.

**CUST Students Complete VIS Programme at PATHWEL**

The second batch of students from Capital University of Science & Technology (CUST) successfully completed their Volunteer in Service (VIS) programme at PATHWEL in August 2026, completing 65 credit hours of meaningful community service. Throughout their placement, the students demonstrated enthusiasm, discipline, and a strong spirit of volunteerism. They actively participated in PATHWEL's blood drives and supported various in-house departments, gaining valuable exposure to the organization's operations and patient-care environment. Their contributions were particularly valuable in the Thalassemia Ward, Blood Bank, and Laboratory, where they assisted with routine activities and supported staff. The

programme was conducted in close coordination with Mr. Naeem Saud and Ms. Dur-e-Shehwar Sagheer, Director VIS, who guided and facilitated the students throughout their placement. PATHWEL appreciates their dedication and looks forward to welcoming more young volunteers.

**Foundation University Rawalpindi Students Bring Smiles to PATHWEL**

Students from the Foundation University Rawalpindi Campus (FURC) visited PATHWEL as part of their Civics & Community Engagement project. The visit provided an opportunity for the students to connect with thalassemia patients and understand their experiences.

They spent quality time with the patients, distributed gifts among everyone, and participated in various fun games and activities. Their warm interaction brought smiles, joy, and a welcome sense of companionship to the patients. PATHWEL appreciates the students' thoughtful initiative and their spirit of community service.



PATHWEL on Radio Pakistan: A Voice for Thalassemia Prevention

On 29th June, PATHWEL participated in a special podcast series at Radio Pakistan Headquarters, Islamabad, focusing on thalassemia prevention and the vital importance of voluntary blood donation. Prof Dr Parvez Ahmed shared valuable insights on preventing thalassemia and appealed to the public to support patients through regular blood donation. The podcast was hosted by Mr Imran Javed, Director, Radio Pakistan Headquarters, providing an important platform to raise awareness and promote community responsibility.



PATHWEL Team Attends Blood Conference

On 1st August, PATHWEL's Medical Superintendent Dr Nasir Mahmood, PRO, Thalassemia Ward staff, and patients attended a blood conference at the Islamabad Chamber of Commerce & Industry (ICCI), organized by Blood Chain Pakistan. The event, attended by healthcare professionals and stakeholders, was graced by Faisal Karim Kundi, Governor Khyber Pakhtunkhwa, as Chief Guest. The conference highlighted the importance of voluntary blood donation.



Picture Quiz: Answer

Peripheral Blood Erythrophagocytosis in Plasmodium falciparum Malaria

Teresa Almeida^{1,2} | Cristina Avelar Ferreira¹

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²Dept. of Biomedicine, Faculty of Medicine, University of Porto, Porto, Portugal

American Journal of Hematology, 2026; 0:1 <https://doi.org/10.1002/ajh.70280>

The engulfed red blood cell contains a clearly identifiable intraerythrocytic trophozoite. The diagnosis of *P. falciparum* malaria was confirmed by a rapid diagnostic test, observation of characteristic gametocytes on the thin blood smear, & detection of parasite DNA by PCR. Parasitemia at admission was 3.3%.

Hemophagocytosis is most commonly observed in the bone marrow or reticuloendothelial organs and is rarely identified in peripheral blood. In malaria, parasitized erythrocytes undergo membrane alterations and opsonization, recognition and clearance by cells of the monocyte-macrophage system, contributing to anemia as part of the host immune response [1]. Direct erythro-

phagocytosis by circulating monocytes reflects targeted immune clearance rather than dysregulated hemophagocytic syndromes and contributes to malarial anemia, even in the absence of severe or complicated disease.

Acknowledgment

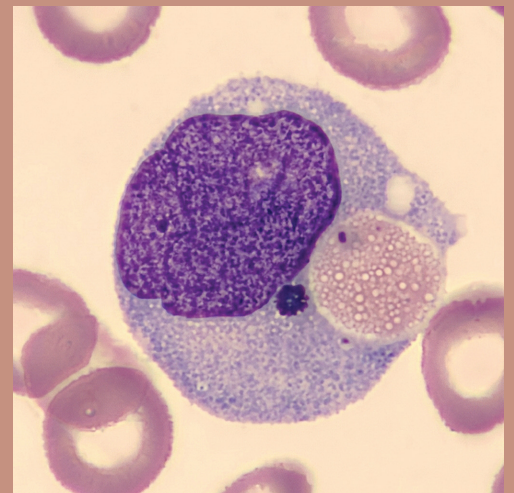
Open access publication funding provided by FCT (b-on).

Conflicts of Interest

The authors declare no conflicts of interest.

Reference

1. P. A. Buffet, I. Safeukui, G. Deplaine, et al., "The Pathogenesis of Plasmodium falciparum Malaria in Humans: Insights From Splenic Physiology," *Blood* 117, no. 2 (2011): 381–392.



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PATHWEL Stars by Dr Khalil Ur Rahman, Consultant Clinical Hematology & BMT

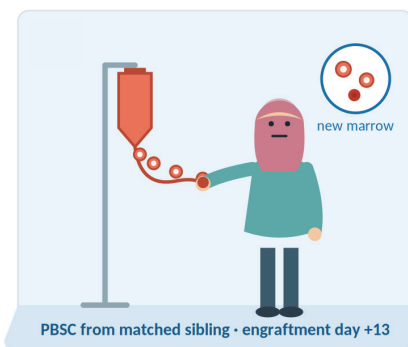
From a Life-Threatening Leukemia to a New Lease on Life



In February 2024, 49-year-old Fatima Ahmed arrived with fever and bleeding gums. Tests revealed acute myelomonocytic leukemia, a form of acute myeloid leukemia (AML), with about 65% blasts in her bone marrow. Molecular testing also detected FLT3-ITD, a mutation linked with a higher risk of relapse. The diagnosis was frightening, but Fatima and her family committed themselves to the demanding treatment ahead.

She began intensive chemotherapy and achieved remission. Follow-up marrow examinations showed a dramatic fall in leukemia cells, and FLT3 testing became negative. After consolidation therapy, another source of hope emerged: her brother, Ahmed Khan, was a fully HLA-matched donor and could provide the stem cells needed for transplantation.

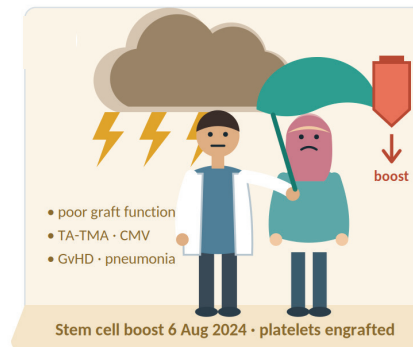
A Major Step: Bone Marrow Transplantation



On 7 May 2024, while in her first complete remission, Fatima underwent an allogeneic hematopoietic stem cell transplant using peripheral blood stem cells from her brother. Her new cells began producing neutrophils by day +13, an encouraging early milestone. Recovery, however, was far from straightforward. Fatima developed poor graft function, transplant-associated thrombotic microangiopathy, neutropenic fever, severe mucositis, liver and kidney dysfunction, diarrhea, cytomegalovirus reactivation, and

repeated electrolyte disturbances. Through each setback, the transplant team provided intensive monitoring, infection control, transfusions, medicines, and supportive care.

When the Graft Needed a Boost



Because her graft remained weak, she received an additional peripheral blood stem cell boost from the same donor on 6 August 2024. The boost helped her platelets engraft. In the months that followed, she returned several times with low potassium, gastrointestinal symptoms, graft-versus-host disease, and generalized weakness. Each episode required careful treatment, yet she repeatedly recovered enough to leave hospital in stable condition.

Another Major Challenge

In November 2025, Fatima faced another life-threatening crisis. Fever, cough, breathlessness, and dangerously low oxygen levels led to admission. Chest imaging initially suggested pulmonary tuberculosis, and treatment was started, but her breathing worsened and she needed intensive care, oxygen, and broad-spectrum antimicrobial therapy.

After specialist review, *Pneumocystis jirovecii* pneumonia was considered more likely. Fatima was treated with high-dose co-trimoxazole and corticosteroids. Her response was remarkable: within 48 hours, her breathing improved significantly and she no longer required supplemental oxygen.

Fatima's journey—from high-risk molecular AML through chemotherapy, transplantation, severe complications, a stem-cell boost, and a major respiratory infection—reflects extraordinary resilience. Today, she is stable and living without significant health problems. Her recovery demonstrates what coordinated multidisciplinary care, timely intervention, and determined follow-up can achieve.

Her brother's role as a fully matched donor was pivotal, as was the continuous support of her family. Their presence helped sustain her through prolonged treatment, repeated admissions, uncertainty, and physical exhaustion. The care team's persistence matched her own, turning a series of medical emergencies into steps toward lasting recovery.

A Message of Hope



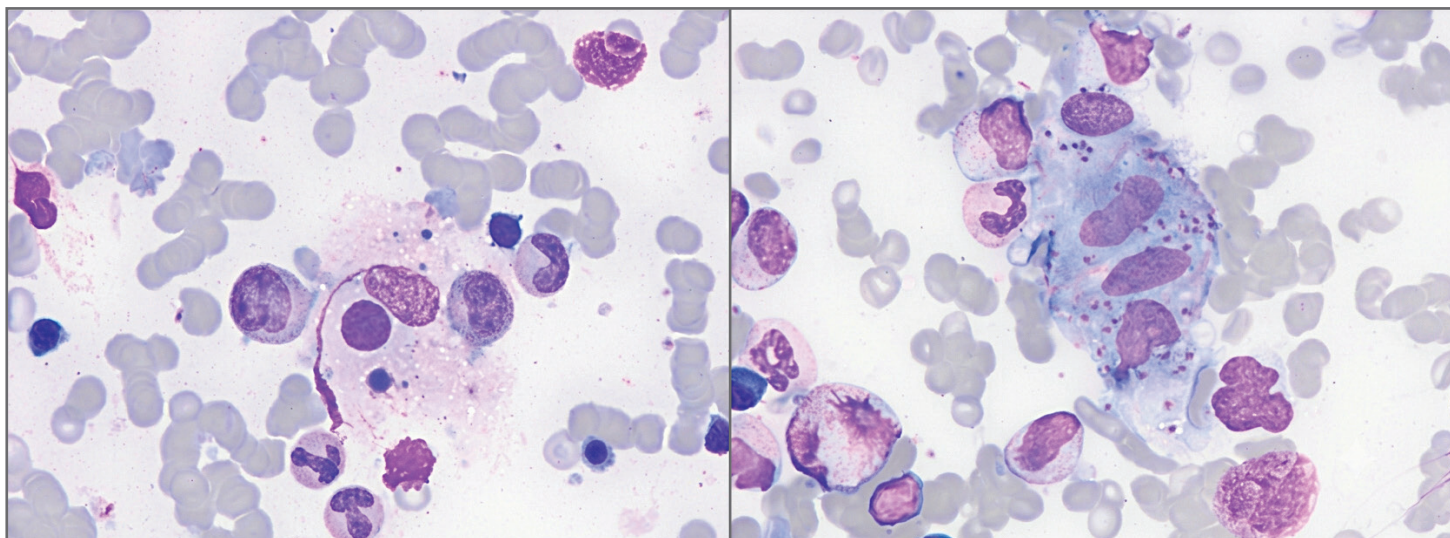
Fatima's story is not only about leukemia or transplantation. It is about courage, family, skilled care, and the refusal to surrender when recovery becomes difficult. For patients and families confronting blood cancer, her experience offers a realistic but hopeful message: the path may include setbacks, yet sustained treatment and support can still lead to a meaningful future.

At PATHWEL Center of Hematology & Bone Marrow Transplant, every successful transplant represents more than a medical achievement—it represents a life given another chance.

Morphology Updates

When macrophages have more than one thing to show

Hachem Abou Moustafa, Maillys Le Guyader, Pierre Loiseau, Yohann Le Govic, Thomas Boyer; DOI: 10.1111/bjh.70618



A 31-year-old man with no prior medical history was hospitalised in the internal medicine department for asthenia, fluctuating pyrexia at 39–40°C for 3 weeks, night sweats and anorexia (10 kg weight loss in 1 month). Computed tomography of the thorax, abdomen and pelvis imaging revealed hepatosplenomegaly. He reported a stay in Ardèche (France) 15 months before the onset of symptoms. A full blood count revealed pancytopenia: leucocyte count of $1.7 \times 10^9/L$ (with no hypereosinophilia), haemoglobin concentration of 81 g/L and platelet count of $67 \times 10^9/L$. Due to the persistence of cytopenias, a bone marrow aspiration was performed, showing signs of haemophagocytosis (left, May–Grünwald–Giemsa staining, objective $\times 100$) and Leishman–Donovan bodies (right, MayGrünwald–Giemsa staining, objective $\times 100$). The diagnosis of visceral leishmaniasis (VL), later supported by polymerase chain reaction (PCR), associated with macrophage activation syndrome (MAS), as the patient fulfilled several diagnostic criteria including fever, organomegaly, pancytopenia, hyperferritinaemia, hypertriglyceridaemia,

hypofibrinogenaemia and elevated aspartate aminotransferase (AST).¹ For VL, treatment with liposomal amphotericin B was initiated for 5 days, in combination with hydrocortisone for MAS. At the 1-month follow-up, a dramatic improvement of clinical and biological parameters was observed, with apyrexia, disappearance of hepatosplenomegaly and normalisation of the blood count.

MAS or haemophagocytic lymphohistiocytosis is a rare but life-threatening syndrome. It can arise from genetic disorders (rare) or secondary causes such as infection (mostly viral), autoimmunity or malignancy. The pathophysiological mechanism of MAS is thought to be based on a major dysregulation of the immune response, marked by excessive and uncontrolled production of pro-inflammatory mediators, responsible for systemic inflammation and multiorgan failure. Identifying the underlying trigger of a MAS episode is essential, as adjunctive therapies in the acute setting may vary depending on associated disorders. VL is a rare cause of MAS and remains a diagnostic challenge due to similar

clinical presentations; however, the frequency of MAS in patients diagnosed with VL is high, at around 40%.² Physicians should consider the diagnosis of VL in patients presenting with fever and pancytopenia who have travelled to a department located in an endemic area, as in the present case.

ACKNOWLEDGEMENTS

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The authors have nothing to report.

ETHICS STATEMENT

The authors have nothing to report.

PATIENT CONSENT STATEMENT

The patient's consent has been obtained.

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2. Horrillo L, Castro A, al Matia B e. Clinical aspects of visceral leishmaniasis caused by *L. infantum* in adults. Ten years of experience of the largest outbreak in Europe: what have we learned? *Parasit Vectors*. 2019;12(1):359. <https://doi.org/10.1186/s13071-019-3628-z>

Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

Gut Feeling: How the Microbiome Shapes Outcomes after Bone Marrow Transplant

Hao W, Stocker N, Gaugler B, Mohty M, Malard F. The Role of the Gut Microbiota in Allogeneic Hematopoietic Cell Transplantation. *American Journal of Hematology*. 2026;101:1980-1996. doi:10.1002/ajh.70360.

Allogeneic hematopoietic cell transplantation (allo-HCT) remains the only curative option for many high-risk blood cancers, but conditioning chemotherapy, radiotherapy, and broad-spectrum antibiotics disrupt the gut's bacterial ecosystem, a state called dysbiosis. This review by Hao et al. (Sorbonne Universite, Paris) synthesizes evidence that a diverse, intact gut microbiota protects the intestinal barrier, regulates donor T-cell and regulatory T-cell (Treg) responses, and lowers the risk of graft-versus-host disease (GVHD), infection, and non-relapse mortality. Loss of microbial diversity, often driven by broad-spectrum antibiotics and conditioning intensity, correlates with worse survival and higher acute GVHD rates, and specific bacterial taxa are

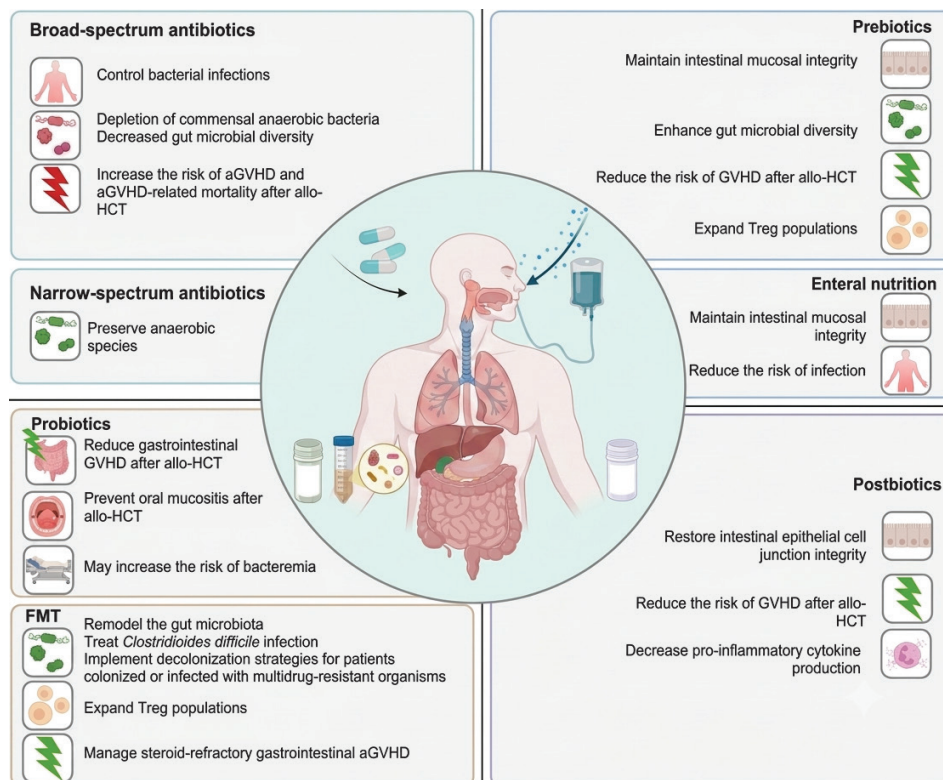
being explored as biomarkers of risk.

Microbial metabolites act as key mediators: short-chain fatty acids, secondary bile acids, and tryptophan-derived indoles strengthen intestinal tight junctions, expand Tregs, and dampen inflammation.

The review outlines emerging strategies to restore a healthy microbiome around transplant: antibiotic stewardship, enteral nutrition, prebiotics, probiotics, fecal microbiota transplantation (FMT), and postbiotics (summarized in Figure 2, below). FMT and the microbiome therapy MaaT013 have shown genuine efficacy against steroid-refractory gastrointestinal GVHD in phase III data, while probiotics carry a caution, as over-the-count-

er formulations have been linked to bacteremia in immunocompromised patients.

For transplant setups in Pakistan, the appeal is cost as much as biology. Antibiotic stewardship, early enteral feeding, dietary prebiotics, and judicious probiotic or FMT use are inexpensive relative to second- and third-line GVHD therapies such as ruxolitinib, extracorporeal photopheresis, or novel biologics. In resource-limited, donation-funded centers such as ours, these low-cost, microbiota-conscious measures could meaningfully reduce GVHD incidence and the downstream cost of treating it, though most interventions still need confirmatory randomized trials before routine adoption.



Probiotics

Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host (e.g., select *Lactobacillus* strains).

Prebiotics

Substrates selectively utilized by host microorganisms that confer a health benefit (e.g., inulin, fructo-oligosaccharides, resistant starch).

Postbiotics

Preparations of inanimate microorganisms and/or their components (e.g., short-chain fatty acids, indole derivatives) that confer a health benefit on the host.

FMT

Fecal microbiota transplantation: infusion of stool from a healthy donor (or the patient's own pre-treatment stool) to restore a disrupted gut microbiota.

SCFAs

Short-chain fatty acids (e.g., butyrate, propionate, acetate) produced by bacterial fermentation of dietary fiber; strengthen the gut barrier and regulate immune cells.

Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

Assessment of response in Hairy cell leukemia Source: Clive S. Zent, et al (Updated consensus guidelines for the diagnosis and management of patients with HCL and HCL variant) <https://doi.org/10.1182/blood.2025032757>

Response	Definition
CR	- Peripheral blood counts (without transfusions or growth factors): hemoglobin > 11 g/dL, platelets >100 x 10⁹/L, and absolute neutrophil count > 1.5 x 10⁹/L* - Absence of morphologic evidence of HCL on both the peripheral blood smear and the bone marrow biopsy† - Resolution of splenomegaly on physical examination
CR MRD‡	In patients who achieve CR, MRD can be assessed by IHC on the bone marrow biopsy and/or by flow cytometry or molecular techniques in the bone marrow aspirate and/or blood to separate CR with or without MRD in the marrow and/or blood.
PR	- Peripheral blood counts as in CR* - An improvement of ≥50% in bone marrow infiltration by HCL assessed in the bone marrow biopsy using IHC - An improvement of ≥50% in splenomegaly
NR	No CR, PR, or PD
PD	A decline of ≥25% in blood count(s) (not because of iatrogenic myelosuppression) and/or ≥25% increase in splenomegaly and/or worsening of HCL-related symptoms
Relapse after response (CR or PR)	HCL-induced reappearance of cytopenia(s) below the thresholds defined above for CR and PR§.

Response to treatment with cladribine, which is usually delivered in a 5-day course, should be assessed 4 to 6 months later because bone marrow recovery and HCL cell clearance can be slow. Following treatment with pentostatin (which is delivered every 2 weeks for up to 12 doses), response should be assessed when blood counts reach the criteria for CR.

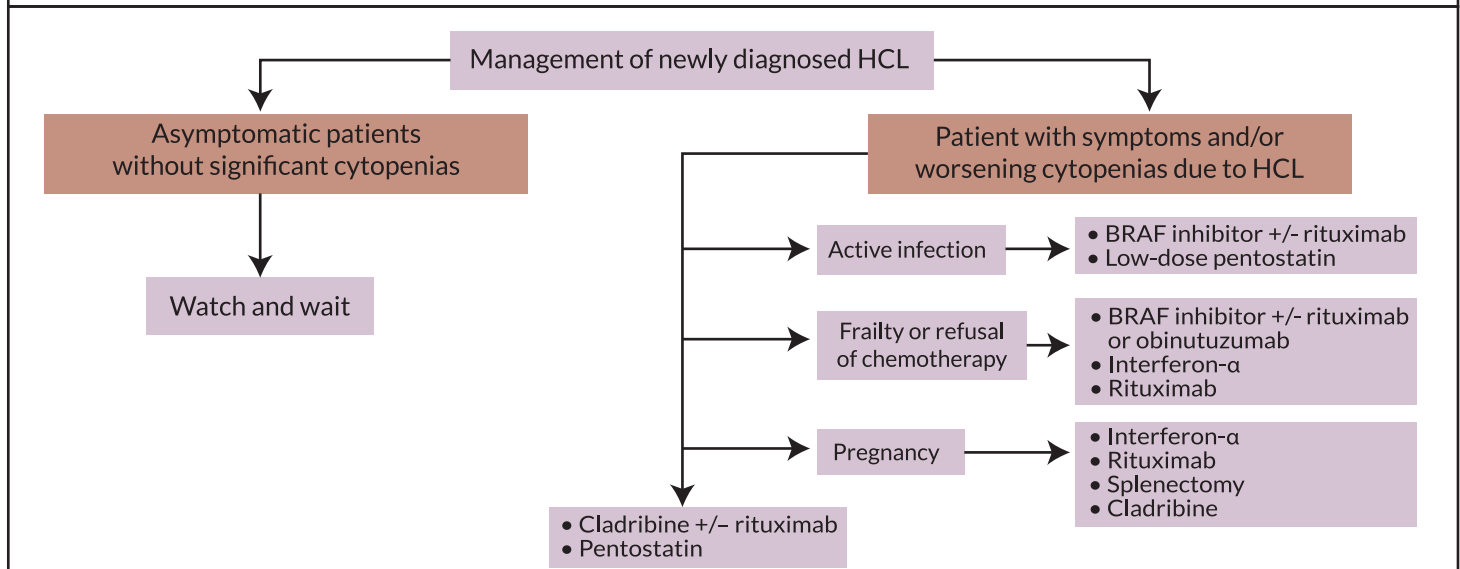
IHC, immunohistochemistry; NR, no response; PD, progressive disease.

*In the setting of a supportive bone marrow biopsy (criterion 2), CR or PR can be declared even if the thresholds for improvement of cytopenias are not met because of causes other than HCL (eg, CR with incomplete resolution of anemia because of concomitant iron deficiency). Similarly, splenomegaly may not fully resolve after therapy because of causes other than HCL.

†Due to the intrinsic subjectivity of, and variability in, evaluating a bone marrow or blood sample without the help of immunophenotyping, an additional criterion has been used by some investigators. This requires that the bone marrow biopsy has ≤10% HCL infiltration by IHC to confirm CR.

‡The clinical value of MRD is uncertain, especially after first-line treatment with purine analogues, and MRD testing in HCL is currently not standardized.

§The simple reappearance in the blood and/or marrow of MRD or even of HCL cells recognizable by morphological stains may not be followed by relapse of cytopenias for years (especially after first-line treatment); therefore, its clinical significance remains uncertain.



TransplantTidings

TransplantTidings

TransplantTidings

PTCy or ATG for HLA-Matched Transplantation in Myelofibrosis

Chiusolo P, et al. Am J Hematol. 2026;101:1192–1195. Retrospective, propensity-score weighted, 21 centers

STUDY	KEY RESULTS (4-YR, ATG VS PTCY)		KEY TAKEAWAY
- 539 adults, HLA-matched HSCT for myelofibrosis, 2010–2024 - 427 received ATG · 112 received PTCy - IPTW propensity-score adjustment + matched cohort analysis - Endpoints: engraftment, GVHD, relapse, NRM, OS, GRFS	14 vs 23d Neutrophil engraftment (p<0.001)	1 vs 7% Primary graft failure (p<0.001)	
	14 vs 33% Relapse incidence (p<0.001)	50 vs 23% Chronic GVHD (p<0.001)	• KEY TAKEAWAY 01 OS and GRFS were similar with ATG and PTCy. ATG gave faster engraftment and less relapse; PTCy halved chronic GVHD (HR 0.60). Choose prophylaxis by dominant risk: relapse vs. chronic GVHD.

DOI: 10.1002/ajh.70244

Refining Busulfan Exposure Improves Pediatric ALL HSCT Outcomes

FORUM StudyBen Hassine K, et al. Blood Adv. 2026;10:3719–3730. Prospective international phase 3 cohort.

STUDY	KEY RESULTS		KEY TAKEAWAY
- 145 children with ALL, fludarabine–busulfan–thiotepa conditioning - IPK-modelled busulfan exposure (cumulative AUC) - Matched vs. 51 TBI-conditioned recipients (post-hoc) - Endpoints: EFS, GRFS, OS, relapse, toxicity	73–98 Optimal busulfan cAUC, mg·h/L	1.93× 02 EFS risk if non-optimal (p=0.008)	
	2.01× GRFS risk if nonoptimal (p=0.002)	≈ TBI EFS/GRFS/OS if exposure optimal	• KEY TAKEAWAY Keeping busulfan cAUC within 73.398.0 mg·h/L (underexposure raises relapse, overexposure raises toxicity/GVHD) matches TBI-level outcomes – supporting TDM-guided busulfan as an irradiation-free option.

DOI: 10.1182/bloodadvances.2025019142

Treosulfan–Fludarabine Conditioning in Infants with SCID

Extended UK StudyLum SH, et al. Br J Haematol. 2026;208:1713–1723. UK multicentre retrospective cohort, 2006–2022.

STUDY	KEY RESULTS		KEY TAKEAWAY
- 104 infants with SCID, first HSCT, treosulfan–fludarabine conditioning - Median follow-up 5.4 years - Multivariable analysis of OS/EFS predictors - Endpoints: OS, EFS, endothelial toxicity, chimerism, Ig freedom	81 / 77% 5-yr overall / eventfree survival	1 vs 7% Endothelial cell dysfunction	
	92% Survivors free of Ig replacement	HR 3.9–5.6 Chronic GVHD (p<0.001)	• KEY TAKEAWAY Treosulfan–fludarabine gives 81% 5yr survival with low endothelial toxicity in infant SCID HSCT. Pretransplant CMV infection and undefined genotype are the strongest predictors of failure – supports early diagnosis and referral.

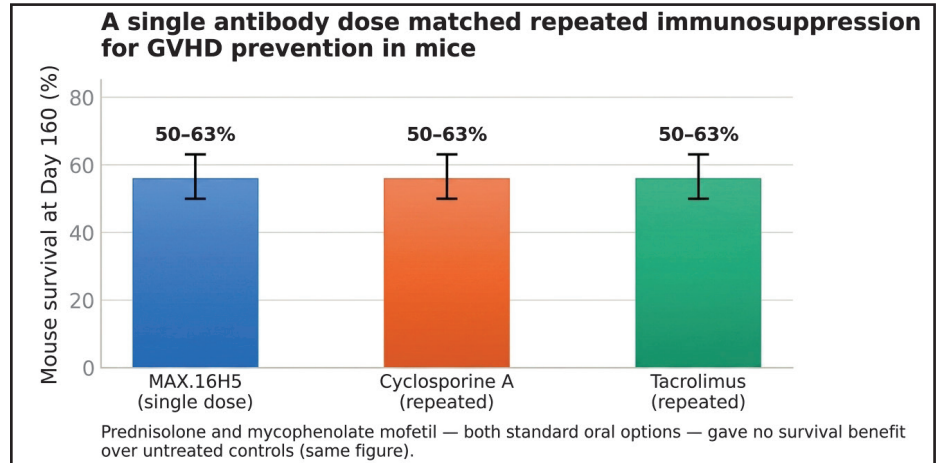
DOI: 10.1111/bjh.70453

Transplant Tidings Transplant Tidings Transplant Tidings

A one-time antibody “dip” of the graft may replace months of GVHD drugs

Preventing GVHD currently means months of immunosuppressive drugs that raise the risk of infection and leukaemia relapse. A German team tested a different approach: treating the donor graft itself, once, before infusion, with a non-depleting antibody (MAX.16H5) that quiets CD4+ T-cells rather than killing them.

In laboratory assays, the antibody cut T-cell proliferation by about 59% and pushed cells toward a calming, IL-10-driven state rather than classic regulatory T-cells. In a humanised mouse model followed for 160 days, this single pre-treatment prevented GVHD as effectively as repeated



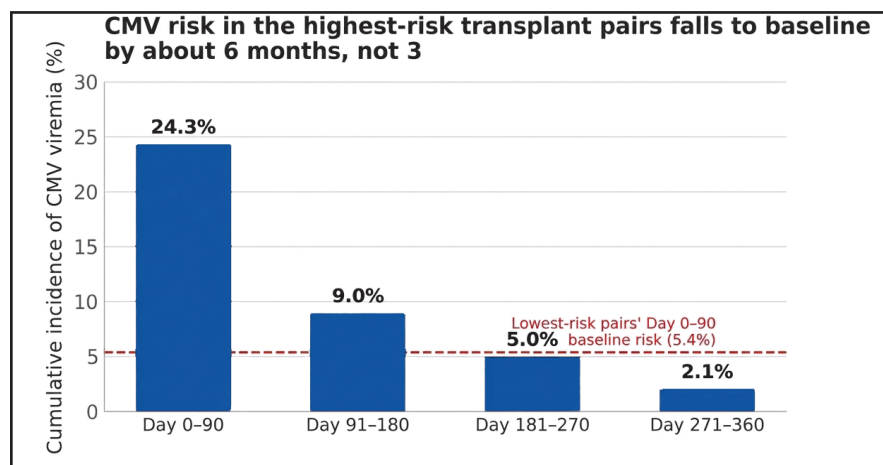
dosing with cyclosporine or tacrolimus (50-63% survival), while standard steroids and mycophenolate mofetil failed outright. If confirmed in humans, a one-time graft treatment

could replace months of systemic immunosuppression, sparing patients its infection and organ-toxicity burden. A first-in-human phase 1 trial is now being prepared.

Roth K, Loeffler D, Blumert C, et al. Anti-CD4 antibody-modulated transplants for GVHD prevention in hematopoietic cell transplantation. *Blood*. 2026;147(20):2402–2412. doi:10.1182/blood.2025031370 — Blood · 2024 Impact Factor 23.1

When is it safe to stop CMV prophylaxis? New data point to about 6 months

Letermovir has transformed early cytomegalovirus (CMV) prevention after stem cell transplant, but how long the risk lasts, and how long prophylaxis should continue, has been unclear. In the largest single-centre study to date (2,106 patients), researchers tracked CMV reactivation from day 90 to day 360 post-transplant. In the highest-risk pairs (CMV-negative donor, CMV-positive recipient), the chance of significant CMV viraemia fell steadily: from 24% in the first 90 days to 9% by day 180, 5% by day 270, and just 2% by day 360, converging on the baseline risk of the lowest-risk pairs by around day 180-270. Active graft-versus-host disease was consistently the strongest



driver of late CMV, outweighing every other factor studied. Letermovir's protective effect was clear only in the first 90 days. These findings suggest letermovir prophylaxis could reason-

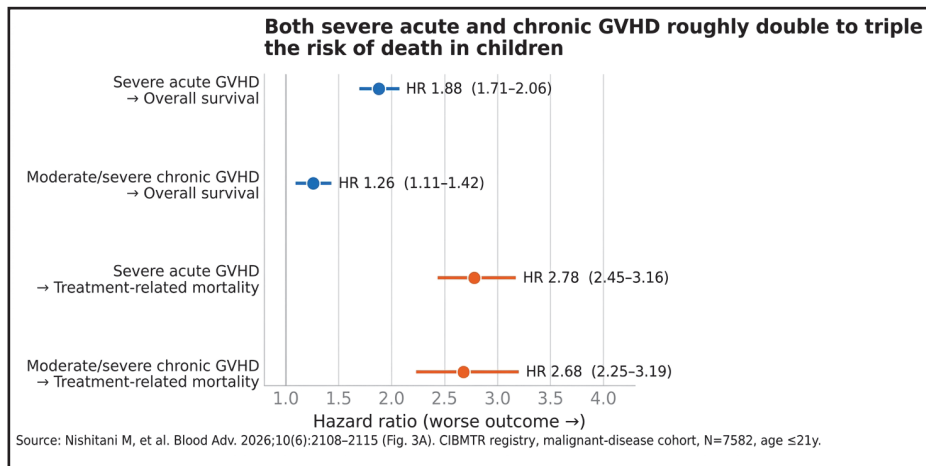
ably be stopped around day 180 in most patients, rather than continued indefinitely, without an apparent rise in CMV risk.

Chen GL, Bassett R, Mehta RS, et al. Late Cytomegalovirus Infections After Allogeneic Hematopoietic Cell Transplant. *Am J Hematol*. 2026;101:1828–1838. doi:10.1002/ajh.70347 — American Journal of Hematology · 2024 Impact Factor 9.9

Transplant Tidings Transplant Tidings Transplant Tidings

Teenagers and young adults carry a heavier GVHD burden than younger children

Does a child's age at transplant change their risk from graft-versus-host disease (GVHD)? This CIBMTR registry study of over 14,000 children and young adults (aged 0-21) transplanted for cancer or non-cancer blood disorders found that adolescents and young adults (13-21 years) had a higher risk of moderate-to-severe chronic GVHD than younger children, and, among those transplanted for non-malignant disease, a higher risk of severe acute GVHD too. Regardless of age, both severe acute GVHD and significant chronic GVHD roughly doubled to nearly tripled the risk of death. Five-year survival was lowest in the oldest group (51% in adoles-



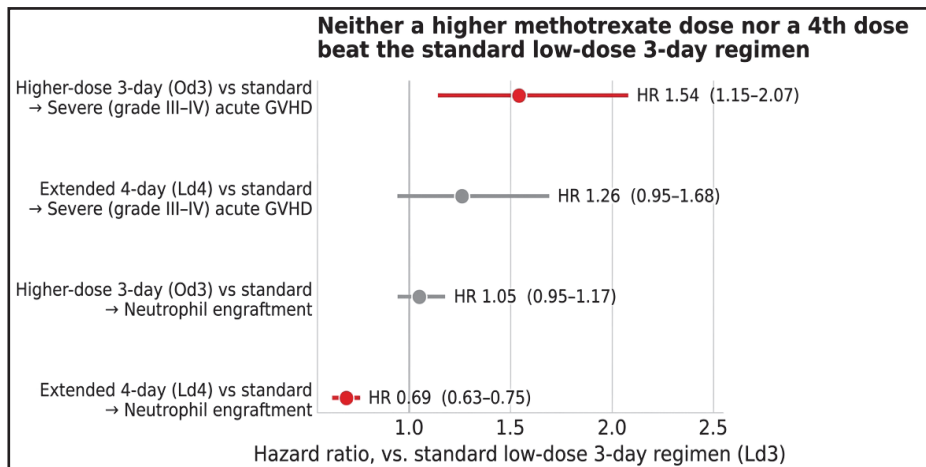
cents/young adults with cancer, versus 58% in school-age children). The findings argue for age-aware counseling before transplant and support including teenagers and young adults

more deliberately in trials testing newer GVHD-prevention strategies, since this group carries a measurably higher burden of this life-threatening complication than younger children do.

Nishitani M, Graham RA, Wang T, et al. Impact of age on graft-versus-host disease and overall survival in pediatric hematopoietic cell transplant recipients. Blood Adv. 2026;10(6):2108-2115. doi:10.1182/bloodadvances.2025017393 — Blood Advances · 2024

More methotrexate is not better methotrexate for GVHD prevention

Methotrexate (MTX) combined with a calcineurin inhibitor remains the most widely used regimen worldwide for preventing GVHD, yet the ideal MTX dose and schedule has never been rigorously tested. This nationwide Japanese registry study compared three regimens in 2,537 patients receiving matched transplants: the now-common low-dose 3-day schedule, a low-dose 4-day schedule (adding a day-11 dose), and the original, higher-dose 3-day schedule. All three gave similar rates of overall acute & chronic GVHD, survival, relapse, & infection. However, the higher original dose unexpectedly raised the risk of severe (grade III-IV) acute GVHD by 54%, & the extended



4-day schedule meaningfully delayed neutrophil engraftment without any GVHD benefit. In other words, giving more MTX, or giving it for longer, bought no extra protection and cost

more toxicity. This is reassuring, practice-affirming evidence that the standard low-dose, 3-day regimen already in widespread use remains the sensible default choice.

Suzuki T, Jo T, Yoshifuji K, et al. Impact of methotrexate-dosing regimens for GVHD prophylaxis on clinical outcomes of HLA-matched allogeneic HSCT. Br J Haematol. 2026;208:219-228. doi:10.1111/bjh.70213 — British Journal of Haematology · 2024

Persistent and Recurrent Bleeding in Severe Haemophilia A With a Previous Factor-VIII Inhibitor

Reported by Ms. Hina Fatima



The development of factor VIII (FVIII) inhibitors remains one of the most challenging complications in the management of severe haemophilia A. Patients with a previous inhibitor may experience bleeding that is difficult to control even when no inhibitor is detectable during a subsequent episode. In such circumstances, treatment decisions should be guided not only by laboratory findings but also by the patient's inhibitor history and, importantly, the clinical response to replacement therapy.

Case Presentation

We report the case of a child with severe haemophilia A and a previous FVIII inhibitor who developed persistent traumatic bleeding despite repeated FVIII administration. He subsequently experienced recurrent dental bleeding. Although the inhibitor assay was negative during admission, both episodes improved after administration of recombinant activated factor VII (rFVIIa).

A 7-year-old boy weighing 16 kg, with severe haemophilia A and a documented FVIII inhibitor in 2024, presented to the Emergency Department at the Pakistan Institute of Medical Sciences (PIMS), Islamabad, in March 2026 with persistent bleeding from a traumatic chin wound. He had a history of recurrent haemarthroses and haematomas requiring multiple hospital admissions. Despite repeated FVIII administration, adequate haemostasis was not achieved; his activated partial thromboplastin time (APTT) was prolonged at 81 seconds. Significant blood loss led to hypovolaemic shock, requiring packed red blood cell and fresh frozen plasma transfusions. Repeat inhibitor testing on 1 April 2026 detected neither an immediately acting nor a time-dependent FVIII inhibitor. Nevertheless, the clinical



response to repeated FVIII administration remained inadequate. rFVIIa was therefore administered, resulting in substantial improvement in bleeding control. Intermittent bleeding from the chin wound persisted and required further haemostatic intervention and surgical review. Approximately one week after control of the chin bleeding, the patient developed recurrent dental bleeding. This again responded poorly to FVIII alone & subsequently required rFVIIa. The patient was then transitioned to prophylaxis with emicizumab.

Discussion

This case highlights several important considerations in the management of severe haemophilia A.

1. Clinical Response in the Absence of a Detectable Inhibitor

In this patient, the following features provided important clinical evidence that FVIII replacement alone was

insufficient during the episode: history of an FVIII inhibitor; persistent bleeding despite repeated FVIII administration; an inadequate clinical response to replacement therapy; and subsequent improvement following rFVIIa administration.

2. Role of Bypassing Therapy

rFVIIa is an established bypassing agent for the management of acute bleeding in patients with haemophilia A and inhibitors. In this case, its introduction was associated with a clear improvement in haemostatic control.

3. Relevance of Previous Inhibitor History

The patient's inhibitor history from 2024 remained clinically relevant despite the absence of a detectable inhibitor during the current admission. A negative assay should therefore be interpreted alongside treatment history & observed clinical response.

4. Comprehensive Management of Recurrent Mucocutaneous Bleeding

The initial traumatic chin wound was followed by recurrent dental bleeding. These episodes required more than replacement therapy alone. Local wound care, surgical review, transfusion support, antifibrinolytic therapy, & bypassing therapy formed part of the comprehensive management approach.

5. Access to Bypassing Agents

A key feature of this case was the availability of rFVIIa. However, its high cost can severely limit access in low- and middle-income countries. In resource-constrained settings, obtaining bypassing therapy can be particularly difficult. Reliable access to appropriate haemostatic products, comprehensive haemophilia care, and prophylactic treatment is essential to reduce morbidity and prevent recur-



rent bleeding.

6. Transition to Prophylaxis

Prophylaxis is essential to prevent recurrent joint bleeding, chronic arthropathy, and disability. For patients with inhibitors, emicizumab—a non-factor therapy—has substantially expanded prophylactic treatment options.

The World Federation of Hemophilia Humanitarian Aid Program supports access to emicizumab in low- and middle-income countries.

Lessons From the Case

This case offers several practical lessons for clinicians caring for

children with severe haemophilia A:

1. A previous FVIII inhibitor remains clinically relevant even when a subsequent inhibitor assay is negative.
2. Persistent bleeding despite appropriate FVIII administration should prompt early reassessment of treatment efficacy: treat the patient, not the laboratory result alone.
3. Clinical response should be interpreted alongside laboratory inhibitor results.
4. Bypassing therapy should be considered when FVIII fails to achieve adequate haemostasis in a patient with a previous inhibitor.
5. Mucosal and dental bleeding may recur even after apparently successful

control of a major traumatic bleed.

6. Local haemostatic measures and antifibrinolytic therapy can be valuable adjuncts, particularly for dental and mucosal bleeding.
7. Reliable access to bypassing agents is critical for patients with current or previous inhibitors.
8. Patients with recurrent breakthrough bleeding should be assessed for an appropriate prophylactic strategy rather than managed solely with episodic treatment.
9. Multidisciplinary management involving haematology, surgery, emergency medicine, transfusion services, dentistry, and the haemophilia treatment team is essential in complex cases.

A once-a-month injection that outperforms intravenous factor prophylaxis

Mancuso ME, Chan AKC, Shanmukhaiah C, et al. Mim8 Bispecific Antibody Prophylaxis in Hemophilia A with or without Inhibitors (FRONTIER2). *N Engl J Med* 2026;394:1696–1709. Published 30 April 2026. doi:10.1056/NEJMoa2517384

Mim8 (denecimig) is a next-generation bispecific antibody that imitates activated factor VIII by bridging factor IXa & factor X. FRONTIER2 randomised 254 people aged 12 years and older with haemophilia A - 84% severe, 12% with inhibitors - to subcutaneous denecimig once weekly or once monthly, compared

against their previous treatment. Among those previously treated on demand, the annualised bleeding rate fell from 15.76 to 0.57 with weekly dosing & 0.20 with monthly dosing, reductions of 96% and 99%. Among those already receiving factor prophylaxis, bleeding fell by a further 54% (weekly) and 43% (monthly). Between

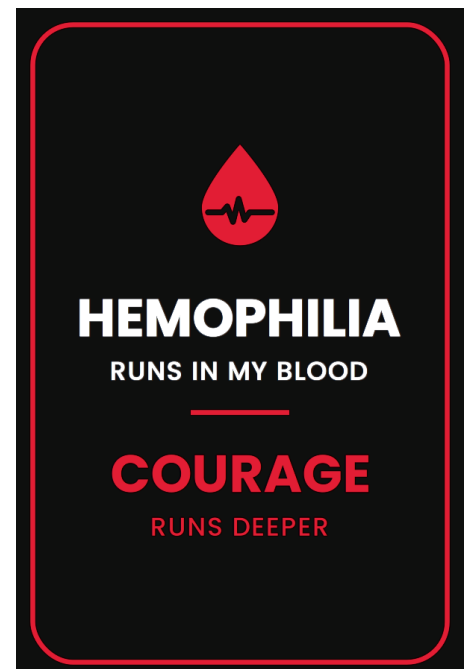
64% & 95% of participants on denecimig had no treated bleeds at all. Injection-site reactions occurred in 10% of participants; there were no thromboembolic events & no clinically significant neutralising antibodies. In short: a monthly subcutaneous injection gave better protection than intravenous factor prophylaxis.

Five years after a single infusion: the final word on HOPE-B

Pipe SW, Miesbach W, Recht M, et al. Final Analysis of a Study of Etranacogene Dezaparvovec for Hemophilia B. *N Engl J Med* 2026;394:463–474. doi:10.1056/NEJMoa2514332

Etranacogene dezaparvovec is a single-dose AAV5 gene therapy carrying the hyperactive Padua variant of factor IX. HOPE-B enrolled 54 men with haemophilia B (factor IX activity ≤ 2 IU/dL) who completed a lead-in period of factor IX prophylaxis before receiving one intravenous infusion; men were included regardless of pre-existing AAV5 antibodies. Five years on, mean factor IX activity was 36.1 ± 15.7 IU/dL — squarely in the mild range — and 96% of participants

showed transgene-derived expression. The annualised bleeding rate fell 63%, from 4.16 to 1.52, and 94% stopped prophylaxis altogether. Exogenous factor consumption dropped 96%, from about 257,000 to 11,000 IU per year. Adverse events attributed to the gene therapy clustered in the first six months and became uncommon thereafter, with no AAV-related malignancy and no late liver toxicity reported. Outcomes were similar in men who had baseline AAV5 antibodies.





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