income countries, factor replacement remains the only feasible option, in line with World Federation of Hemophilia (WFH) recommendations. **Conclusion:** Despite recent paradigm shifts in the treatment of pediatric hemophilia, factor replacement remains indispensable. Gene therapies hold promise for the future, but biological and ethical constraints currently prevent their application in children. Non–factor-based agents have facilitated prophylaxis but are insufficient in emergencies and lack long-term safety data, particularly in major surgical procedures and severe acute bleeding episodes. Factor replacement therapies, with their proven efficacy, predictable pharmacokinetics, established safety, and global accessibility, continue to stand as the gold standard treatment option for both today and the foreseeable future. *"A reference to a Turkish idiomatic saying, originally 'Introducing a new custom to an old village' (bringing new ways to an old place), which means introducing a revolutionary, unusual, or unexpected innovation or behavior into a traditional, clichéd order or way of doing things."

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Abstract 004

IRON CHELATİON İN MYELODYSPLASTİC SYNDROMES: WHO AND WHEN?

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Red blood cell (RBC) transfusions are the cornerstone of supportive care in patients with myelodysplastic syndromes (MDS). While transfusions alleviate symptomatic anemia, they inevitably lead to progressive iron accumulation in patients. This transfusional iron overload may exert toxic effects on the heart, liver, endocrine system, ultimately contributing to increased morbidity and mortality. Timely initiation of iron chelation therapy has become an important consideration in the comprehensive management of MDS. Chelation is primarily indicated for patients with lower-risk MDS (IPSS low or Int-1) who are expected to have longer survival, who remain transfusion-dependent. In such patients, iron overload not only threatens organ function also worsens prognosis. Multiple studies have shown that transfusion dependence is a negative prognostic factor, and retrospective analyses suggest that iron chelation may improve overall survival. Chelation is also particularly important in patients who are candidates for allogeneic stem cell transplantation, since excess iron has been associated with inferior transplant outcomes. By reducing systemic iron burden, chelation help optimize organ function and improve transplant eligibility. The decision is usually guided by transfusion history and serum ferritin levels. Most guidelines recommend considering chelation after approximately 20–30 units of RBC transfusions or when serum ferritin persistently exceeds 2500 ng/mL. The therapeutic goal is to maintain ferritin below 1000 ng/mL, minimizing iron-mediated oxidative stress and tissue damage. While serum ferritin is an imperfect surrogate, it remains a practical marker. More advanced techniques such as MRI T2* or SQUID can provide direct estimates of hepatic iron, but their availability is limited. Three chelators are currently in clinical use. Deferoxamine, administered subcutaneously or intramuscularly, is effective but limited by its parenteral route. Deferasirox, an oral once-daily agent, has become the preferred choice in many cases and is FDA-approved for transfusion-related iron overload. Randomized trials in lower-risk MDS demonstrated that deferasirox reduced ferritin, improved event-free survival, and even enhanced hematologic response in some patients. However, renal, hepatic toxicity require careful monitoring. Deferiprone, another oral agent, is mainly approved for thalassemia, can be considered when other chelators fail, though its use in MDS remains limited due to risk of agranulocytosis. Chelation has been associated with improved overall survival in observational studies, prospective trials provide encouraging evidence. Beyond survival, reversal of some iron-related cardiac, hepatic damage has been documented, underscoring its importance. Monitoring should include serial ferritin, renal, liver function, vigilance for adverse events. Individualization is critical: patients with advanced or high-risk MDS, limited life expectancy are less likely to benefit, and chelation is generally not recommended in such settings. Iron chelation therapy plays a vital role in selected MDS patients. It should be considered in lower-risk individuals with substantial transfusion requirements and elevated ferritin, especially in those with preserved organ function or who are candidates for transplantation. As evidence grows, iron chelation continues to evolve from a supportive measure into a prognostically meaningful intervention in the management of MDS.

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Abstract 005

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

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Thrombotic thrombocytopenic purpura (TTP) is a rare but life-threatening thrombotic microangiopathy caused by severe ADAMTS-13 deficiency due to either autoantibodies (immune TTP, iTTP) or biallelic mutations (congenital TTP, cTTP). The first International Society on Thrombosis and Haemostasis (ISTH) guidelines were issued in 2020. Since then, substantial advances in therapeutic strategies and real-world evidence have prompted an ISTH 2025 focused update. The most significant change relates to cTTP prophylaxis. A new strong recommendation was issued in favor of recombinant ADAMTS-13 (rADAMTS-13) over fresh frozen plasma (FFP) in patients in remission. This decision, supported by a phase 3 randomized crossover trial, demonstrated that rADAMTS-13 provides higher and sustained ADAMTS-13 activity and fewer TTP-related manifestations, with a favorable safety profile [1]. Where rADAMTS-13 is unavailable, the panel conditionally recommends FFP over a watch-and-wait strategy, shifting from the neutral stance in 2020 [1,2]. Pregnancy-related cTTP remains a high-risk setting, and prophylactic therapy—preferably rADAMTS-13, or intensified FFP when rADAMTS-13 is

not accessible—is emphasized due to high maternal and fetal morbidity and mortality [1]. For iTTP, no major directional changes were made. Therapeutic plasma exchange (TPE) with corticosteroids remains standard of care. The addition of rituximab is conditionally suggested for both initial and relapsed events. Caplacizumab continues to be conditionally recommended, supported by real-world registry and cohort data showing faster platelet recovery, fewer exacerbations, reduced TPE sessions, shorter hospitalization, and mortality consistently below 5% [3,4]. Evidence highlights that early initiation, ideally within three days of diagnosis, maximizes benefit [4]. The update also provides revised good practice statements on antithrombotic therapy. Prophylactic anticoagulation (most often low-molecular-weight heparin) may be considered once platelet counts recover above 50×10^9/L in patients at elevated thromboembolic risk, while antiplatelet agents remain discouraged during the acute phase [1]. Importantly, registry data highlight the long-term morbidity of cTTP, including ischemic stroke, end-stage renal disease, and cardiac dysfunction, as well as pregnancy complications. These findings strengthen the rationale for early and consistent prophylaxis. Regulatory approval of rADAMTS-13 in the United States, Europe, and Japan for both prophylaxis and acute treatment represents a transformative milestone in cTTP management [5]. Conclusion: The ISTH 2025 focused update establishes rADAMTS-13 as the new standard for prophylaxis in cTTP and reaffirms the existing evidence-based triple therapy (TPE, corticosteroids, and caplacizumab ± rituximab) in iTTP. These recommendations, integrating randomized trial results, real-world data, and international consensus, provide globally harmonized, evidence-based guidance to improve outcomes and quality of life for patients with TTP.

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Abstract 006

THE TREATMENT ALGORITHM FOR SICKLE CELL DISEASE

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Sickle cell disease (SCD) is an autosomal recessive hemoglobinopathy characterized by the polymerization of Hemoglobin S (HbS), which results from a point mutation in the β-globin gene. The clinical heterogeneity of the disease is dictated by a complex interplay of three core pathophysiological mechanisms: vaso-occlusion (VOC), driven by erythrocyte rigidity secondary to deoxy-HbS polymerization; chronic hemolytic anemia, resulting from a shortened erythrocyte lifespan; and a state of chronic sterile inflammation and ischemia-reperfusion injury, triggered by the scavenging of nitric oxide (NO) by cell-free hemoglobin. While HbSS and HbS/β^0-thalassemia genotypes constitute the most severe phenotypes, therapeutic algorithms are designed to target these fundamental molecular underpinnings. **Foundational Management and Prevention in SCD:** The cornerstone of modern SCD management is rooted in proactive and preventive medicine. Early diagnosis through newborn screening programs facilitates the immediate initiation of penicillin prophylaxis (from 2 months to 5 years of age) and comprehensive vaccinations (against *Pneumococcus*, *Meningococcus*, and *H. influenzae*), which dramatically reduce the risk of invasive pneumococcal disease secondary to functional asplenia. Primary stroke prevention in the pediatric population (ages 2-16) relies on annual Transcranial Doppler (TCD) screening. A time-averaged mean of maximum velocity exceeding 200 cm/sec is an absolute indication for initiating a chronic transfusion program, a measure proven to reduce stroke risk by over 90%. Hydroxyurea remains the cornerstone of this foundational care, recommended for all patients with severe genotypes over the age of 9 months. When titrated to the maximum tolerated dose (MTD), its pleiotropic effects—including the induction of fetal hemoglobin (HbF) and its anti-inflammatory and anti-adhesive properties—significantly modify the disease course. **Management of Acute Complications:** Acute complications warrant standardized and aggressive intervention. The management of vaso-occlusive crises (VOCs) necessitates rapid, multimodal analgesia, featuring the administration of parenteral opioids and non-steroidal anti-inflammatory drugs (NSAIDs) within 30 to 60 minutes of presentation. Acute Chest Syndrome (ACS), a leading cause of mortality, is managed with broad-spectrum antibiotics, supplemental oxygen, and transfusion support. In cases of severe ACS, the 2020 American Society of Hematology (ASH) guidelines recommend exchange transfusion over simple transfusion to rapidly decrease the HbS fraction to less than 30%. Similarly, acute ischemic stroke constitutes a hematologic emergency that mandates immediate exchange transfusion to reduce the HbS level to below 30%. **Chronic Complications and Disease-Modifying Therapies:** For patients with a suboptimal response to or intolerance of hydroxyurea, therapy is personalized with phenotype-specific agents. In the vaso-occlusive-dominant phenotype, options include the P-selectin inhibitor crizanlizumab and the oxidative stress-targeting agent L-glutamine. However, the role of crizanlizumab in the treatment algorithm has become contentious following the failure of its post-approval STAND study to meet its primary endpoint. For the hemolysis-dominant phenotype, voxelotor, a direct inhibitor of HbS polymerization, is effective in increasing hemoglobin levels. Nevertheless, its use has become debatable following the non-renewal of its marketing authorization by the European Medicines Agency (EMA) due to insufficient evidence of clinical benefit and the company's subsequent global withdrawal decision. **Transfusion Support and Associated Management:** Chronic transfusion therapy is a life-saving intervention, particularly for stroke prophylaxis, but inevitably leads to iron overload. Iron chelation therapy should be initiated when serum ferritin levels exceed 1000-1500 ng/mL. The gold standard for monitoring chelation efficacy is the quantitative assessment of hepatic and cardiac iron burden via T2* MRI. To minimize iron accumulation and more precisely achieve target HbS levels, the 2020 ASH guidelines advocate for automated red cell exchange (RCE) over simple transfusions for patients on chronic transfusion regimens. **Conclusion:** The management paradigm for SCD has evolved from reactive care to a multifaceted approach encompassing proactive foundational