Laboratory findings[2,5,14,15]

a Abnormal complete blood count parameters, including platelet count and MPV may be detected incidentally in many cases. Platelet count below 150,000/μL and significantly increased platelet size (MPV >12 fL) are pathognomonic findings.
b Abnormal platelet morphology may be observed in peripheral blood smear. In patients with IMTP, on average, 20% of platelets are large (>4μm diameter), and 12% are giant (>8 μm diameter) (normal platelets size are between 1.5 μm and 3 μm in diameter). As well, *vacuolated platelets* for GATA1 related disease, *giant platelets* for MYH9 related disease, biallelic Bernard Soulier syndrome (BSS) (GP1bα, GP1bβ and GP9-moderate to severe phenotype), GPS, FLNA related and TUBB1 related disease, *large platelet* for monoallelic BSS (GP1bα-mild phenotype), Paris-Trousseau/ Jacobsen syndrome, GATA1 related-, ITGA2B- and ITGB3 related-disorders are diagnostic signs in peripheral blood smear.
c Abnormal platelet function by light transmission aggregometry may be observed in patients with BSS (*e.g.*, Ristosetin induced platelet aggregation response is absent).
d Immunofluorescence testing with antibody against nonmuscle myosin heavy chain reveals a spotty abnormal distribution of these molecules in patients with MYH9 disorders.
e Flow cytometry reveals lack of GP1bα, GP1bβ and GP IX receptor in patients with BSS.
f Two-dimensional sodium dodecyl sulfate-polyacrylamide gel electrophoresis of the surface radio iodinated platelet glycoproteins results show the absence of GPIb which identifies BSS.
g Electron microscopy reveals abnormal ultrastructure of platelets (*e.g.*, lack of alpha granules and inclusions in MYH9 disorders, giant fused alpha granules in Paris-Trousseau syndrome).
h The next-generation sequencing technology has enabled comprehensive genetic testing using broad diagnostic panels for IMTP related disorders. Recent studies using whole-exome sequencing and whole-genome sequencing have greatly contributed to the early recognition of IMTP related genes and the detection of pathogenic variants within these genes.

v. Treatment: No definitive guidelines are available for managing asymptomatic or mildly symptomatic patients with IMTP; however, platelet transfusion, antifibrinolytic therapy, and recombinant FVIIa are usually recommended for those with severe bleeding manifestations.[5,15] Recently, it has been reported that TPO-receptor agonists can be used in some patients with MYH9 related disorders.[5]

Conclusion: The International Society of Thrombosis and Haemostasis' scientific subcommittee on platelet physiology has published guidelines for diagnosing IMTP. In this approach, personal and family history, and physical examination are the key, followed by *i*) investigation of platelet count and morphology, *ii*) evaluation of platelet function by light transmission aggregometry, and *iii*) a panel of tests to assess granule contents and platelet surface markers by electron microscopy and flow cytometry studies. Further, next-generation sequencing has greatly expanded the molecular repertoire of IMTP, thus enabling the identification of new disorders.

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Sp 11

Treatment of sickle cell in 2021

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Sickle cell disease (SCD) is an inherited disorder prevalent in many areas of the world including Africa, Middle East and parts of India. It is characterized by repetitive episodes of vaso- occlusive (VOC) process leading to recurrent painful episodes, hemolytic anemia, and predisposition to infection. Sickle cell manifestations varies and it includes VOC leading to recurrent painful episodes, or organ specific complications such as acute chest syndrome, stroke, splenic sequestration, and many skeletal complications. Although the prognosis of patients with SCD has improved, due to introduction of vaccination, use of antibiotics prophylaxis and blood transfusions, however still patients are dying prematurely. Better understanding of pathophysiology of the disease as well as worldwide interest in the disease has allowed more progress on preventing these complications and development of more focused pharmacological therapies. Hemoglobin polymerization is a primary triggering event in the pathophysiology of the disease, leading to the sickling process, this usually ignite an inflammatory process/ tissue ischemia and increased adhesions. This understanding of the pathophysiology has allowed scientist to develop drugs (three FDA approved within 2 years) that interfere with these processes such as Voxelotor & Hydroxyurea (interfere with polymerization), L-glutamine and Omega 3 (interfere with inflammatory process and oxidative stress) and Crizanluzimab and Tinzaparin (works by inhibiting adhesion molecules). The availability of these therapeutic interventions will allow patients and physicians the freedom to have patient specific therapeutic interventions including development of combinations protocols. SCD is very complex and this meant that drug with multi-faceted action such as Hydroxyurea will remain with us for some time. Further progress also made in the area of bone marrow transplant (including alternative donor pool) and gene therapy /gene editing.

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