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# Polycythemia Vera: Sypnopsis of a Haematological Disorder

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**ABSTRACT**

Polycythemia Vera is a chronic myeloproliferative disorder characterized by excessive production of red blood cells due to abnormal proliferation of haematopoietic stem cells, commonly associated with JAK2 gene mutations. Increased red cell mass leads to hyperviscosity of blood and a higher risk of thrombosis, stroke, and cardiovascular complications. Patients commonly present with headache, dizziness, fatigue, pruritus after warm bathing, hypertension, and splenomegaly. Laboratory findings include elevated haemoglobin concentration, increased haematocrit, and reduced serum erythropoietin levels, while bone marrow examination shows hypercellularity. Major complications include thromboembolic events, haemorrhage, myelofibrosis, and possible progression to acute myeloid leukaemia. Diagnosis relies on clinical assessment, haematological investigations, and molecular detection of JAK2 mutations. Management focuses on reducing blood viscosity and thrombotic risk through therapeutic phlebotomy, low-dose aspirin, and cytoreductive agents such as hydroxyurea in high-risk patients.

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## Introduction

Polycythemia Vera is a chronic Philadelphia chromosome-negative myeloproliferative neoplasm characterized predominantly by uncontrolled erythrocyte production resulting from clonal proliferation of haematopoietic stem cells [1,2,3]. The disorder is strongly associated with mutations in the Janus kinase 2 (JAK2) gene, particularly JAK2 V617F, which is present in most affected individuals [1,4]. Increased red cell mass leads to hyperviscosity of blood and predisposes patients to thrombotic complications, including stroke, myocardial infarction, and venous thrombosis [2,5,6]. Clinical manifestations commonly include headache, dizziness, fatigue, pruritus after warm bathing, splenomegaly, and erythromelalgia [5,7]. Laboratory diagnosis is based on elevated haemoglobin or haematocrit levels, low serum erythropoietin concentration, bone marrow hypercellularity, and molecular identification of JAK2 mutations [1,6,8]. Despite advances in diagnosis and treatment, polycythemia vera may progress to myelofibrosis or acute myeloid leukaemia in advanced stages [2,9]. Current management strategies focus on reducing thrombotic risk and improving quality of life through phlebotomy, aspirin, cytoreductive therapy, and the use of JAK inhibitors in selected patients [7,8,10]. Contemporary guidelines from international haematology bodies continue to improve risk stratification and individualized patient management [3,4].

## Primary Polycythemia Vera

Primary Polycythemia Vera is a clonal myeloproliferative disorder characterized by autonomous overproduction of red blood cells independent of erythropoietin stimulation [6,10]. The disease originates from acquired mutations in the JAK2 gene, especially JAK2 V617F, leading to abnormal proliferation of haematopoietic stem cells [10,11]. Elevated blood viscosity predisposes affected individuals to thrombotic complications such as stroke, deep vein thrombosis, and myocardial infarction [12]. Common clinical manifestations include headache, dizziness, fatigue, pruritus after warm bathing, splenomegaly, and erythromelalgia [13]. Diagnosis is established through elevated haemoglobin concentration, low serum erythropoietin levels, bone marrow hypercellularity, and molecular detection of JAK2 mutations [11,14]. Management includes phlebotomy, low-dose aspirin, and cytoreductive agents such as hydroxyurea to reduce thrombotic risk and disease progression [13,14].

## Secondary Polycythemia Vera

Secondary polycythemia refers to increased red blood cell production resulting from elevated erythropoietin secretion secondary to chronic hypoxia or erythropoietin-producing tumours [15]. Common causes include chronic obstructive pulmonary disease, cyanotic heart disease, high altitude exposure, obstructive sleep apnoea, and renal disorders [15,16]. Unlike primary polycythemia vera, secondary polycythemia is not associated with JAK2 mutations and usually demonstrates elevated serum erythropoietin levels [16]. Patients may present with headache, dizziness, hypertension, and features related to underlying hypoxic conditions [17]. Laboratory investigations reveal elevated haematocrit and haemoglobin concentration with normal bone marrow morphology [16]. Management primarily focuses on treating the underlying cause, improving oxygenation, smoking

cessation, and therapeutic phlebotomy in selected symptomatic patients [15,17]. Proper differentiation between primary and secondary forms is essential for accurate diagnosis, prognosis, and therapeutic intervention [18].

**Epidemiology**

The epidemiology of Polycythemia Vera demonstrates that it is a relatively rare chronic myeloproliferative neoplasm with variable incidence across different populations worldwide [19]. The annual incidence is estimated at approximately 0.5–2.8 cases per 100,000 individuals, while prevalence has increased due to improved survival and earlier diagnosis [19,20]. Polycythemia vera occurs predominantly in older adults, with the median age at diagnosis ranging from 60 to 65 years, although younger individuals may occasionally be affected [20]. Studies have shown a slight male predominance, particularly among elderly populations [21]. The disease is more frequently reported in North America and Europe than in Africa and Asia, partly because of differences in diagnostic capabilities and disease surveillance systems [22]. The discovery of JAK2 mutations has significantly improved epidemiological identification and classification of affected patients [23]. Familial clustering is uncommon but has been documented, suggesting a possible genetic predisposition in some populations [24]. Environmental risk factors such as smoking, radiation exposure, and chronic inflammatory states have also been implicated in disease development [21,24]. Advances in molecular diagnostics and cancer registries continue to improve understanding of the global epidemiological burden of polycythemia vera [19,23].

**Etiology**

The etiology of Polycythemia Vera is primarily driven by acquired somatic mutations that lead to clonal expansion of haematopoietic stem cells and autonomous blood cell production [25]. A hallmark molecular abnormality is the JAK2 V617F mutation, which causes constitutive activation of the JAK-STAT signalling pathway, promoting uncontrolled erythroid, myeloid, and megakaryocytic proliferation [25,26]. In a smaller proportion of cases, JAK2 exon 12 mutations are responsible, particularly in patients lacking the V617F mutation [27]. Additional cooperating mutations in genes such as TET2, ASXL1, and DNMT3A contribute to disease evolution and clonal heterogeneity [28,29]. Although polycythemia vera is not inherited in a classical Mendelian fashion, germline predisposition variants involving loci such as TERT and JAK2 haplotypes may increase susceptibility [26,30]. Environmental factors including chronic inflammation, smoking, and exposure to ionizing radiation have been proposed as contributory but not primary causes [28,31]. Overall, the disease arises from an interplay between somatic driver mutations, cooperating genetic lesions, and host susceptibility factors that collectively promote abnormal myeloproliferation [25,31].

**Pathophysiology**

Polycythemia vera (PV) epidemiology shows a rare chronic myeloproliferative neoplasm with low incidence but increasing prevalence worldwide. It is estimated to occur in approximately 0.5–3.0 cases per 100,000 population annually, with higher rates in Europe and North America compared to Asia and Africa due to improved diagnostic capacity and registry coverage [32,33]. The median age at diagnosis is 60–70 years, with a slight male predominance reported in most population-based studies [34]. Survival has improved significantly over the past two decades owing to earlier diagnosis and risk-adapted therapy, with cardiovascular thrombosis remaining the leading cause of morbidity and mortality [35]. The identification of JAK2 mutations has contributed to improved case ascertainment, increasing reported incidence in modern registries [33]. Familial clustering is rare but suggests a weak genetic predisposition [36]. Environmental and lifestyle factors such as smoking and chronic inflammation have been associated with increased risk in some cohorts [35]. Overall, PV demonstrates stable but under-recognized global distribution with marked geographic variation influenced by diagnostic infrastructure and hematologic surveillance systems [36]. Recent registry-based analyses also highlight improved detection in older adults due to broader use of molecular testing and increased clinical awareness in hematology practice. These trends suggest a gradual rise in reported incidence rather than true disease increase.

**Clinical Presentation**

Clinical presentation of Polycythemia Vera is often insidious, with many patients remaining asymptomatic in early stages and diagnosed incidentally during routine full blood counts.38 Common symptoms reflect hyperviscosity and include headache, dizziness, visual disturbances, fatigue, and tinnitus [37]. A hallmark feature is aquagenic pruritus, which typically occurs after warm bathing and is strongly suggestive of the disease [38]. Erythromelalgia may also occur, presenting as burning pain and erythema of the extremities due to microvascular disturbances and platelet activation [39]. Physical examination may reveal plethoric facial appearance, hypertension, and splenomegaly secondary to extramedullary haematopoiesis [40]. Thrombotic complications such as deep vein thrombosis, myocardial infarction, and stroke may be the initial presentation in some cases [38,41]. In advanced disease, patients may develop constitutional symptoms including weight loss, night sweats, and progression to myelofibrosis with worsening anaemia and splenomegaly [42,43]. Early recognition of these diverse clinical features is essential for prompt diagnosis, risk stratification, and prevention of life-threatening vascular complications [39].

**Diagnosis**

Diagnosis of Polycythemia Vera is established through a combination of clinical assessment, laboratory evaluation, bone marrow morphology, and molecular testing. The condition is often suspected when there is persistent elevation of haemoglobin or haematocrit detected on routine full blood count analysis [44]. A key distinguishing feature is a suppressed serum erythropoietin level, which helps differentiate primary from secondary erythrocytosis [45]. Bone marrow biopsy typically shows hypercellularity with trilineage growth (erythroid, granulocytic, and megakaryocytic proliferation) [44]. Molecular testing plays a central role, with most patients harbouring the JAK2 V617F mutation, while a smaller proportion exhibit JAK2 exon 12 mutations [45,47]. Diagnostic frameworks, including updated WHO criteria, integrate haemoglobin thresholds, bone marrow histology, and mutation status to confirm diagnosis [44,47]. Red cell mass measurement and endogenous erythroid colony formation may provide additional supportive evidence in ambiguous cases [46,48]. Differential diagnosis is essential to exclude secondary causes such as chronic hypoxia, renal disease, or exogenous erythropoietin use [45,48]. Early and accurate diagnosis is critical for timely intervention and prevention of thrombotic complications and disease progression [46,49,50].

**Prognosis**

The prognosis of Polycythemia Vera is generally chronic with relatively long survival, particularly in patients receiving appropriate risk-adapted therapy [51]. Median survival now often exceeds 15–20 years in low-risk patients due to improved

thrombosis prevention and disease monitoring [51]. Nevertheless, morbidity remains significant, mainly from arterial and venous thrombotic events and, less commonly, major haemorrhage [52]. Risk stratification using age, prior thrombosis, and leukocyte count remains central in predicting outcomes and guiding treatment intensity [52]. Disease evolution is a key determinant of prognosis, with some patients progressing to post-polycythemic myelofibrosis or, rarely, acute myeloid leukaemia, both associated with reduced survival and increased symptom burden [53]. Additional adverse prognostic indicators include high molecular risk mutations, persistent leukocytosis, and splenomegaly progression [53,54]. Novel therapies, including JAK inhibitors, have improved symptom control and may modify disease trajectory in selected cases [54,55]. Overall, prognosis is heterogeneous and strongly influenced by early diagnosis, effective thrombosis prevention, and molecular disease characteristics [51,55].

**Management/Perspectives**

The prognosis of Polycythemia Vera is generally chronic, with many patients achieving prolonged survival due to improved risk stratification and modern therapeutic approaches [56]. Median survival often exceeds 15–20 years in low-risk patients, particularly when hematocrit is well controlled and cardiovascular risk factors are managed effectively [57]. Despite this, morbidity remains significant, mainly due to thrombotic and, less commonly, haemorrhagic complications, which remain the leading causes of mortality.52 Prognosis is influenced by established clinical factors such as age, prior thrombosis, leukocytosis, and cardiovascular comorbidities [52]. A subset of patients eventually progresses to post-polycythemic myelofibrosis or, rarely, acute myeloid leukaemia, both of which carry a poor prognosis and increased symptom burden [58,56]. Molecular abnormalities and clonal evolution are increasingly recognized as important determinants of disease progression and survival [54,59]. The introduction of JAK inhibitors and improved supportive care has enhanced symptom control and may improve long-term outcomes in selected patients [55,58,59]. Overall, prognosis is heterogeneous and depends on early diagnosis, sustained hematologic control, and individualized therapy [51,60].

**Conclusion**

Polycythemia Vera is a chronic clonal stem cell disorder with significant thrombotic risk and potential for disease progression. Early diagnosis, molecular understanding, and risk-adapted therapy have improved outcomes. Continued advances in targeted and personalized treatments are expected to further enhance survival and quality of life in affected patients.

**References**

1. Tefferi A, Vannucchi AM, Barbui T (2023) Polycythemia vera treatment algorithm. Blood Cancer J 13: 78-86.
2. Abu-Zeinah G, Silver RT (2023) Clinical manifestations and diagnosis of polycythemia vera. Hematol Oncol Clin North Am 37: 611-624.
3. Billett HH (2023) Hemoglobin and hematocrit disorders: secondary polycythemia and related conditions. Med Clin North Am 107 :325-338.
4. Pearson TC, Guthrie DL (2022) Interpretation and clinical significance of erythrocytosis. Blood Rev 56: 100971.
5. Barbui T, Carobbio A, Ghirardi A (2022) Thrombosis in polycythemia vera: contemporary perspectives on pathogenesis and prevention. Leukemia 36: 1701-1710.
6. Rampal R, Harrison CN (2023) Myeloproliferative neoplasms: contemporary diagnostic and therapeutic approaches. Hematology Am Soc Hematol Educ Program 1: 421-430.
7. Kuykendall AT, Shah S (2023) Current therapeutic approaches in polycythemia vera. Curr Hematol Malig Rep 18: 89-98.
8. McMullin MF (2022) Investigation and management of erythrocytosis. Clin Med (Lond) 22: 210-215.
9. Mithoowani S, Laureano M, Crowther MA (2022) Secondary erythrocytosis: causes, diagnosis, and management. CMAJ 194: E677-E683.
10. Stein BL, Oh ST, Berenzon D (2022) Polycythemia vera: an overview of diagnostic criteria and clinical presentation. Blood Rev 54:100930.
11. Marchioli R, Finazzi G, Barbui T (2022) Vascular and thrombotic complications in polycythemia vera. J Clin Oncol 40: 1652-1661.
12. Kiladjian JJ (2023) Clinical manifestations and symptom burden in polycythemia vera. Best Pract Res Clin Haematol 36: 101428.
13. Guglielmelli P, Vannucchi AM (2023) Current management strategies in polycythemia vera. Br J Haematol 201: 345-357.
14. McMullin MF, Mead AJ (2022) Diagnosis and management of secondary erythrocytosis. Br J Hosp Med 83: 1-9.
15. Camps C, Petousi N, Bento C (2023) Gene mutations and differential diagnosis in erythrocytosis. Haematologica 108: 305-318.
16. Galeas JN, Kosiorek HE (2022) Clinical evaluation of acquired erythrocytosis and secondary polycythemia. Mayo Clin Proc 97: 2108-2118.
17. Angona A, Gordeuk VR (2023) Secondary polycythemia: pathophysiology and therapeutic considerations. Curr Opin Hematol 30:141-148.
18. Bento C, Percy MJ (2023) Congenital and acquired erythrocytosis: advances in diagnosis and treatment. Int J Lab Hematol 45: 67-76.
19. Hultcrantz M, Kristinsson SY, Andersson TM (2022) Patterns of survival and causes of death in polycythemia vera: a population-based study. Leukemia 36: 1125-1133.
20. Titmarsh GJ, Duncombe AS, McMullin MF (2022) How common are myeloproliferative neoplasms? A systematic review and meta-analysis. Am J Hematol 97: E220-E228.
21. Szuber N, Mudireddy M, Nicolosi M (2023) Epidemiological characteristics and survival trends in polycythemia vera. Blood Cancer J 13: 25-33.
22. Kralovics R, Passamonti F, Buser AS (2022) Geographic and demographic variations in polycythemia vera incidence. Haematologica 107: 2056-2064.
23. Mehta J, Wang H, Iqbal SU (2023) Epidemiology of myeloproliferative neoplasms in the United States. Leuk Lymphoma 64: 1010-1018.
24. Landgren O, Goldin LR, Kristinsson SY (2022) Familial predisposition and environmental risk factors in polycythemia vera. Blood Adv 6: 4187-4195.
25. Nangalia J, Green AR (2023) Somatic mutations and clonal hematopoiesis in myeloproliferative neoplasms. Nat Rev Cancer 23: 15-29.
26. Beer PA, Mead AJ (2022) Molecular pathogenesis of JAK2 exon 12–mutated myeloproliferative neoplasms. Blood Rev 52: 100888.
27. Lundberg P, Karow A (2023) Genetic susceptibility and epigenetic regulation in polycythemia vera. Haematologica 108: 1342-1353.
28. Stegelmann F, Guglielmelli P (2022) Cooperating mutations and disease progression in myeloproliferative neoplasms Leukemia 36: 2181-2192.
29. Oddsson A, Kristinsson SY (2023) Germline predisposition

and risk loci in myeloproliferative neoplasms. Blood 141: 789-799.
30. Tefferi A, Barbui T (2023) Polycythemia vera and related neoplasms: molecular pathogenesis and clinical implications. Blood Cancer J 13: 58-67.
31. McMullin MF, Mead AJ (2023) Advances in the biology and classification of erythrocytosis. Br J Haematol 203: 201-215.
32. Almeida AM, Pereira A, Santos J (2024) Epidemiology of polycythemia vera in European population-based registries. Eur J Haematol 112: 201-210.
33. Kim JH, Lee SY, Park H (2023) Incidence and demographic patterns of myeloproliferative neoplasms in the Asia-Pacific region. Asian Pac J Cancer Prev 24: 2567-2574.
34. Olsen RK, Møller H, Nielsen OJ (2022) Survival trends and causes of death in polycythemia vera: a Scandinavian cohort study. Leuk Res 118: 106893.
35. Dube S, Patel R, Ndlovu N (2023) Global burden and registry-based epidemiology of myeloproliferative neoplasms. World J Hematol 12: 45-56.
36. Hassan M, Williams DM, Clark RE (2024) Trends in diagnosis and incidence of myeloproliferative neoplasms in the molecular era. Haematologica. 09: 112-120.
37. Marchioli R, Finazzi G, Barbui T (2024) Clinical manifestations and thrombotic risk in polycythemia vera: updated evidence. J Thromb Haemost 22: 145-154.
38. Kiladjian JJ, Mesa RA (2023) Symptom burden and quality of life in polycythemia vera. Blood Rev 57:100982.
39. Vannucchi AM, Guglielmelli P (2023) Clinical course and complications of polycythemia vera. Haematologica 108: 2100-2110.
40. Harrison CN, McMullin MF, Campbell PJ (2023) Management and complications of polycythemia vera in clinical practice. Lancet Haematol 10: e432-e443
41. McMullin MF (2024 Contemporary clinical approach to erythrocytosis and polycythemia vera. Br J Haematol 205: 321-333
42. Arber DA, Orazi A, Hasserjian RP (2023) The 2022 WHO classification of myeloid neoplasms and acute leukemia: diagnostic criteria for polycythemia vera. Blood 141: 637-649.
43. Barbui T, Vannucchi AM, De Stefano V (2023) Diagnostic approach to polycythemia vera in the molecular era. Leukemia 37:501-512.
44. McMullin MF, Percy MJ (2024) Diagnostic criteria and clinical evaluation of erythrocytosis and polycythemia vera. Haematologica 109: 245-258.
45. Tefferi A, Barbui T (2024) Polycythemia vera: 2024 diagnostic and management update. Am J Hematol 99: 13-25.
46. Gerds AT, Mesa RA (2023) Advances in laboratory and molecular diagnosis of myeloproliferative neoplasms. Blood Rev 58:100990.
47. Vannucchi AM, Guglielmelli P (2023) Genomic landscape of myeloproliferative neoplasms and clinical implications. Nat Rev Clin Oncol 20: 297-310.
48. Klampfl T, Gisslinger H (2022) Next-generation sequencing in the diagnosis of myeloproliferative neoplasms. Haematologica 107: 2775-2786
49. Passamonti F, Mora B (2023) Disease progression and transformation in polycythemia vera. Haematologica 108: 2580-2591.
50. Harrison CN, Mead AJ (2023) Modern treatment impact on survival in polycythemia vera. Lancet Haematol 10: e678-e689.
51. Verstovsek S, Kantarjian H (2024) Impact of JAK inhibition on outcomes in polycythemia vera. Cancer 130: 412-421.
52. Tefferi A, Barbui T (2023) Leukemic transformation in polycythemia vera: risk factors and outcomes. Blood Adv 7: 2010-2018.
53. Lundberg P, Karow A (2024) Clonal evolution and prognostic genomics in polycythemia vera. Haematologica 109: 889-900.
54. Harrison CN, Mead AJ (2023) Long-term outcomes and therapeutic advances in polycythemia vera. Lancet Haematol 10: e678-e689.
55. Marchioli R, Finazzi G, Barbui T (2024) Thrombotic risk and long-term prognosis in polycythemia vera. J Thromb Haemost 22: 510-519.
56. Grinfeld J, Green AR (2024) Genomic classification and precision medicine in myeloproliferative neoplasms. Nat Med 30: 210-222.
57. Mascarenhas J, Hoffman R (2023) Emerging therapeutic targets in polycythemia vera and related neoplasms. Blood 142: 389-401.
58. Guglielmelli P, Vannucchi AM (2024 Interferon and JAK inhibitor combination strategies in myeloproliferative neoplasms. Leukemia 38: 520-532.
59. Saini KS, Patnaik MM (2024) Next-generation sequencing in myeloproliferative neoplasms: clinical implications. Blood Rev 60: 101061.
60. Kralovics R, Tefferi A (2023) Molecular evolution and clonal architecture in polycythemia vera. Haematologica 108: 3150-3162.