A guide to the diagnosis of polycythaemia

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

JOHN H. GALLO
MB BS, FRACP, FRCPA

Dr Gallo is Senior Staff Haematologist, Liverpool Hospital, Liverpool, NSW.

Series Editor
CHRISTOPHER S. POKORNY
MB BS, FRACP

Dr Pokorny is Honorary Secretary, Board of Continuing Education, Royal Australasian College of Physicians, and a gastroenterologist in private practice, Sydney, NSW.

True polycythaemia (polycythaemia vera) is a myeloproliferative disorder characterised by an increase in the number of red cells in the blood. It results in an increase in the haemoglobin level and red cell count and, in some patients, increases in granulocyte and platelet counts. Clinical features include pruritus (which is related to the release of histamine from basophils) and splenomegaly.

True polycythaemia needs to be distinguished from other causes of an elevated haemoglobin concentration (Table). A high haemoglobin level can also be caused by a reduction in the plasma volume (relative polycythaemia) or an increase in erythropoietin secretion (polycythaemia secondary to cyanotic heart disease, hypoxic lung disease, and renal or other tumours); less common causes include sleep apnoea (Figure), androgen therapy, and blood doping of athletes. Smoking causes another type of polycythaemia.

Interpreting a borderline high haemoglobin finding

If a patient's haemoglobin level seems to be borderline between normal and high, look for possible clinical causes such as dehydration or smoking. Remember that such findings may be normal in young men. Polycythaemia vera occasionally presents with a borderline high haemoglobin level if masked by iron deficiency, inapparent due to increased plasma volume or in the spent phase when myelofibrosis develops. The finding is more important if intercurrent vascular disease is present.

A high haemoglobin level is more significant when associated with increased neutrophils and platelets or with other symptoms and signs of polycythaemia vera.

Diagnosing polycythaemia vera

No single diagnostic test yet exists to confirm the presence of polycythaemia vera so the diagnosis rests on a combination of criteria defined by the Polycythemia Vera Study Group in 1975 and a modification proposed in 1997.[1,2] According to these criteria, a diagnosis is made if the following three 'major' findings are present:

- increased red cell mass
- oxygen saturation of at least 92%
- splenomegaly.

IN SUMMARY

- **True polycythaemia is a myeloproliferative disorder that needs to be distinguished from other causes of an elevated haemoglobin level. A reduction in the plasma volume (relative polycythaemia), an increase in erythropoietin secretion (secondary polycythaemia) and smoking (smoker's polycythaemia) can all increase the haemoglobin level.**
- **If a patient's haemoglobin level is borderline between normal and high, look for possible clinical causes such as dehydration or smoking. Remember that such findings may be normal in young males.**
- **A high haemoglobin level is more important if intercurrent vascular disease is present because polycythaemia vera is a risk factor for both arterial and venous thrombosis.**

Investigating the patient with a raised haemoglobin level

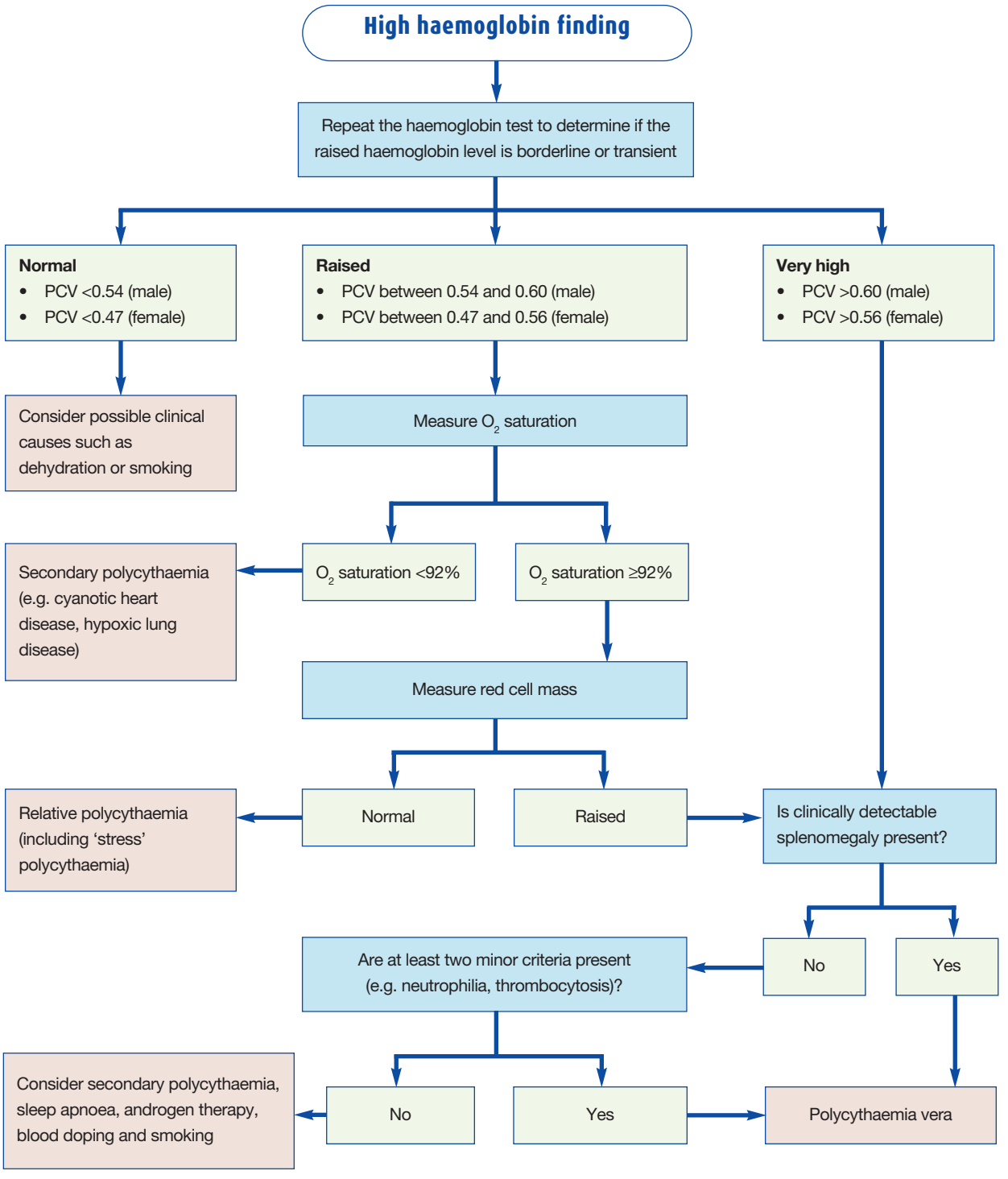

Table. Causes of a high haemoglobin level

	Red cell mass	Plasma volume	Erythropoietin level
True polycythaemia	Increased	No change	Decreased
Relative polycythaemia	No change	Decreased	No change
Secondary polycythaemia	Increased	No change	Increased
Smoker's polycythaemia	Increased	Decreased	Increased

Polycythaemia vera can also be diagnosed if the first two of the three major criteria are satisfied provided that at least two of the following 'minor' criteria are also present:

- neutrophilia
- thrombocytosis
- a raised neutrophil alkaline phosphatase score
- a raised serum vitamin B_{12} level.

A practical approach to the investigation of a high haemoglobin finding that addresses the diagnostic criteria for polycythaemia vera is suggested in the flowchart on page 71. A red cell mass test should be performed to confirm polycythaemia unless the packed cell volume (PCV) is over 0.60 for a male or 0.56 for a female (in such cases, one can assume the red cell mass is raised). The test is available in larger hospitals using either chromium labelling of red cells or, more recently, a nonradioactive method using biotin.

Splenomegaly that is detected clinically is a major diagnostic criterion. In some patients, however, it may be detectable following ultrasound examination only – in these cases, splenomegaly is a minor diagnostic criterion.

Other clinically useful tests

Serum erythropoietin is generally reduced in polycythaemia vera, so this finding is a useful additional minor criterion in the investigation. Bone marrow biopsy and cytogenetics are not routine diagnostic tests for polycythaemia vera but may be useful in difficult cases, particularly if a clonal karyotypic abnormality is found (10 to 20% of patients).

Consultant's comment

Concern about a high haemoglobin level is important because the consequences of hyperviscosity can be serious and the risk of thrombosis in major circulations is imminent when the PCV is in excess of 0.60. The clinical setting will usually be informative. In the young, a high haemoglobin level is rare and likely to be a consequence of an abnormal haemoglobin with a high affinity for oxygen or of cyanotic heart disease. In the older person, a plethoric facies makes one think of chronic airways disease or sleep apnoea, and a few questions will point the direction. If splenomegaly is detected, a myeloproliferative disorder is most likely and the pathway for tests clarified.

It pays to bear in mind circumstances in which erythropoietin is in excess, but these occasions are uncommon and would be sought only if other directions prove negative. It is a satisfying clinical challenge to make the right diagnosis because treatment is often effective.

Professor Peter Castaldi
Consultant Haematologist
Westmead Hospital, Sydney

Figure. Plethoric facies of a patient with a haemoglobin level of 199 g/L caused by sleep apnoea.

Follow up

A high haemoglobin level can be due to one or more of many causes. Just as anaemia can be the presenting sign of many underlying illnesses, so do the causes and management of an elevated haemoglobin level vary. Sometimes the cause will be clear and the management simple, such as in the case of dehydration or smoking. In more difficult cases or when polycythaemia vera is suspected, referral to a haematologist will be required for diagnosis and appropriate treatment.

Concluding remarks

Polycythaemia vera is a challenging diagnosis because it relies on a combination of clinical and laboratory features rather than a single diagnostic test. In addition, the finding of an elevated haemoglobin level has a wide differential diagnosis that includes many organ systems. MT

References

1. Berlin NI. Diagnosis and classification of polycythemia. Semin Hematol 1975; 12(4): 339-351.
2. Michiels JJ, Juvonen E. Proposal for revised diagnostic criteria of essential thrombocythemia and polycythemia vera by the Thrombocythemia Vera Study Group. Semin Thromb Hemost 1997; 23(4): 339-347.