**Keywords:** anaemia, genetics, haematology, cation transport, polymorphism, polymerase chain reaction

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Fig S1.** Forward DNA sequences of the region surrounding *RHAG* codon 65. All sequences represent genomic DNA except for the cDNA sequence from patient II:1 (right lower panel). Right middle panel genomic sequence II:1 (*S/S* in red italics) was from the *RHAG* exon 2 PCR amplicon produced with oligonucleotide primer "I3R1," which encompasses intronic SNP rs9473627 (c.22956G>C; 29% minor allele frequency).

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# Diagnostic pathway for the investigation of thrombocytosis

Chronic myeloid leukaemia (CML) may present with an isolated thrombocytosis and thus mimic essential thrombocythaemia (ET). The diagnostic criteria for ET proposed within the British Committee for Standards in Haematology guidelines (Harrison *et al*, 2010) are listed in Table I. Here, A3 requires exclusion of CML, usually by demonstrating the absence of a *BCR-ABL1* fusion gene or transcript in samples from bone marrow or peripheral blood. However the text of the guideline indicated that *BCR-ABL1* testing could be restricted to patients with atypical features, such as basophilia, left shift of neutrophils or the presence of small hypolobated megakaryocytes. Such features are easily overlooked and missing a diagnosis of CML has major consequences for the patient. We would therefore like to clarify that we recommend testing for the presence of a *BCR-ABL1* fusion in all patients lacking *JAK2* V617F or *MPL* mutations, as well as in patients with any atypical features in order to ensure that category A3 is fulfilled. We have therefore modified the diagnostic flow diagram from the guidelines (Fig 1).

There are reports of individuals who harbour two distinct clones, one carrying the *JAK2* V617F mutation and the other positive for *BCR-ABL1* (Curtin *et al*, 2005; Bee *et al*, 2010; Toogeh *et al*, 2011). This possibility needs to be kept in mind when investigating and managing a patient with either disorder whose disease is behaving in an atypical manner.

## Author contributions

CH and MFM lead the discussion and wrote the paper. NB, PC, EC, MD, AG, RM, DR and JR contributed to the discussion and reviewed and approved this work.

**Table I.** Proposed diagnostic criteria for essential thrombocythaemia.

| | |
|---|---|
| Diagnosis requires A1–A3 or A1 + A3–A5 | |
| A1 | Sustained platelet count >450 × $10^9$/l |
| A2 | Presence of an acquired pathogenetic mutation (e.g. in the *JAK2* or *MPL* genes) |
| A3 | No other myeloid malignancy, especially PV*, PMF†, CML‡ or MDS§ |
| A4 | No reactive cause for thrombocytosis and normal iron stores |
| A5 | Bone marrow aspirate and trephine biopsy showing increased megakaryocyte numbers displaying a spectrum of morphology with predominant large megakaryocytes with hyperlobated nuclei and abundant cytoplasm. Reticulin is generally not increased (grades 0–2/4 or grade 0/3) |

*Polycythaemia vera; excluded by a normal haematocrit in an iron-replete patient.
†Primary myelofibrosis; indicated by presence of significant marrow bone marrow fibrosis (greater or equal to 2/3 or 3/4 reticulin) AND palpable splenomegaly, blood film abnormalities (circulating progenitors and tear-drop cells) or unexplained anaemia (Barosi *et al*, 1999; Mesa *et al*, 2007).
‡Chronic myeloid leukaemia; excluded by absence of *BCR-ABL1* fusion from bone marrow or peripheral blood.
§Myelodysplastic syndrome; excluded by absence of dysplasia on examination of blood film and bone marrow aspirate.

## Conflict of interest

The authors have no conflicts of interest to disclose.

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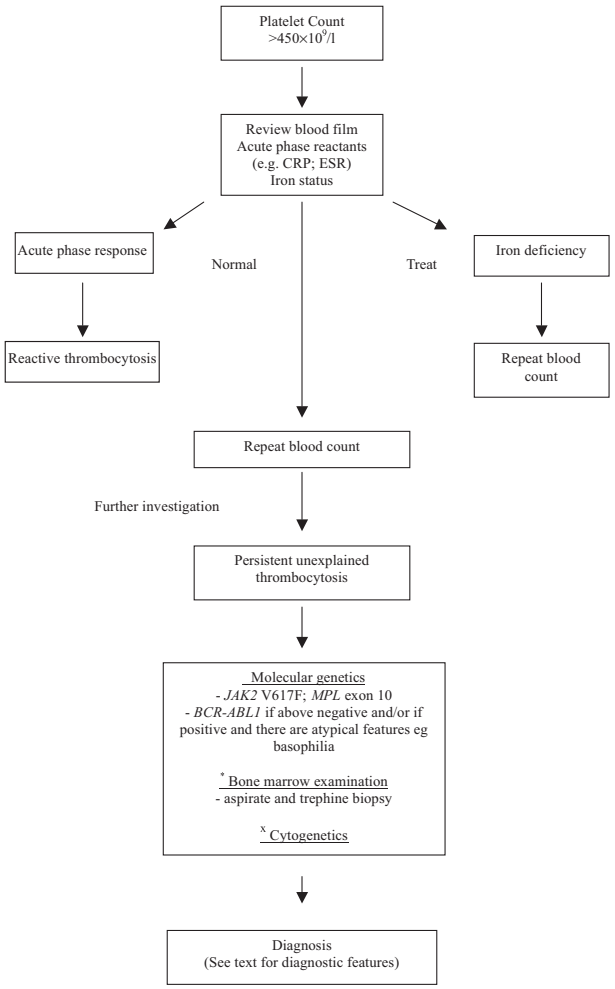


**Fig 1.** Diagnostic pathway for the investigation of thrombocytosis. *Bone marrow examination is recommended to confirm the diagnosis, as per the World Health Organization Classification (Swerdlow, 2008). In some circumstances this may not be clinically indicated, × The need for Cytogenetics on the bone marrow should be guided by the blood and bone marrow morphology.

**Keywords:** myeloproliferative neoplasms, thrombocytosis, *BCR-ABL1*, chronic myeloid leukaemia

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