To the Editor,

I have read with interest the paper entitled "Polycythemia Vera with Ph' Chromosomes in Two Brothers", by Levin, Houston and Ritzmann in Blood 30:503, October, 1967. The paper is based upon the observation of an apparent Ph' chromosome in cells of direct bone marrow preparations. To me the claim by the authors that these patients have such a structurally altered chromosome is completely unsupported by the karyotypic evidence provided their readers. In neither Figure 1A nor 2A is the morphology of the small acrocentrics demonstrated adequately enough for positive identification of the Y chromosome. None of the chromosomes identified as Y in the composite partial karyotypes of Figures 1B and 2B meet the criteria for identification as a Y; as a matter of fact, the quality of these chromosomes is not good enough for positive identification of the Y. If anything, they resemble more closely pairs 21 and 22. In Figure 1B it seems that the only chromosome that can be even tentatively labeled Y is the right-hand member of pair 21 in the fourth row from the top (the chromosome apparently identified by the authors as Ph'). In Figure 2B the only chromosome that can be even tentatively identified as Y is the right-hand member, again, of pair 21 of the bottom row, the presumptive Ph'. The point to be made is that without positive identification of the Y the possibility remains that the small chromosome is a Y and that pairs 21 and 22 are morphologically normal. If positive identification of any chromosome as a Ph' is to be made, better evidence must be provided.

I would like to suggest that the chromosomes of the G group are structurally normal. If a small G-Y chromosome is present, and I cannot even be sure of this, then I suggest that the small one may be Y, a chromosome the size of which can be quite variable in the normal population, and that this small chromosome is unrelated to the polycythemia vera of the patients. Evidence in support of or in opposition to this possibility might be gained by chromosomal analysis of leukocytes of the patients from short term culture, or better yet, by analysis of chromosomes from the father of the patients if he is still living, any unaffected brothers of the patients and any unaffected sons of the patients, with careful evaluation of the size of their Y chromosomes. Evidence for a "familial small Y" might be found.

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To the Editor,

In response to the letter from Dr. Robert L. Summitt and to letters received personally from Drs. Hirschhorn, Hsu, Shapiro and Lieber, and from Dr. H. E. M. Kay, we have reevaluated the chromosomal findings in the family reported in Blood 30:503, 1967.

Direct preparations from a second marrow aspirate and 48- and 72-hour cultures of peripheral blood from patient E.P. were studied, and at a later date, 51- and 70-hour cultures of phytohemagglutinin (PHA) stimulated blood lymphocytes from patients E.P. and A.P.; an additional male sibling of the two affected brothers, V.P.; a son of one affected brother, B.P.; and a son of the third unaffected sibling, J.P., were analyzed. Hemograms and leucocyte alkaline phosphatase determinations were performed in all five individuals. The chromosomal patterns of group G chromosomes and the Y chromosomes from karyotypes of the male members of the family studied. Note the small Y chromosome characterized by less distinct short arms, parallel chromatids which are usually closely approximated, less clarity in the distal portions of the long arms, etc. From top in descending order:

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Source of Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.P.</td>
<td>Original Marrow</td>
</tr>
<tr>
<td>A.P.</td>
<td>51-hour Blood Culture</td>
</tr>
<tr>
<td>E.P.</td>
<td>Second Marrow</td>
</tr>
<tr>
<td>E.P.</td>
<td>72-hour Blood Culture</td>
</tr>
<tr>
<td>V.P.</td>
<td>51-hour Blood Culture</td>
</tr>
<tr>
<td>B.P.</td>
<td>70-hour Blood Culture</td>
</tr>
<tr>
<td>J.P.</td>
<td>51-hour Blood Culture</td>
</tr>
</tbody>
</table>
chromosomes from each subject are shown in Figure 1. A pedigree of the
family members studied is depicted in Figure 2.

A small acrocentric chromosome, similar to the one we interpreted as a
Ph\(^1\) chromosome in the original report, was present in all male family
members available for study. It is apparently unrelated to the presence or absence
of polycythemia vera, and it probably represents a familial small Y chromo-
some, based upon the following evidence:

1. This chromosome was present in all of the 231 cells counted and analyzed
from all the cultures described and in both marrow cells and PHA stimulated
lymphocytes. The chromosome in question is about two-thirds the length of
the group G autosomes, with long-arm chromatids which are thinner than
those of the group G autosomes.

2. One small acrocentric chromosome, significantly smaller than the other
four small acrocentrics, was found in all cells evaluated from the three male
siblings and two of their sons, thus establishing it as a probable heritable
feature of the karyotype; no such size discrepancy among the four group G
autosomes was reported in the cultured blood cells of a female sibling, who
was kindly studied for us by Dr. William Dameshek.

3. Satellite formation and satellite association between the acrocentric
chromosomes was a frequent finding in the 51- and 70-hour cultures from
four of the five family members studied; no instance of satellite formation
or participation in satellite association with other acrocentric chromosomes
was observed in the smallest of the five potential group G chromosomes.

4. Rarely, a cell was observed, in which all four group G autosomes were clearly satellite, thus eliminating these as candidates for the Y chromosome, since the Y is not known to carry satellites. In all such cells, the satellite chromosomes were the four largest of the five small acentric chromosomes.

It may be of interest that J.P., the 35-year-old son of V.P., exhibits an abnormal hemogram. His hemoglobin concentration is 18.2 Gm. per cent; RBC, $6.07 \times 10^6$/mm.$^3$; hematocrit, 49 per cent, with normal platelets, WBC and differential. The leucocyte alkaline phosphatase score (Kaplow) was 216 (normal 88 ± 25). Follow-up studies of this individual are planned, to determine whether he may later develop polycythemia vera.

We are indebted to Dr. Summitt, Drs. Hirschhorn et al., and to Dr. Kay for calling to our attention the possibility that the presumed Ph$^+$ chromosome may actually represent a familial small Y chromosome. Since the occurrence of the small Y chromosome is infrequent in normal individuals (3 of 207 males), it is unusually fortuitous to have encountered this phenomenon as a familial trait in a kindred which includes two brothers with polycythemia vera. An obvious corollary to be drawn from this observation is the need to be alert to the possibility of a small Y chromosome when searching for Ph$^+$ chromosomes.

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