POLYCYTHEMIA is a descriptive term that simply denotes an elevated hemoglobin and hematocrit. As previously described,\(^1\) polycythemia could be classified into three groups: polycythemia vera (PV) and secondary polycythemia (SP) from increased production of erythropoietin (Epo); if the underlying cause of this abnormal production is eliminated, the excess RBCs disappear. These first two groups represent an absolute polycythemia, i.e., an abnormal increase in the total volume of circulating RBCs (TRCV). The third group, relative or spurious polycythemias, is characterized by an elevated hematocrit but has only a normal or slightly increased TRCV.

PV is a chronic myeloproliferative disorder characterized by an elevated TRCV and usually leukocytosis, thrombocytosis, and splenomegaly. The Polycythemia Vera Study Group (PVSG) has developed a useful set of clinical criteria\(^2\) for the diagnosis and the treatment of PV. The classification of polycythemia and the set of criteria of PVSG have two disadvantages, however. First, the classification into three groups excludes many who have only a true increase of TRCV and absence of an underlying cause, pure erythrocytosis (PE),\(^3\) or so-called idiopathic erythrocytosis.\(^4\) Second, some individuals who do have PV will be excluded by these criteria, mainly at an early stage.

The demonstration in 1974 by Prchal and Axelrad\(^5\) that erythroid colonies derived from bone marrow cells of PV can develop in a semisolid culture medium without the addition of Epo (EECs) marked an important turning point. Although EECs have been observed in other diseases as well, including erythroleukemias,\(^6,7\) some cases of sickle cell anemia,\(^8\) and myeloproliferative diseases other than PV,\(^9,10-11\) their presence in polycythemia could, for the first time, constitute a characteristic sign for the diagnosis of PV. EECs were always reported in PV and never in SP.\(^12-14\)

To determine the diagnostic value of the presence or absence of EECs in polycythemias, we made a prospective study on 108 patients with suspected polycythemia, comparing the standard criteria with the results of bone marrow cultures, with or without Epo. Our aim was to distinguish PV from SP and to recognize PV in the possible absence of all the standard criteria, hoping to simplify and improve the diagnosis of PV.

MATERIALS AND METHODS

Patients. This study was made of 108 patients (69 men, 39 women) with a mean age of 59.4 ± 17 years (19 to 91 years) referred for suspected polycythemia to the department of hematology of the Saint Antoine Hospital between 1979 and 1985. The question of polycythemia was raised when the hemoglobin exceeded 18 g/dL in men and 16 g/dL in women. All patients with relative polycythemia from reduced plasma volume were excluded. None had received treatment before the study. Although familial polycythemia vera is rare,\(^15,16\) 5 patients belonged to 3 families in which 1 parent and 1 child have this disease.

Criteria. The criteria established by the PVSG were used in all the cases except for LAP scoring and serum B, estimations, which were made only when the other criteria were absent; bone marrow
cultures were made prior to treatment. Bone marrow biopsy was performed in 56 patients. Epo level in serum was measured in 54 cases. When necessary, special studies were done to find the cause of polycythemia: blood oxygen affinity; hemoglobin electrophoresis; carboxy-hemoglobin evaluation; kidney echographic examination; and cerebral, abdominal, and thoracic computed tomographic scans. All patients were advised of procedures and attendant risks in accordance with institutional guidelines and gave informed consent.

The TRCV was measured by the $^{57}$Cr-labeled RBC dilution method. The TRCV was considered abnormally elevated when it was >32 mL/kg in women (normal 25 mL/kg) and 36 mL/kg in men (normal 30 mL/kg).

WBC counts, platelet counts, and arterial oxygen saturation were determined by standard techniques. LAP scoring was based on the standard techniques. Each histological section was examined independently by two histopathologists. Examination was done under a 400x magnification, and only colonies visible at 400x magnification were counted. The grade of megakaryocytes was: normal, I to 2; slight increase, 2 to 3; moderate increase, 3 to 6; marked increase, 6 to 12. The TRCV was measured by the 5tCR-labeled RBC dilution method. Serum B12 estimations were performed by radioisotope dilution. Spleen volume was determined by physical examination. Percutaneous trephine biopsies were taken from the anterior iliac crest with Tanzer or Jamshidi needles. Sections of marrow were prepared and stained by routine techniques described elsewhere. Each histological section was examined independently by two histopathologists. Examination was done under a 400x Zeiss microscope. An area of 16 x 16 mm was measured (mean ± SD). The grade of megakaryocytes was: normal, I to 2; slight increase, 2 to 3; moderate increase, 3 to 6; marked increase, 6 to 12. The final grading was established by comparing the results of cellularity grade and megakaryocyte concentration.

**Epo assay.** Epo activity was determined in vitro by incorporation of radioactive iron into cultured fetal mouse liver cells. Embryos were harvested from 13-day-pregnant Balb/c mice (Charles River, France). The mechanically dissociated liver cells were suspended in RPMI 1640 medium at 1.6 x 10^6 cells/mL containing 7% fetal calf serum (FCS), 85 umol/L of bovine serum albumin, and 0.4 μmol/L of human transferrin. Cell suspension was distributed in a small volume (200 μL) into the wells of Nunclon culture plates. After incubation for 21 hours, human Fe-transferrin was added, followed by 5 hours of additional incubation. Epo fraction prepared from whole patient serum was used in the assay and calibrated against a standard of pig serum Epo (Centre National de Transfusion Sanguine, Paris) referred to as the second international reference preparation (courtesy of the WHO for biological standards, Mill Hill, London) and NIH standard (specific activity: 1,546 UI/A 280) generously donated by E. Goldwasser. Each sample was cultured at three or four protein concentrations and in four replicate assays, and results were expressed in milliunits per milliliter: mean ± SEM: 14 ± 4 for normal human serum.

**Bone marrow culture.** Bone marrow aspirate (1.2 mL) was collected in 200 U of sterile preservative-free heparin. Mononuclear cells, isolated by using Hypaque-Ficoll (density 1.077) were washed three times with Iscove-modified Dulbecco's medium (IMDM, GIBCO, Grand Island, NY). The nucleated cells collected were plated at a final concentration of 2.5 x 10^6/mL by the plasma clot method described by MacLeod in 30 x 10-mm Petri dishes containing 20% heat-inactivated FCS, 1% deionized bovine serum albumin (BSA, Sigma, St Louis) prepared according to the method of Worton and colleagues. CaCl2 34 mL, thrombin 1 U/mL, citrated beef plasma (GIBCO) 10%, with or without 1 U/mL Epo (step III, Connaught, Toronto). All tests were done at least twice. Clots were incubated at 37°C in 5% CO2. After 7 days of incubation, the clots were stained with benzidine and hematoxylin to determine the number of colonies with hemoglobin that had formed. Each clot was examined under 100x magnification, and only colonies consisting of eight or more benzidine-positive cells were counted. These colonies were derived from CFU-E that normally proliferate and differentiate into proerythroblasts in response to Epo. The presence of erythroid colonies that grew without the addition of exogenous Epo was defined as a positive culture; the occurrence of erythroid colonies only in the presence of exogenous Epo was defined as a negative culture.

**Statistical methods.** All results are given as means ± SE. The Wilcoxon Mann-Whitney rank-sum test was used to compare erythropoietin levels from patients with or without endogenous erythroid colonies. The analysis of variance (ANOVA) test was used to compare the means of the level of erythropoietin among patients with PV, with SP, with UP and EECs, and with UP without EECs. The Chi-square test was used to analyze contingency tables of patients with and without EEC obtained by several cut-offs: presence or not of standard criteria, and grade of the bone marrow.

**RESULTS**

**Standard criteria.** The main clinical and laboratory data from the 108 patients are summarized in Table 1. The TRCV delineated two groups: group A, consisting of 87 patients (50 men, 37 women) in which it was >36 mL/kg (49 ± 12.5 mL/kg) in men and >32 mL/kg (42 ± 9.5 mL/kg) in women; and group B, consisting of 21 patients (19 men, 2 women) with a TRCV between 30 and 36 mL/kg (32.8 ± 2.1 mL/kg) in men, and 27.8 ± 28.6 mL/kg/kg for the two women, respectively. None of these 21 group B patients had a reduction of plasma volume; therefore, there was no hemococoncentration. None was obese or had phlebotomies prior to diagnosis. The mean corpuscular volume of the RBCs was normal in each case of this group.

According to the criteria of the PVSG, 46 of the 87 patients of group A had PV (mean TRCV: 49 ± 11.5 mL/kg). Twelve patients from group A and 5 of group B had SP:

<table>
<thead>
<tr>
<th>Data</th>
<th>Group A</th>
<th>Group B</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>87</td>
<td>21</td>
</tr>
<tr>
<td>Total (%)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>58</td>
<td>90</td>
</tr>
<tr>
<td>F</td>
<td>42</td>
<td>10</td>
</tr>
<tr>
<td>Sex ratio</td>
<td>1.41/1</td>
<td>NS</td>
</tr>
<tr>
<td>(M vs F)</td>
<td></td>
<td></td>
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<tr>
<td>Arterial oxygen</td>
<td></td>
<td></td>
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<tr>
<td>saturation 92%</td>
<td>93</td>
<td>100</td>
</tr>
<tr>
<td>Spleenomegaly</td>
<td>33</td>
<td>15</td>
</tr>
<tr>
<td>Leucocytosis</td>
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<td></td>
</tr>
<tr>
<td>≥12 x 10^9/L</td>
<td>39</td>
<td>20</td>
</tr>
<tr>
<td>Thrombocytosis</td>
<td></td>
<td></td>
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<tr>
<td>≥400 x 10^9/L</td>
<td>44</td>
<td>15</td>
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Group A is defined by a total volume of circulating RBCs (TRCV) ≥ 36 mL/kg in males and TRCV ≥ 32 mL/kg in females. Group B is defined by a TRCV between 30 and 36 mL/kg in males and between 25 and 32 mL/kg/kg in females.
7 from chronic respiratory insufficiency, 3 from smoking excess, 4 from hepatomas, 1 from adrenal cancer, 1 from renal cancer, and 1 from essential thrombocythemia. Forty-five patients (29 of group A and 16 of group B) lacked the criteria for PV or SP and were considered to have unclassified polycythemia (UP).

Culture of bone marrow erythroid progenitors. In 65 of 108 cases (60%), colonies derived from CFU-E were observed without addition of Epo (EECs): 61 of 87 cases (70%) of group A and 4 of 21 cases (20%) of group B. In the remaining 43 cases, no growth occurred in the absence of Epo. The mean of EECs was 213 ± 334 colonies for 2.5 x 10^5 cells plated with a range from 12 to 1,455 colonies. In 34 cases, the number of colonies was also counted at the optimal concentration of 1 U/mL Epo: the mean was 439 ± 621 colonies for 2.5 x 10^5 cells plated with a range from 69 to 2,255 colonies. To appreciate the importance of the abnormal clonal population in relation to total erythroid progenitors, in these 34 cases we counted and compared the number of EECs with the number of colonies stimulated by Epo in the concentration of 1 U/mL. The ratio of EECs to Epo-stimulated colonies was 39.5% ± 18% (range 10% to 80%).

Comparative study of standard criteria and presence or absence of EECs. In group A (Table 2), 43 of 46 patients (93%) with PV had positive cultures. Three, in spite of fitting the standard criteria, had negative cultures. The first two were technical failures. In all three cases, the cultures could not be repeated. Two of these patients have died, one from a Blast transformation of PV, the second from an astrocytoma. None of the 12 patients with SP had a positive culture. For diagnosis of PV, there was an excellent statistical correlation (P < .0001) in this group of 46 PV and 12 SPs between the standard criteria and positive cultures. The study of the 29 patients with unclassified polycythemia showed positive cultures in 18 cases (62%): 11 of 12 patients (6 men, 5 women) with 2 major and 1 minor criterion, 7 of 17 patients (4 men, 3 women) with 2 major and no minor criteria, and one of whom belonged to a PV family. In all group A, the presence of at least 2 major criteria and 1 minor criterion makes the probability of the culture being positive statistically significant (P < .0001).

In group B, 4 patients (3 men, 1 woman) (20%) had positive cultures: one with 2 major and 2 minor criteria who belonged to a PV family, one with 2 major criteria, one with 1 major criterion and 2 minor criteria, and the last one with only 1 major criterion but with a positive family history. The 5 patients with a disposition toward polycythemia had negative cultures. The remaining 12 had negative cultures.

In group B, the presence of at least 1 major criterion and 2 minor criteria or a family background makes the probability of the culture being positive statistically significant (P < 0.0001), in spite of the small size of the series (n = 21).

Thus, the culture of bone marrow erythroid progenitors has allowed differentiation among the 45 unclassified polycythemias (UP), 22 cases with EECs (18 cases from group A and 4 from group B), and 23 cases without EECs (11 from group A and 12 from group B).

To evaluate the significance of the presence of EECs in the absence of criteria for PV, we studied other laboratory tests that can help in the diagnosis of PV and the prognosis of the disease of these patients.

Unclassified polycythemias with EECs in the bone marrow. The 22 patients were 13 men and 9 women with a mean age of 56.3 ± 15.6 years (range 19 to 81 years); 18 of 22 have had in common a high TRVC (mean 48 ± 13 mL/kg), a normal arterial oxygen saturation, and the absence of splenomegaly. The WBCs count was >12 x 10^9/L in three cases, and the platelet count was >400 x 10^9/L in eight cases. The LAP score was elevated in one case, but became high in two other cases during progression of the disease. Four of 22 have had a slightly increased TRVC (mean 32.6 ± 2.6 mL/kg) with a normal arterial oxygen saturation. Splenomegaly was present in two cases. WBCs and platelets were elevated in two cases.

Bone marrow biopsies were done in 15 of 22 patients. The results are shown in Table 3. The grade of the bone marrow was normal in 3 cases, slightly increased in 1 case, and

<table>
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<tr>
<th>Table 2. Comparative Study of Standard Criteria of Polycythemia and Results of Bone Marrow Erythroid Progenitor Cultures</th>
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<tr>
<td>Group</td>
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<tr>
<td>-------</td>
</tr>
<tr>
<td>A</td>
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<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>B</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Total</td>
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EECs, endogenous erythroid colonies derived from bone marrow cells developing without exogenous erythropoietin.

Standard criteria, criteria proposed by the Polycythemia Vera Study Group and criteria of secondary polycythemia. Group A is defined by a TRCV of > 36 mL/kg in males and TRCV > 32 mL/kg in females; group B is defined by a TRCV between 30 and 36 mL/kg in males and between 25 and 32 mL/kg in females.

<table>
<thead>
<tr>
<th>Table 3. Grade of Bone Marrow in Patients With Polycythemia Vera and With Unclassified Polycythemias With or Without Endogenous Erythroid Colonies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Marrow (Grade)</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>PV</td>
</tr>
<tr>
<td>UP (A + B)</td>
</tr>
<tr>
<td>UP (A)</td>
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<tr>
<td>UP (B)</td>
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<table>
<thead>
<tr>
<th>UP, unclassified polycythemias.</th>
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</thead>
<tbody>
<tr>
<td>Grade of bone marrow: cellularity. N, normal; +, slight increase; ++, moderate increase; ++++, marked increase. A, patients with a total volume of circulating RBCs (TRVC) &gt;36 mL/kg in males and &gt;32 mL/kg in females; B, patients with a TRVC between 30 and 36 mL/kg in males and between 25 and 32 mL/kg in females. All numbers indicate number of cases.</td>
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<tr>
<td>*Patient had a normal number of megakaryocytes.</td>
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<td>†One-third had a normal number of megakaryocytes.</td>
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increased in 11 cases. There was no difference between the patients who lacked one or more standard criteria. In the meantime, 22 bone marrow biopsies were done among the 46 patients with PV: the grade of the bone marrow was normal in one case and increased in 21 cases. When a cut-off point between normal and slightly increased cellularity on one hand and moderate or marked cellularity on the other hand was chosen, there was no difference between the two groups (NS).

Epo level in the serum was measured in 12 of 22 patients; the results are presented in Fig 1. The Epo level was low in 5 cases, normal in 6 cases, and high in only 1 case. The mean level was 11.75 ± 6.78 mU/mL of serum, ranging from 4 to 30 mU/mL. There was no difference between the patients who lacked one or more standard criteria. Meanwhile, Epo levels were measured also in 16 patients with PV; they were low in 5 cases, normal in 9 cases, and high in 2 cases. The mean level in this group was 13.5 ± 10.5 mU/mL of serum, ranging from 4 to 42 mU/mL. The comparison between the two groups has not shown any statistically significant difference (NS).

The course of the disease could be followed in 21 of 22 cases with a mean follow-up of 4.25 ± 2 years (extremes: 1.5 to 7 years).

Sixteen of 18 patients of group A were treated. In 15 cases, the disease was continuously active with relapses under treatment. In three of these cases, PV became evident on the standard criteria during follow-up. Thrombophlebitis occurred in five cases. Five patients died: one from agnogenic metaplasia after a course of 6 years, and four from vascular thrombosis. One patient had a stable disease under treatment for 4 years, and the patient who was not treated but followed had a permanent and nonevolving polycythemia.

The four patients with a slightly increased TRCV received treatment and achieved complete remission. Two patients have had an active disease with an increasing TRCV, and one died from agnogenic metaplasia after a course of 6 years. The two other patients are always in complete remission, under treatment.

Unclassified polycythemias without EECs in the bone marrow. All but one of the 23 patients were men, with a mean age of 49 ± 15.5 years (range 22 to 76 years). They have had in common an absence of splenomegaly, normal arterial oxygen saturation, normal WBC and platelet counts; the LAP scores and the B-12 serum levels were also normal. Eleven patients have had a clearly increased TRCV (mean 40 ± 3.4 mL/kg) whereas the 12 others have had a slightly increased TRCV (mean 32.8 ± 2.1 mL/kg).

Bone marrow biopsy was done in 13 of 23 cases. The results are shown in Table 3. The grade of the bone marrow was normal in 8 cases, slightly increased in 4 cases, and increased in 1 case. There was a striking difference between the bone marrow in these patients and the patients with PV (P < .01) as well as the patients with unclassified polycythemias with EECs (P < .01).

Epo level was measured in 15 of 23 cases (Fig 1). It was low in two cases, normal in eight cases, and high in five cases, with a mean of 17.16 ± 9.25 mU/mL and a range of values from 4 to 31 mU/mL. Among the patients with high levels, three had increased TRCV (group A) and two had a slightly increased TRCV (group B). None of these patients had tumors; blood oxygen affinity was studied in three cases and was normal. In two cases, excessive smoking was suspected but the level of carboxyhemoglobin was not evaluated. In all five patients, the significance of the high level of erythropoietin remains to be found. There is no significant difference between this group and patients with PV or with UP and EEC (NS). There is a statistically significant difference, however, between this group and a group of 11 SPs studied in the meantime (P < .001).

All these patients but one were followed in absence of treatment with a mean follow-up of 3.25 ± 1.5 years (range 1.5 to 7 years). There were no significant changes in the blood counts, and no complications occurred.

**DISCUSSION**

Two observations stand out in this study of an unselected series of patients with different forms of polycythemia. First, the standard criteria for the etiologic diagnosis were applicable in only 63 of 108 (57%) of the cases: 46 PV and 17 secondary type. If one considers the group with definitely abnormal TRCV, the etiologic diagnosis was possible in 57 of 87 (66%) of the cases.

Second, the presence of an abnormal population of erythroid progenitors was observed not only when all the standard criteria of PV were present, but also (in many cases) when they were lacking. In group A, the culture was positive in 93% of patients having all the criteria of PV and in 63% in
whom some of these criteria were missing. In group B, the culture was also positive in 20%.

The criteria proposed by the PVSG in 1965 have had the merit of distinguishing a homogenous group of patients with PV but lead to the exclusion of atypical and early forms. Therefore, an important number of polycythemias could not be classified as PV even though the TRCVs were very elevated: 29 of 87 cases in our series. Moreover, the definition of PV as a value of TRCV >2 SD (+2 SD) of the average value likewise contributed to the exclusion of definite cases with abnormally high blood counts, a moderate elevation of TRCV, and no reduction of total plasma volume. These cases, classified by some as spurious polycythemias, may equally well be forms of PV at a stage just starting or smoldering cases of PV. The long absence of a specific measurable criterion for a primary disorder involving the production of the erythroblastic line explains these difficulties.

Although the initial cause of PV remains unknown, abnormality of the erythroblastic line is now well established through recent findings. PV can be considered the result of an abnormality of a clone from myeloid stem cells from which a population of erythroid progenitors recognized by its behavior in in vitro semisolid medium derives.

The diagnostic value of the presence of this population during the course of polycythemia has not been the object of important prospective studies, as far as we know. The presence of spontaneous erythroid colonies in SP has been reported by many authors. Clement and colleagues reported finding spontaneous colonies in 8 of 18 patients with pure erythrocytosis, a debatable term used for cases characterized by an important and isolated increase in TRCV. Analysis of our results indicates that the finding of spontaneous colonies is of great value in differentiating PV from secondary forms.

The means of the two groups are <2 SD of the average of PV, all the more so because the hemoglobin and hematocrit of the patients with PV. Fifteen of 21 patients who could be followed have had an active disease which has required treatment. Several cases of thrombophlebitis were noted. Six patients died from vascular complications and from myelofibrosis, as happens in PV. Conversely, the patients with unclassified polycythemias without EEC have had a quiet course, without treatment.

We believe that the varying combinations of the hematological data in the patients with polycythemia and EECs are related to the diversity of lineage involvement in the chronic myeloproliferative syndromes, the reasons for which have been unclear. These varied manifestations may be dependent on the predominant impaired stem cell and its proliferative strength. Thus, the 18 of 29 cases of unclassified polycythemias of group A were PV with variable hemato poeticin in the serum of patients with PV and unclassified polycythemias with EECs. The means of the two groups are <2 SD, whereas it is high in secondary forms. Discrepancies can be noted, however, despite the method of dosage used, which reduces the diagnostic importance of this test for individuals. In one patient with UP and EECs, the level was as high as it was in two patients with PV. High levels of Epo were also observed in PV by Koeffler and Goldwasser with a radioimmunological method. Conversely, there was a greater proportion of patients (5 of 15) with high Epo levels in the group with unclassified polycythemias without EECs.

The cause of the increase that produced a true polycythemia in three patients and a slight increase of TRCV in the two others was not found until now. The higher mean of Epo in this group, although not significantly different from the mean of Epo in PV or in patients with EECs, leads to the consideration of these patients as a heterogenous population. Some of them may have SPs, some real unclassified polycythemias, and some may have spurious polycythemias.

Finally, the course of the disease in the patients with unclassified polycythemias with EECs was very similar to that of the patients with PV. Fifteen of 21 patients who could be followed have had an active disease which has required treatment. Several cases of thrombophlebitis were noted. Six patients died from vascular complications and from myelofibrosis, as happens in PV. Conversely, the patients with unclassified polycythemas without EEC have had a quiet course, without treatment.

We believe that the varying combinations of the hematological data in the patients with polycythemia and EECs are related to the diversity of lineage involvement in the chronic myeloproliferative syndromes, the reasons for which have been unclear. These varied manifestations may be dependent on the predominant impaired stem cell and its proliferative strength. Thus, the 18 of 29 cases of unclassified polycythemias of group A were PV with variable hematologic findings. Of the four patients of group B with positive cultures, three had all the standard criteria of PV except for a sufficiently high TRCV. The absence of this first criterion is easily explained if it concerns a beginning case or one that has hardly evolved. The fourth patient had only one major criterion but had a parent with PV. The rarity of familial forms of PV, which represent only 0.8% of all PV cases, is an important argument in linking this case to a beginning stage of PV, all the more so because the hemoglobin and hematocrit were elevated and the TRCV slightly increased without any decrease in plasma volume.

The unclassified polycythemias without EECs were a
heterogenous group. The cause of the polycytherias in the patients with a high TRCV (group A) remains to be found, especially for the patients with a normal Epo level.

The 12 cases of group B cannot be better defined for the moment. The patients with normal bone marrow biopsies and normal Epo levels were perhaps normal subjects corresponding to group A of Weinreb and Shin in framework of spurious polycythemia. The two patients with increased Epo levels were perhaps cases in a very early stage.

The better evaluation of PV by the bone marrow erythroid progenitor cultures in polycytherias in the study we report (+22%) leads us to reconsider the recommended diagnostic steps to follow in a suspected case of polycythemia. That investigation must occur at an earlier diagnostic step, at the same time that the TRCV and the arterial oxygen saturation are measured. Likewise, one must now consider the possibility of diagnosing PV at an early stage when the TRCV increase is still minimal. As early treatment and control improve the survival median of PV, one may expect that early diagnosis will improve the outlook.

ACKNOWLEDGMENT

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A prospective study of the value of bone marrow erythroid progenitor cultures in polycythemia