Thrombocythemia and Pulmonary Intra-Alveolar Coagulum in a Young Woman

By B. Levinson, R. S. Jones, M. M. Winthrobe and G. E. Cartwright

An increased number of circulating platelets (thrombocytosis, thrombocythemia, piastreninia) has been known to occur in response to a variety of nonhematologic conditions. Thrombocythemia, a term applied to persistently increased platelet levels, is also an integral part of certain diseases primarily affecting the blood-forming organs. The authors have had the opportunity to study a young woman in the terminal phase of an illness characterized by a markedly increased number of circulating blood platelets as well as a very unusual type of lung pathology. The purpose of this report is to describe the clinical course and pertinent postmortem findings in this patient. A preliminary report of this case has been published. The possibility of Pneumocystis carinii infestation of the lung as well as the question of interrelationship between the thrombocythemia and the lung pathology are considered.

Case History

S.O. (C.M. No. 4887) (SLCGH No. 35–30)

This 19-year-old white female was first seen by the writers on October 15, 1954. Her chief complaint at that time was shortness of breath of three months' duration. She had been well until August, 1952, when a tonsillectomy was performed for "tonsillitis." This procedure was complicated by hemorrhage from the tonsillar fossae which required transfusion of four units of whole blood. At that time, her physician noted that there was a strikingly increased buffy coat in the hematocrit tube. During the next year, the patient noted excessive menstrual bleeding, and anemia was found. This was treated intermittently with iron by mouth and vitamin B₁₂ by injection. A routine chest x-ray taken in November, 1953, was not reported to the patient as being abnormal. She had no further symptoms until August, 1954, when she began to notice progressive exertional dyspnea associated with an intermittent nonproductive cough and mild cyanosis. She had lost 14 pounds in weight during the preceding three months. The past and family histories were noncontributory.

Her blood pressure was 110/70, pulse rate 90 per minute and respirations 23 per minute; oral temperature was 98.2° F., weight 108 pounds, and height 65 inches. The patient was apprehensive, well-nourished but slender. There were plethora and slight cyanosis of the lips and nail beds, but there was no clubbing of the distal phalanges. Three soft, freely...
movable, non-tender lymph nodes, each measuring 5 mm. in diameter, were present in the left axilla. Examination of the chest was normal. A strong precordial impulse was noted 2 cm. to the left of the sternum at the fourth intercostal space, but the heart was not enlarged. The second pulmonic sound was accentuated and a soft systolic murmur was heard at the apex. The spleen was palpable 5 cm. and the liver 3 cm. below the costal margins in the midclavicular line during quiet respiration. There was slight sternal but no tibial tenderness. The remainder of the physical examination was essentially negative.

The laboratory data included the following: volume of packed red cells (V.P.R.C.), 49 ml. per 100 ml., and volume of packed white cells plus platelets (V.P.W.C. & P1.), 7.5 ml. per 100 ml. of blood; hemoglobin 15.7 Gm. per 100 ml. of blood; red blood cells 6.33 million and platelets greater than 3 million per cu.mm. of blood (there were many additional platelets in clumps); leukocytes 20,250 per cu.mm. The differential count is shown in table 1. The red cells appeared normocytic and normochromic, but slight polychromatophilia was present.

In essence, the patient had marked thrombocytosis and moderate leukocytosis with neutrophilia, eosinophilia, increased basophilic leukocytes and occasional nucleated red cells in the blood. Of special interest was the 7.5 mm. layer of creamy white-yellow material above the layer of packed red cells in the hematocrit. A stained smear of this material indicated that it consisted almost entirely of platelets. A sternal bone marrow specimen was cellular; the differential count was normal and the M:E ratio was 3:1 (table 2). The megakaryocytes were abundant, but they were not obviously increased in number.

### Table 1—WBC and Differential

<table>
<thead>
<tr>
<th>Hosp. Day</th>
<th>Date</th>
<th>WBC per mm.</th>
<th>Myeloocytes</th>
<th>Juvenile</th>
<th>Neutro.</th>
<th>P.M.N.</th>
<th>Eos.</th>
<th>Basophil</th>
<th>Lympho</th>
<th>Monos.</th>
<th>NRBC* (per 100 WBC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/15/54</td>
<td>20,250</td>
<td>0</td>
<td>1</td>
<td>55</td>
<td>12</td>
<td>12</td>
<td>20</td>
<td>0</td>
<td>occ.</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>12/20/54</td>
<td>10,900</td>
<td>0</td>
<td>0</td>
<td>69</td>
<td>7</td>
<td>5</td>
<td>16</td>
<td>3</td>
<td>occ.</td>
<td></td>
</tr>
<tr>
<td>79</td>
<td>1/3/55</td>
<td>15,800</td>
<td>0</td>
<td>2</td>
<td>74</td>
<td>1</td>
<td>1</td>
<td>22</td>
<td>0</td>
<td>occ.</td>
<td></td>
</tr>
<tr>
<td>86</td>
<td>1/10/55</td>
<td>10,000</td>
<td>4</td>
<td>13</td>
<td>67</td>
<td>3</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>93</td>
<td>1/17/55</td>
<td>20,200</td>
<td>4</td>
<td>10</td>
<td>48</td>
<td>5</td>
<td>2</td>
<td>31</td>
<td>0</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>101</td>
<td>1/25/55</td>
<td>45,000</td>
<td>2</td>
<td>5</td>
<td>68</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>110</td>
<td>2/3/55</td>
<td>11,200</td>
<td>5</td>
<td>72</td>
<td>18</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>occ.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Nucleated red blood cells.

### Table 2—Bone Marrow

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10/15/54</td>
<td>6</td>
<td>—</td>
<td>16</td>
<td>15</td>
<td>2</td>
<td>2</td>
<td>24</td>
<td>6</td>
<td>2</td>
<td>16</td>
<td>1</td>
<td>6</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>1/15/55</td>
<td>6</td>
<td>—</td>
<td>16</td>
<td>15</td>
<td>2</td>
<td>2</td>
<td>24</td>
<td>6</td>
<td>2</td>
<td>16</td>
<td>1</td>
<td>6</td>
<td>27</td>
<td>27</td>
</tr>
</tbody>
</table>

*Cellular spec.; normal number of megakaryocytes.**

*Cellular spec.; mild increase in megakaryocytes.*
THROMBOCYTHEMIA AND PULMONARY INTRA-ALVEOLAR COAGULUM

FIGURE 1

A. Smear of peripheral blood showing a mass of platelets (X 350).
B. Megakaryocytes in pre-mortem bone marrow (X 350).
C. Numerous megakaryocytes are uniformly distributed throughout the section of vertebral marrow (X 75).
D. Higher magnification of figure 3C shows megakaryocytes with enlarged and hyperchromatic nuclei. Some leukocytes appear to be within the cytoplasm of the megakaryocytes (X 350).

(fig. 1B). The tourniquet test was negative, the bleeding time (Ivy) was 5 minutes, clot retraction satisfactory at two hours and Lee-White clotting time 9 minutes. Urinalysis showed a specific gravity of 1.028, pH 6 and a trace of protein. Roentgen examination of the chest (fig. 2A) revealed an extensive, bilateral, diffuse, finely nodular infiltration with some coalescence in the left second anterior intercostal space. An electrocardiogram indicated a normal, vertical heart with a sinus tachycardia of 107 beats per minute.

The initial impression was that the patient was suffering primarily from pulmonary insufficiency due to an infiltrative process in the lungs which was of unknown etiology.
Fig. 2.—Roentgenograms of the chest.

A. First examination. A diffuse, symmetrical infiltrative process involves the lower three-fourths of the lung fields bilaterally. Both costophrenic angles are spared, as are the apices. On the lateral projection the diffuse increase in density was seen to involve all lobes.

B. Third hospital day. Note the coalescence of the infiltrative process in the left upper lung field.

C. Eighty-eighth hospital day. There are interlacing densities throughout both lung fields, more marked in the right. The left upper field is now relatively clear. The heart is enlarged in transverse diameter.

D. One hundred and fourteenth hospital day. There has been some increase in the extent of the pulmonary involvement and the transverse diameter of the heart is still further enlarged.

In addition there were signs of a myeloproliferative disorder characterized mainly by a marked thrombocytosis but with many features resembling chronic myelocytic leukemia. A single explanation for these findings was not apparent.

On October 16, 1954, the patient suddenly developed fever to 104° F., shaking chills, sharp left pleuritic chest pain and a slightly productive hacking cough. The following day she was admitted to the Salt Lake County General Hospital. Physical and roentgen examination (fig. 2B) indicated the presence of an area of consolidation in the left upper lobe. Sputum cultures revealed many pneumococci and a few nonhemolytic streptococci.
Procaine penicillin therapy, 300,000 units twice daily, was ineffective. Administration of tetracycline, 2 grams per day, was associated with gradual improvement in the signs and symptoms of the pneumonia. On the seventh hospital day, the patient became more dyspneic, a gallop rhythm was heard along the left sternal border and the cardiac silhouette appeared enlarged on x-ray. Digitalization produced substantial improvement in the dyspnea and the gallop rhythm disappeared. On the twelfth hospital day, a transthoracic liver biopsy was performed; no abnormalities were found in the liver upon histologic examination. A few hours after the procedure, a right-sided tension pneumothorax developed. This resolved completely, after two days, following the application of negative pressure through an intrapleural catheter. By this time the patient had recovered from the acute febrile illness but her general condition had gradually deteriorated.

The patient's hospital course is partially represented in figure 3. Additional studies included the following.

**Bacteriology:** Nose, throat and sputum cultures at various times during the course of the illness revealed the following predominant organisms: nonhemolytic, alpha hemolytic and beta hemolytic streptococci; nonhemolytic coagulase-positive Staphylococcus aureus; *Candida albicans*. All 17 blood cultures were negative and two cultures of the bone marrow were negative for fungi and acid-fast bacilli. Skin tests for histoplasmosis, blastomycosis, coccidioidomycosis and first and second strength P.P.D. were all negative.

**Chemistries:** Van den Bergh 0.05 mg. % direct and 0.3 mg. % indirect; alkaline phosphatase 3.5 to 9 King-Armstrong units; serum albumin 3.1 to 4.2 Gm. %; serum globulin 3.0 to 3.2 Gm. %; prothrombin time 42 to 66% of normal; bromsulfalein retention 4% at 45 minutes; thymol turbidity 2.5 to 8.5 units (normal up to 5 units); cephalin flocculation 2+; CO₂ 25 mEq. per liter; chlorides 95 to 102 mEq. per liter; B.U.N. 7.5 to 11.5 mg. %; uric acid 4.7 mg. %; calcium 10 mg. %; phosphorus 7.2 mg. %; a 24-hour urine collection contained no beryllium.

**Miscellaneous hematologic data:** Direct and indirect Coombs' tests, negative; reticulocytes 1 to 2.5%; urinary urobilinogen (2-hour collection) 0.1 to 0.3 Ehrlich units.

**Pulmonary function studies** carried out on the 33rd hospital day are shown in summarized form.
form in table 3. These were interpreted as indicating considerable restriction of lung volume and a moderate reduction of maximal ventilatory capacity. There was mild hyper-ventilation and severe arterial oxygen unsaturation at rest. Since full saturation did not occur when 100% oxygen was inhaled, it would seem likely that the hypoxia was due, at least in part, to physiologic venous admixture. The possibility that there was impairment of diffusion of gases through the alveolo-capillary membrane could not be excluded by these studies since the diffusing capacity of the lung for O₂ was not measured.

**Circulatory:** On the seventh hospital day the decholin arm to tongue circulation time was 11 seconds and the venous pressure in the antecubital vein was 120 mm. of normal saline. On the 108th hospital day the corresponding values were 15 seconds and 270 mm., respectively.

On the 37th hospital day a thoracotomy was performed and biopsies were taken from portions of the right middle lobe. At the time of surgery the lung was found to be involved by a diffuse, widespread multinodular infiltration. There were a number of individual lesions from 1 to 6 mm. in diameter but in most places these were confluent. As the lung was divided, sticky secretions exuded generally from the cut surfaces. The excised portions of the right middle lobe were tan-gray in color and were rather friable. Histologic examination of the lung revealed that an amorphous, acidophilic material filled the alveolar sacs and that the alveolar septae were thickened in some areas. Sections of a hilar lymph node revealed changes corresponding to those of chronic lymphadenitis. Cultures and smears of the lung tissue and lymph node were negative for tubercle bacilli and fungi but a few gram positive rods were cultured from the lung tissue.

The patient was discharged on the 49th hospital day in fairly good general condition and advised to return in four weeks. However, two weeks later (62nd day), she was readmitted to the hospital acutely ill with fever, nausea, vomiting and anorexia and was marked dyspneic and cyanotic. A grade III basilar systolic murmur, gallop rhythm and slight clubbing of the fingernails were noted. She was treated with various antibiotics without response. Combined therapy with cortisol 200 mg. per day, erythromycin, penicillin, and streptomycin was associated with marked subjective improvement and return of the temperature and pulse to normal. The steroid therapy was associated with a marked rise of leukocytes to 45,000 per cu.mm. The tachycardia recurred when the antibiotic therapy was discontinued and, when cortisol administration was interrupted, the temperature gradually rose to parallel the pulse rate. Serial electrocardiograms showed evidence of progressive right ventricular hypertrophy. The patient's weight had declined to 88 pounds.

In the hope that a myelosuppressive agent would alter the unfavorable course, therapy with Myleran (1,4-dimethanesulfonyloxybutane), 4 mg. per day, was initiated and was continued for 10 days. This was without effect on the temperature, pulse or size of the

<table>
<thead>
<tr>
<th>Table 3.—Pulmonary Function Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Observed</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Vital Capacity (cc.)</td>
</tr>
<tr>
<td>Residual Volume (cc.)</td>
</tr>
<tr>
<td>Total Capacity (cc.)</td>
</tr>
<tr>
<td>Resid. Vol./Tot. Cap. (%)</td>
</tr>
<tr>
<td>Max. Vent. Cap. (L./min.)</td>
</tr>
<tr>
<td>Ventilation (L./min./met.² BSA)</td>
</tr>
<tr>
<td>Arterial Oxygen Saturation (%)</td>
</tr>
<tr>
<td>Art. Oxygen Sat. while breathing 99.85% oxygen (%)</td>
</tr>
<tr>
<td>Alveolar oxygen tension (mm. Hg)</td>
</tr>
<tr>
<td>Arterial oxygen tension (mm. Hg)</td>
</tr>
<tr>
<td>Arterial CO₂ tension (mm. Hg)</td>
</tr>
</tbody>
</table>

Spirograms showed no evidence of airway obstruction. Lung volumes, maximum ventilatory capacity and ventilation were calculated at body temperature, ambient barometric pressure, and saturated with water vapor.
spleen or liver but did produce a drop in the leukocyte count and volume of packed red cells (V.P.R.C.). The numbers of white and red cells, however, continued to decline even after discontinuation of the therapy. An early pulmonary diastolic murmur appeared. Re-digitalization did not affect the tachycardia or progressive shortness of breath. Hydrocortisone, 180 mg. per day, had no effect on the anemia or leukopenia but did induce a decline in the temperature and pulse rate.

When the V.P.R.C. had dropped to 18 per cent, 250 ml. of packed red cells was slowly administered. The following day the patient appeared to be more uncomfortable. She suddenly became more severely dyspneic, moist rales were heard throughout the chest and, despite all measures, the patient expired on the 127th hospital day (2/20/55).

Pathologic findings: Autopsy was performed 14 hours after demise. The outstanding changes were a diffuse intra-alveolar, non-cellular coagulum in the lungs and a marked increase in megakaryocytes in the bone marrow. Death seemed attributable to the pulmonary disease.

The pericardial sac contained 75 ml. and each pleural cavity held 100 ml. of clear serous fluid. The right lung weighed 1300 Gm. and the left 1100 Gm. The pulmonary vessels were unchanged. Copious yellow serous fluid welled from the transected trachea and bronchi. There was no evidence of fibrosis or granuloma formation in the pulmonary tissue or in the soft, moderate-sized hilar lymph nodes. Opaque yellow mottled zones of consolidation were scattered throughout the pulmonary tissue; this was most marked in the right lung and least noticeable in the lung apices.

The microsections of the original lung biopsy were similar to those of tissue obtained at autopsy. Filling and distending the alveoli was a granular eosinophilic material (figs. 4A, 4B) which was shown by differential staining to consist of variable quantities of lipid, carbohydrate and protein. Throughout this eosinophilic coagulum were zones of PAS positive material (fig. 4C) and uniformly dispersed fat droplets as well as occasional masses of lipid (fig. 4D). The aggregation of some fat droplets suggested an original location within macrophages, now disintegrated (fig. 4D). In isolated areas, compact masses of protein were seen in the alveoli partially organized by fibroblasts and usually surrounded by the lipid and PAS positive material. There was a striking absence of leukocytic exudation, even in the rare areas where clusters of bacteria were found within the coagulum. The alveolar walls were generally normal in appearance. However, in many places, they were thickened to several times the normal by fibroblastic proliferation and collagen deposition (figs. 4B, 4C). In their walls were occasional, pale brown, fat-laden macrophages and masses of lipid similar to those found within the intra-alveolar coagulum. No tubercle bacilli or fungi were detected by special stains. Stains of the fixed lung tissue, made in an attempt to demonstrate Pneumocystis carinii, included Trichrome, P.A.S., Alcian blue plus P.A.S., Giemsa, Gridley and Warthin's. No cystic form of this agent could be found but innumerable discrete angular black dots about 1 micron in diameter were observed to be scattered throughout the coagulum on sections stained by Warthin's silver technic.

The heart weighed 300 Gm. with the right ventricle 5 mm. and the left ventricle 15 mm. in diameter. The valves and myocardium were unchanged.

Bone marrow from the ribs, vertebrae and mid-femoral areas revealed engorged venous channels and diminished numbers of myelopoietic cells without apparent reduction in the cells of the erythropoietic series. Megakaryocytes were markedly increased in number (fig. 1C) and in microscopic fields of 75 X magnification, 35 megakaryocytes could be identified. Often the megakaryocytes were of normal size but contained enlarged nuclei or were of smaller size with rounded nuclei (fig. 1D). In addition, alterations seemed to have occurred in the megakaryocytes, for macrophages and polymorphonuclear leukocytes often appeared within a clear vacuolated zone or in an indented area of the megakaryocytic cytoplasm. Nuclei of these as well as other megakaryocytes often appeared as indistinct basophilic masses. There was no fibrosis in the marrow and the osseous trabeculae were unaltered.

Although megakaryocytes were present within the distended venous channels of the bone marrow, none was seen within the arteries. Megakaryocytes with pyknotic nuclei and
A. The alveoli of the lung are distended with a non-cellular material (Hematoxylin and eosin) (X 100).
B. Some alveolar walls are thickened and the intra-alveolar exudate shows occasional areas of early organization (Hematoxylin and eosin (X 100).
C. Periodic acid-leucaofuchsin stains many areas of the intra-alveolar exudate (X 100).
D. Sudan IV stain for fat reveals an aggregation of fat droplets, suggesting original location in disintegrated alveolar macrophages (X 100).

Sparse cytoplasm were observed, however, within the capillaries of the alveolar walls and occasionally within the hepatic sinusoids, myocardial capillaries, splenic pulp and lymph nodes. There was no extra-medullary hematopoiesis, and megakaryocytes in the visceral capillaries did not have the hyperchromatism of those in the marrow. The capillaries were unchanged at all sites and no platelet thrombi were encountered.
The capsular surface of the 800 Gm. spleen was smooth and showed marked engorge-
ment of the red pulp with occasional hemorrhages in the small Malpighian centers. The
red pulp showed no prominence of sinusoidal endothelium; occasional eosinophils or
pyknotic megakaryocytes were encountered within the sinuses. There were a few fine
granular masses suggestive of loose aggregates of platelets in the sinuses.

As in the spleen, the follicles of the tracheobronchial and mesenteric lymph nodes were
of small size and usually without germinal centers. Macrophages often encircled small ves-
sels and capillaries in the lymph nodes.

The liver weighed 2100 Gm. No changes were seen in the cord cells or bile ducts of this
organ.

There were no other tissue changes except for a thin adrenal cortex, a 4.5 mm. cyst in
the pars intermedia of the pituitary and multiple small ovarian follicular cysts, sparsely
lined with granulosa cells. Proteus organisms were recovered from the heart blood. Splenic
and lymph node tissue gave a negative dye test for toxoplasmosis.

**DISCUSSION**

Thrombocytosis is known to occur in a variety of circumstances. As a tempo-
rary phenomenon, an increase in platelets may occur following surgical
operations, after asphyxiation and following trauma, especially when bones
are fractured. Acute blood loss causes thrombocytosis and an increase in
platelets may occur in acute rheumatic fever and in suppurative infections.
More persistent thrombocytosis (thrombocythemia) and an increase of greater
magnitude follows splenectomy. This is also seen in association with splenic
atrophy and is common in chronic myelocytic leukemia and in polycythemia
vera. Thrombocythemia may be encountered in Hodgkin's disease and, rarely,
in association with carcinoma, hyperadrenalism, splenic vein thrombosis,
Beck's sarcoïd, and myelosclerosis. In addition, a number of reports des-
cribing "idiopathic" or "essential" thrombocythemia have appeared in the
literature.

Scrutiny of reported instances of thrombocythemia reveals that some were
quite clearly examples of the entities mentioned above (case 2, Case 1, Case
1-410-14,24). Other cases were incompletely reported or complicating fac-
tors were present (case 1, case 3, case 415-21,25). There remain, however,
several cases of thrombocythemia in which no underlying disease was appar-
ent (case 2, case 540,22,23). To these the term "idiopathic" or "essential" throb-
ocythemia may be applicable.

"Idiopathic" thrombocythemia has been observed in adults in both sexes. Easy fatigability and weakness have been the chief complaints. Frequently
slight to moderate leukocytosis has been observed, as well as some splenic en-
largement. Of special note is the fact that, in spite of the large number of platelets, a hemorrhagic diathesis has been described in a number of instances
of thrombocythemia, whether "idiopathic" or secondary. The platelets were studied in some of these cases and were found to be qualita-
tively deficient as determined in the thromboplastin generation test, and the
5-hydroxytryptamine (serotonin) content of the platelets in some of the cases
was found to be below the normal range. The significance of the observed
changes in thromboplastin generation has been questioned, however, and
it has been suggested that thrombocythemic platelets are functionally normal
but that excessive numbers of platelets impair the process of coagulation both
by interfering with thromboplastin formation and by inhibiting the action of thromboplastin already formed. Exhaustive coagulation studies of 27 patients with chronic thrombocytopenia by Soulier et al. indicated marked variability from patient to patient as well as from test to test in the same patient. Thus, increased clotting tendency could be demonstrated by an increase in tolerance to heparin and increased thromboplastin generation by platelets, while increased fragmentation of the clot and decreased pro-accelerin activity could also be shown. It becomes apparent that further investigation is necessary in order to arrive at a clear understanding of the defect in the coagulation mechanism in thrombocytopenia.

Our patient presented a picture in some ways suggesting chronic myelocytic leukemia but could hardly be classified as such. The preponderance of platelets in the blood and megakaryocytes in the bone marrow, as well as the bizarre character of her illness, would lead one to think that this unique disorder was indeed an example of “idiopathic hemorrhagic thrombocytopenia.”

The pulmonary disease was of a distinctly unusual nature. Pulmonary function studies suggested that the hypoxia was due to a physiologic venous admixture and a possible, but not proved, “alveolo-capillary block.” This is to be expected from the histologic changes in the lung tissue. There was an extensive intra-alveolar, honey-combed coagulum with little inflammatory reaction. In a few areas the alveolar septae were thickened by a mononuclear infiltration. This combination has been previously described only in interstitial plasma cellular pneumonia due to Pneumocystis carinii.

Gajdusek reviewed the problem of Pneumocystis carinii infections. Pneumonia due to this organism has been described almost exclusively in Europe but recently a few cases have been reported from England, Canada, and the United States. Although the vast majority of cases have occurred in premature or dystrophic infants, otherwise healthy children have also been afflicted with this disease. Only six adults are known to have been affected (van der Meer’s case, McMillan’s case and Vanek’s two cases). The etiologic agent has yet to be definitively identified. Cystic structures measuring 5 to 12 microns in diameter have been demonstrated within the intra-alveolar coagulum in histologic sections as well as in imprints of lung tissue (Vanek and Jirovec) obtained at autopsy. These structures consist of one to eight angular rods taking nuclear stains which are surrounded by a thick mass of P.A.S. positive material, and this in turn is encased within a thin-walled capsule. Most investigators claim that the angular rods are the organism Pneumocystis carinii, which has been considered to be a stage of a protozoan by some and of a fungus by others. In either case, it still remains to be proven that these structures are related to the pathogenesis of the disease.

The cysts of Pneumocystis carinii could not be found in the lung tissue of our patient. However, the characteristic extensive intra-alveolar honey-combed coagulum with little inflammatory reaction, the mononuclear infiltration of the alveolar septae and the demonstration of small black dots within the coagulum on silver stains suggest the possibility, at least, of an infection due to Pneumocystis carinii. Since our patient had a disease involving the hemo-
poietic tissues, it is of special interest that of the two adults reported by Vanek (quoted by Hamperl) one had Hodgkin’s disease and the other a “myelosis.”

An alternate explanation for the etiology of the intra-alveolar coagulum in our patient lies in the possible relationship between the coagulum and the thrombocythemia. The simultaneous occurrence of two unusual pathologic processes in a relatively young individual suggests that the two processes are closely related in cause and effect. If so, the probability that the lung pathology was secondary to the myeloproliferative disorder is suggested by the demonstration of thrombocytosis at least two years before the onset of respiratory symptoms. There is evidence that megakaryocytes are filtered out by the lung and that the lung may serve as a reservoir for platelets; platelets actually being formed there. It is possible that the destruction of an extremely large number of platelets in the lung led to the deposition of a coagulum rich in lipid, since the lipid content of platelets is known to be approximately 15 per cent of their dry weight.

On the other hand, Schwarz has theorized that megakarocytosis and thrombocythemia may be directly related to anoxemia. Although the evidence for this is rather meager, the possibility that the hematologic manifestations in our patient were secondary to the lung pathology must still be considered. Further, it is not inconceivable that the pulmonary and hematologic findings were all manifestations of a response to a third hitherto undefined stimulus.

**SUMMARY**

A description is given of the clinical course and findings at autopsy in a 19-year-old girl with a myeloproliferative syndrome characterized primarily by thrombocythemia. This was associated with an unusual pulmonary disorder in which the alveoli were filled by a non-cellular exudate comprised of carbohydrate, fat and protein which resembled in some respects pneumonia attributed to *Pneumocystis carinii*. The possible interrelationship of the thrombocythemia and the intra-alveolar coagulum is discussed.

**SUMMARIO IN INTERLINGUA**

Es presentate un description del curso clinic e del constatationes necroptic in le caso de un puera de 19 annos de etate qui habeva un syndrome myeloproliferative characterisate primarimente per thrombocythemia. Isto essea associate con un inusual disordine pulmonar, in que le alveolos essea plenate de un exsudato non-cellular composte de hydrato de carbon, grassia, e proteina. In certe respectos le disordine pulmonar resimilava pneumonia del typo attribuite a *Pneumocystis carinii*. Le relation possibile inter le thrombocythemia e le coagulo intra-alveolar es discutite.

**REFERENCES**

Thrombocythemia and Pulmonary Intra-Alveolar Coagulum in a Young Woman

B. LEVINSON, R. S. JONES, M. M. WINTROBE and G. E. CARTWRIGHT