Circulating Megakaryocytes and Platelet Release in the Lung

By Richard M. Kaufman, Romano Airo, Simeon Pollack and William H. Crosby

It has become evident in recent years that megakaryocytes, the progenitors of blood platelets, regularly inhabit the capillaries of the lung. The presence in the lungs of these large cells has generated much discussion, yet their physiologic significance has remained obscure. In 1937 Howell and Donohue contended (1) that megakaryocytes were produced in the lungs, and (2) that platelets were released in that organ. Recently, we have disproved the first contention by demonstrating that pulmonary megakaryocytes originate in the bone marrow, enter the bloodstream and migrate to the lungs, but we have also presented data which support the second contention. Ten per cent of megakaryocytes found in the dog lung contain cytoplasm; platelets derived from such cells no doubt enter the circulation within the pulmonary capillaries. Other investigators have also suggested that the lungs play a role in the delivery of platelets to blood, but the magnitude of pulmonary platelet release has not yet been defined.

It has generally been accepted that the finding of megakaryocytes in the blood almost always heralds a "serious disorder of the bone marrow," such as myelosclerosis or granulocytic leukemia. But the presence of megakaryocytes in the lungs implies that these cells normally circulate, for if they originate in the marrow, they must enter the blood in order to reach the lungs. If this is the case, then a significant number—if not the vast majority—of platelets might be released in the lungs.

For this hypothesis to be correct, megakaryocytes in the blood should contain significant amounts of cytoplasm and should be present in numbers sufficient to account for the production of the platelets in the body. In an attempt to validate this theory we have undertaken, as Schwarz once proposed, to study the incidence and morphology of megakaryocytes isolated from the right atrial blood of patients undergoing cardiac catheterization. In addition, we have attempted to quantify platelet release in the lungs.

Methods and Materials

Twenty-three human subjects, 15 females and 8 males, ranging in age from 2 to 54 years, were studied. Twenty-one of these persons had diagnosable cardiac abnormalities; the remaining two were normal volunteers.

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two persons had no heart lesions demonstrable by cardiac catheterization and were considered to be normal. One hour prior to catheterization all patients were given meperazine and pentobarbital (adults) or morphine, meperazine, and pentobarbital (children). Ten ml of blood was obtained from each patient from the right atrium or, when a left to right shunt was present, from high in the inferior vena cava. The blood was collected in a plastic syringe through either a Goodale-Lubin* woven nylon catheter, 5 to 7 French gauge, or an Ödman-Ledin† polyethylene catheter. The catheters were flushed with a dilute heparin-glucose solution (1 unit per ml) before the blood samples were drawn through them.

The blood was placed immediately in a buffered formalin-polyvinylpyrrolidone (PVP) fixative, and the saponin-hemolysis leukocyte concentration procedure of Herbeuval et al.,15 slightly modified, was followed.

**Saponin-Hemolysis Leukoconcentration Technic**

Each 5 ml of blood is thoroughly mixed with 20 ml of a diluted buffered formalin-polyvinylpyrrolidone solution in a 100 ml beaker. A one per cent saponin solution is then added slowly, drop by drop, while rotating the beaker gently, until the blood becomes translucent, indicating that hemolysis has taken place. An additional 10 ml of the dilute buffered formalin-PVP solution is added and then the hemolyzed blood suspension is transferred to a 50 ml round bottom test tube and centrifuged for 15 minutes at 1500 r.p.m. The supernatant hemolysate is decanted and the sediment—containing leukocytes, platelets, and megakaryocytes—is gently suspended in 15 ml of normal saline.

The cell suspension is next divided into 3 aliquots of 5 ml, each of which is diluted with 50 ml of saline and filtered through a Millipore filter. The filters are placed, still moist, in acidified Zenker's fixative for 15–30 minutes. Following this they are dipped in alcoholic iodine solution for 1 minute, rinsed in tap water, placed in a 5 per cent sodium thiosulfate solution for a few minutes, and then washed well in running water. The filters are then stained with hematoxylin and eosin, air-dried, and mounted on a 3 by 2 inch glass slide using Permount and a 48 by 60 mm cover glass. (Immersion oil may be substituted for Permount but does not make permanent preparations.)

In this preparation all cells, except erythrocytes, are well preserved. The different types of leukocytes are evenly distributed and clearly distinguishable, one from the other. The platelets appear as multiple small cells, ovoid, discoid or irregularly shaped, which stain a light pink, providing a rose-colored background for the other cells (fig. 1, parts c and f). The megakaryocytes, with cytoplasm stained the same color as platelets, stand out boldly and are readily identified by their large size and distinctive, basophilic, clumped nuclei (fig. 1, parts a through e).

Each filter is scanned systematically under low power. When a megakaryocyte is observed...

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†Ödman-Ledin, Solna 3, Sweden.
‡Stock formalin-polyvinylpyrrolidone solution is prepared by combining solutions (a) and (b) and is kept refrigerated.

**Solution a:** NaCl 76.5 g., KCl 2.0 g., Na Acetate 15 g., glucose 10 g., NaH₂PO₄ 0.5 g., KH₂PO₄ 1.0 g., NaHCO₃ 7.0 g., ascorbic acid 0.03 g., formalin 100 ml., distilled H₂O q.s. 1000 ml.

**Solution b:** Na Citrate 50 g., PVP 160 g., distilled H₂O q.s. 1000 ml.

Working solution is prepared by diluting 15 ml. of stock solution with 85 ml of distilled H₂O which has been first filtered through a Millipore filter, pore size 0.5 μ. This solution should be made up fresh prior to use.

§Saponin hemolyzing solution is made up as follows: Saponin 1.0 g., 95 per cent ethanol 50 ml., distilled H₂O 50 ml., formalin 2 ml.

¶Millipore filter type HA, 0.45 micron pore size, Millipore Filter Corp., Bedford, Massachusetts.
Fig. 1.—Megakaryocytes isolated from right heart blood.  

- **a** and **b**: Flattened megakaryocytes with intact cytoplasm. Note that the leukocytes, both polymorphonuclears and mononuclears, are well preserved and clearly distinguishable. The smaller, lighter-staining bodies without nuclei, interspersed between the leukocytes, are platelets. (×855).
- **c** and **d**: Two extremely elongated megakaryocytes appear to contain less cytoplasm than the more typical forms. These cells may possibly be in the act of releasing platelets (see text), although their distorted shape may represent artifact. (×855).
- **e**: Megakaryocyte with lesser amount of cytoplasm (×1600).
- **f**: Nucleus with thin rim of cytoplasm (×855). (Figure reduced 25 per cent from sizes given.)

Its identity is verified under greater magnification. Scanning may be accomplished fairly quickly and easily because the cells on the filter are well separated. However, in the presence of thrombocytosis or leukocytosis, overlapping and clumping of cells may occur, making scanning difficult. This problem is obviated by spreading the white cell sediment on 4 or 5 Millipore filters instead of 3.
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Table 1.—The Age, Sex, Cardiac Diagnoses, Megakaryocyte Counts from Right Heart Blood in 23 Patients who Underwent Cardiac Catheterization

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Cardiac Diagnosis</th>
<th>Megakaryocytes/ml.</th>
<th>Per Cent with Cytoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>T. W.</td>
<td>12</td>
<td>F</td>
<td>IASD, PS, PDA, R to L shunt</td>
<td>1.7</td>
<td>47</td>
</tr>
<tr>
<td>E. L.</td>
<td>16</td>
<td>F</td>
<td>Levo-cardia, Sit. Inv., IASD</td>
<td>2.0</td>
<td>20</td>
</tr>
<tr>
<td>S. S.</td>
<td>8</td>
<td>F</td>
<td>IVSD, Pul. Hypertension</td>
<td>2.1</td>
<td>52</td>
</tr>
<tr>
<td>J. W.</td>
<td>2</td>
<td>M</td>
<td>IVSD</td>
<td>1.2</td>
<td>50</td>
</tr>
<tr>
<td>J. G.</td>
<td>19</td>
<td>M</td>
<td>Normal</td>
<td>1.1</td>
<td>22</td>
</tr>
<tr>
<td>T. S.</td>
<td>7</td>
<td>M</td>
<td>Normal</td>
<td>4.4</td>
<td>66</td>
</tr>
<tr>
<td>L. M.</td>
<td>24</td>
<td>F</td>
<td>AI, TI (?)</td>
<td>3.4</td>
<td>41</td>
</tr>
<tr>
<td>W. R.</td>
<td>37</td>
<td>M</td>
<td>Pul. hypertension</td>
<td>0.7</td>
<td>50</td>
</tr>
<tr>
<td>M. S.</td>
<td>8</td>
<td>M</td>
<td>PS, coarc. of PA</td>
<td>1.6</td>
<td>75</td>
</tr>
<tr>
<td>G. J.</td>
<td>8</td>
<td>F</td>
<td>IVSD</td>
<td>1.2</td>
<td>29</td>
</tr>
<tr>
<td>M. T.</td>
<td>12</td>
<td>F</td>
<td>IVSD, L to R shunt</td>
<td>2.9</td>
<td>83</td>
</tr>
<tr>
<td>G. A.</td>
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<td>M</td>
<td>IVSD, Pul. hypertension</td>
<td>1.5</td>
<td>36</td>
</tr>
<tr>
<td>K. G.</td>
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<td>F</td>
<td>IVSD, L to R shunt</td>
<td>4.1</td>
<td>44</td>
</tr>
<tr>
<td>R. L.</td>
<td>5</td>
<td>M</td>
<td>IVSD</td>
<td>4.0</td>
<td>65</td>
</tr>
<tr>
<td>J. C.</td>
<td>54</td>
<td>F</td>
<td>AS</td>
<td>2.6</td>
<td>73</td>
</tr>
<tr>
<td>G. C.</td>
<td>44</td>
<td>F</td>
<td>AS, AI, MS, TI (?)</td>
<td>2.4</td>
<td>58</td>
</tr>
<tr>
<td>J. J.</td>
<td>23</td>
<td>F</td>
<td>IASD</td>
<td>1.2</td>
<td>58</td>
</tr>
<tr>
<td>K. J.</td>
<td>2</td>
<td>F</td>
<td>IASD, IVSD, PS</td>
<td>3.8</td>
<td>58</td>
</tr>
<tr>
<td>M. L.</td>
<td>23</td>
<td>M</td>
<td>IASD</td>
<td>5.9</td>
<td>34</td>
</tr>
<tr>
<td>C. H.</td>
<td>26</td>
<td>F</td>
<td>IASD</td>
<td>2.2</td>
<td>55</td>
</tr>
<tr>
<td>C. L.</td>
<td>5</td>
<td>F</td>
<td>IVSD, L to R shunt</td>
<td>2.2</td>
<td>55</td>
</tr>
<tr>
<td>I. C.</td>
<td>21</td>
<td>F</td>
<td>IASD</td>
<td>0.7</td>
<td>53</td>
</tr>
<tr>
<td>F. H.</td>
<td>52</td>
<td>F</td>
<td>AS, AI, MS</td>
<td>3.4</td>
<td>56</td>
</tr>
</tbody>
</table>

Mean 2.4 51

Key to abbreviations:
IASD = interatrial septal defect.
IVSD = interventricular septal defect.
PS = pulmonic stenosis.
PDA = patent ductus arteriosus.
AS = aortic stenosis.
AI = aortic insufficiency.
MS = mitral stenosis.
TI = tricuspid insufficiency.
Sit. Inv. = situs inversus.
Coarc. of PA = coarctation of the pulmonary artery.
L. to R shunt = left to right shunt.

RESULTS

The results are reported in table 1. Megakaryocytes with intact cytoplasm were found in the blood of every patient. The megakaryocyte count ranged from 0.7 cells per ml. to 5.9 cells per ml., with a mean of 2.4 cells per ml. The percentage of megakaryocytes with intact cytoplasm varied from 22 to 83 per cent per sample, averaging 51 per cent of all the cells observed. Approximately half of these megakaryocytes were considered to have a full complement of cytoplasm, the other half containing less amounts of cytoplasm. Overall, it was estimated that the equivalent of one-third of all megakaryocytes contained a full load of cytoplasm.
Morphologically, the megakaryocytes appeared in a variety of shapes. Some were paddle-shaped (fig. 1, parts a and b), irregular (fig. 1, part e) or rounded. Many were extremely elongated, with the cytoplasm streaming out from the nuclear area in flagella-like processes (fig. 1, parts c and d). Cells which were rated as naked nuclei varied from fragments the size of leukocytes to intact cells with a compact nucleus of condensed chromatin surrounded by a thin rim of cytoplasm (fig. 1, part f).

**Discussion**

The saponin-hemolysis leukoconcentration technic was chosen for use in our studies because it has two advantages over other methods of concentrating megakaryocytes. First, it permits immediate fixation of blood specimens. Megakaryocytes are "sticky cells" with a reactive surface, and delay in fixation may lead to cytoplasmic disintegration. Second, there is a minimum of trauma to the megakaryocyte in this technic; only one centrifugation is required, and this after fixation. In other currently used technics of leukocyte concentration employing fibrinogen or dextran sedimentation, megakaryocytes are not fixed until 40 minutes or more after blood specimens are collected. In addition, when streptolysin 0 is employed as the hemolyzing agent, three separate centrifugations are required prior to cell fixation. These differences in technics may explain in part why we found a larger number of megakaryocytes with intact cytoplasm in circulating blood than previously reported. (Another factor which could influence the megakaryocyte count is the uniformity of dispersion of these cells within the blood stream. For instance, physical factors, such as laminar blood flow, might cause these cells to concentrate along blood vessel walls so that a catheter tip at the center of a vein would receive blood containing relatively few megakaryocytes, whereas a catheter wedged against the vessel wall might obtain blood laden with such cells. Computations, presented later, disregard this possibility and are based upon an assumption of uniform distribution of megakaryocytes.)

The morphology of megakaryocytes found in blood is worth noting. In addition to the typical round, mature megakaryocyte, many cells were observed which were somewhat bizarre in shape. These appeared to have streamers of cytoplasm flowing out from the nucleus and, in general, contained less cytoplasm than the intact normal forms. It is possible that these cells may have been in the act of releasing platelets at the time of fixation since these forms partially resemble the descriptions of megakaryocytes yielding platelets in vitro. However, the possibility that these aberrations in form may be artifactual cannot be excluded with certainty. Naked nuclei are interpreted as representing megakaryocytes stripped of platelets; the release of these platelets obviously occurs distal to the right heart, either in the venous system or in the bone marrow. It is our impression that as the megakaryocyte matures and enters the peripheral blood its nuclei condense into a compact mass. After the cell sheds its platelets, a thin envelope of cytoplasm frequently remains around the nuclear material (fig. 1, parts e and f). However, this cytoplasmic remnant is not observed on every naked nucleus. Therefore, it is not possible to determine with certainty whether each naked nucleus in our
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preparations represents a single megakaryocyte; for the purpose of our computations (see below), however, we make this assumption.

The frequency with which megakaryocytes are found in blood appears to depend upon the site in the body from which the blood was drawn. For example, blood from the vena cava is more likely to contain megakaryocytes than blood from the veins of the forearm\(^2\) and in greater concentrations as well;\(^*\) the cava drains an area rich in bone marrow (the pelvic girdle and spine) whereas the antecubital vein does not (bones of the forearm and hand). It is not surprising, therefore, to read that circulating megakaryocytes are not usually found in the blood of normal persons,\(^2\) since blood is almost always taken from antecubital veins. Thus, the concept that megakaryocytes are seen in the blood only under abnormal conditions is perpetuated.\(^2\)

Probably the best source for the study of circulating megakaryocytes is central venous blood since it represents a mixture of blood from all areas of the body and permits a more accurate assessment of the incidence of megakaryocytes in blood. Understandably, there is little opportunity to obtain such blood from healthy persons. It is possible, however, to obtain it, as we did, from patients who undergo cardiac catheterization. The results of our studies indicate megakaryocytes regularly enter the circulation, for without exception they were present in the right heart blood of each patient studied, including the two normal subjects. These findings lend support to other demonstrations of megakaryocytes as normal constituents of blood.\(^15,30,32\)

We have also examined arterial blood from two humans and found less than 0.3 megakaryocyte per ml. in each case. This indicates that most megakaryocytes arriving via the vena cava are actually arrested in the lungs. Of those cells which escape only 2 to 3 per cent contain any cytoplasm, judging from blood drawn from antecubital veins,\(^2\) suggesting that platelets are shed when megakaryocytes are in the lung. Similar discrepancies between the numbers and nakedness of megakaryocytes from the pulmonary artery versus the pulmonary vein have been found in human blood obtain during surgical operations.\(^2\)

The Significance of Migrating Megakaryocytes

Of what significance are these circulating megakaryocytes in terms of the total requirement for platelet production? Do they represent a mere fraction of the megakaryocytes which must be involved in thrombopoiesis? Does their number exceed the total requirement for megakaryocytes? Or is the number consistent with the concept that the movement from marrow to lung represents a normal phase in the life cycle of the platelet-generating megakaryocyte?

\(^*\)Douglas et al.\(^2\) have reported finding 75 megakaryocytes per ml. of vena caval blood in a severely preeclamptic patient. We have found as many as 80 megakaryocytes per ml. of vena caval blood in women undergoing cesarean section.\(^2\) In nongravid patients 14 cells per ml. of vena caval blood appears to be the greatest concentration of megakaryocytes that Hume\(^2\) encountered in her studies of patients with pelvic malignancy. However, it appears that only wholly intact cells were counted in the latter study so that Hume's figures might actually be higher if naked nuclei had been included in the count.
Whether all megakaryocytes enter the blood stream is not known, but there are reasons to believe that such is the case. The reasons are linked to the mode of platelet release from the megakaryocyte. The classic concept of Wright,\textsuperscript{33} that platelets are delivered to the blood stream by the pinching off of megakaryocyte cytoplasmic processes extended into marrow sinusoids, has never been confirmed by in vivo observation.\textsuperscript{34} The observation in bone marrow smears of platelets streaming from ragged megakaryocytes is often interpreted to represent “platelet production” or “platelet release” in the bone marrow. Such shedding of platelets is not observed when freshly aspirated marrow is suspended in saline with anticoagulant and observed in a hemocytometer chamber. Here each megakaryocyte is spheroid in shape and smooth in outline. We suspect that the “platelet production” which is found in stained smears is an artifact produced by the shearing off of bits of cytoplasm from mature megakaryocytes when bone marrow tissue is crushed and pulled between two glass surfaces in the preparation of the smears.

Furthermore, it is unlikely that platelets are released in the extravascular marrow, since in contrast to reticulocytes and leukocytes they are incapable of amoeboid movement and have not been demonstrated to be able to cross endothelium. Megakaryocytes, on the other hand, are capable of entering the blood vessels of the bone marrow wholly intact. This has been observed in vivo in rabbits\textsuperscript{34} and doubtlessly occurs in man since intact megakaryocytes are demonstrable in the blood. Thus, it is not unlikely that megakaryocytes must first enter vascular channels before platelets are released. From this it would follow that, once intravascular, megakaryocytes are swept out of the marrow and are carried to the lungs.

We have tried to test this hypothesis by calculating whether or not the numbers of megakaryocytes observed in right heart blood are sufficient to maintain the platelet population. In order to make this determination it is necessary to know (1) whether or not the production (and release into blood) of megakaryocytes proceeds at a constant rate, (2) how many platelets are produced by a single megakaryocyte, and (3) what is the average life span of the normal platelet population.

\textit{Megakaryocyte Production and Release:} We do not know for certain that megakaryocyte production and delivery to blood is constant. However, platelet counts tend to remain at fairly constant levels, day to day, so it is assumed that the proliferation and entry into blood of megakaryocytes is maintained at a reasonably uniform rate under normal circumstances. (Hume's studies\textsuperscript{27} revealed a diurnal variation in the pattern of megakaryocyte release to blood in patients with cancer. In these cases, however, blood was obtained from the inferior vena cava and not from the right heart. And, as previously cited, only intact megakaryocytes were counted; naked nuclei were ignored.)

2. \textit{Number of Platelets Produced by a Single Megakaryocyte:} Estimates of the number of platelets produced by a single megakaryocyte range from $2000 \per 26^{35}$ to $7700 \per 27^{36}$ to $11,000.\textsuperscript{3} We have tried to deduce the correct figure by estimating the volume of the average bone marrow megakaryocyte and deriving from it the potential number of platelets contained in the cytoplasm.
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In fresh marrow suspensions megakaryocytes are spheroid in shape. The largest and presumably most mature of these cells measure approximately 50 µ in diameter. Their nuclei are usually clustered together and, though not always tightly packed, may be viewed as a conglomerate mass with a diameter which is, on the average, one-half of the cell diameter. If we consider the nuclei as a spheroid mass, we may thus envision the megakaryocyte and its nuclei as concentric spheres with the larger sphere having a diameter at least twice the smaller one. Since the volume of a sphere is \( \frac{4}{3} \pi r^3 \), the total cell megakaryocyte volume is \( \frac{4}{3} (3.14) (25)^3 = 65,000 \) µ³, and the nuclear volume is \( \frac{4}{3} (3.14) (12.5)^3 = 8000 \) µ³. Therefore, the cytoplasmic volume is 57,000 µ³. The volume of an average platelet as obtained from measurements of platelet mass utilizing a quantitative electron microscopic technic appears to be 12–15 µ³, although published figures vary from 4 to 16 µ³.

If we choose 14 µ³ as the mean platelet volume then the number of platelets contained within the cytoplasm of the megakaryocyte = \( \frac{57,000 \mu^3}{14 \mu^3} = 4000 \).

3. Life Span of the Normal Platelet Population: Although human platelet life span is generally reported to be from 9 to 11 days, the pattern of survival varies with the method of platelet labeling employed. Cr⁵¹ (see refs. 46–52) and DFP (see refs. 53, 54) tagging yield linear survival curves, while Na₃P₂O₄ (see ref. 55) labeling results in curves which are exponential. The distinction between the shapes of the survival curves is important because daily platelet consumption, upon which our calculations are based, is much greater if survival follows an exponential rather than a linear pattern. Thus, the average platelet population survives 10 days when tagged with Cr⁵¹ but only 4 days when tagged with Na₃P₂O₄. Since the problem of the shape of the pattern of platelet survival is not yet resolved, we must consider the results of both methods in our computations.

It is obvious that our calculations are based on data which cannot be considered as exact and final, but the data are accurate enough to permit a rough test of the hypothesis, at least. Thus we may determine whether or not more than just an occasional megakaryocyte migrates to the lung. The calculations are as follows: given a person whose blood volume is 5000 ml. and whose platelet count is 300,000 per mm.³, the total platelet population equals \( 1.5 \times 10^{12} \) cells. If the average platelet population life span is 10 days, then the average number of platelets produced per day is \( 1.5 \times 10^{11} \), and the number produced per minute is \( 1.0 \times 10^9 \). If one megakaryocyte yields 4000 platelets, then the number of megakaryocytes produced per minute is \( 2.5 \times 10^4 \) cells. Thus, if all megakaryocytes circulate, \( 2.5 \times 10^4 \) cells will travel to the lungs each minute. This figure is compared to that actually observed, \( 1.3 \times 10^4 \); the latter is derived by multiplying the number of megakaryocytes per ml. of right heart blood (2.4) by the amount of blood that is pumped to the lungs each minute (5000 ml.). Therefore, if platelet survival follows a linear pattern, the actual number of megakaryocytes observed in the right heart blood represents 50 per cent of the number needed to maintain the platelet population (\( 1.3 \times 10^4/2.5 \times 10^4 \times 100 \)). If platelet survival is exponential...
(average platelet population life span, 4 days), then the number of cells observed is 20 per cent of the requisite number \((6.5 \times 10^4)\). Theoretically, then, the observed numbers of circulating megakaryocytes can account for from 20–50 per cent of the platelet population; we thus infer that from 20–50 per cent of the mature megakaryocyte population enters the blood. Considering the necessarily imprecise nature of the calculations, the probability of sampling errors, and possible imperfections in the collection and treatment of blood specimens, the hypothesis that all megakaryocytes circulate cannot be considered invalid. It seems reasonable to ask that if as many as 5 megakaryocytes in 10 may enter the blood, why not all?

It is apparent that platelets may be released in the bone marrow, in the veins and right heart, or in the lungs. Since on the average the equivalent of one-third of megakaryocytes in the right heart contain a full load of cytoplasm, it would appear from the foregoing figures that from 7–17 per cent of the platelets in the body are released in the lungs. If, indeed, all megakaryocytes reach the lung, then as many as 33 per cent of the body's platelets are delivered in that organ. Further, if during periods of great platelet demand immature megakaryocytes are forced from the bone marrow, an even greater percentage of the body's platelet release may take place in the lungs.

**Summary**

1. Megakaryocytes were demonstrated in central venous blood of each of 23 patients who underwent cardiac catheterization. Cell counts ranged from 0.7 to 5.9 megakaryocytes per ml. of blood; the equivalent of one-third of these cells were considered to contain a full complement of cytoplasm. It has become evident that megakaryocytes are normal constituents of blood.

2. In an attempt to quantify megakaryocyte migration from the bone marrow it was calculated that from 20–50 per cent of the mature megakaryocyte population enters the blood and ultimately reaches the lungs. The possibility that all megakaryocytes migrate from the marrow is not precluded with certainty by these studies.

3. It was estimated that from 7–17 per cent of the body's platelets are released in the pulmonary capillaries. If all megakaryocytes migrate from the bone marrow, then as much as 33 per cent of the platelet population is delivered to the blood in the lungs.

**Summario in Interlingua**

1. Le presentia de megacaryocytos eseva demonstrate in sanguine centron venose de cata-un de 23 patientes subjicite a catheterismo cardiac. Le numerations variava inter 0.7 e 5.9 megacaryocytos per ml de sanguine. Esseva estimate que un tertio de iste cellulas contineva un complete garnitura de cytoplasma. Il deveni de plus in plus evidente que megacaryocytos es constituentes normal del sanguine.

2. In un essayo de quantificar le migration de megacaryocytos ex le medulla ossee il eseva calculate que inter 20 e 50 pro cento del population de megacaryocytos matur entra in le sanguine e arriva in le curso del tempore in le
pulmones. Le presente studios non exclude definitemente le possibilitate que omne megacaryocytos migra ex le medulla.

3. Esseva estimate que inter 7 e 17 pro cento del plachettas del corpores es liberate in le capillares pulmonar. Si omne megacaryocytos migra ab le medulla ossee, non minus que 33 pro cento del population plachettal es transmittite al sanguine in le pulmones.

ACKNOWLEDGMENTS

We wish to express our gratitude to Mrs. Elizabeth Houchin for her valuable technical assistance. Also, thanks are due to Colonel Weldon Walker, Colonel Robert Jones and Captain Richard McCarty, Department of Medicine, Walter Reed General Hospital, for kindly allowing us to study their patients and for providing us with blood specimens.

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