Number and Distribution of Human Hemic Cells

By Edwin E. Osgood

Data now available in the literature\textsuperscript{1} and from our own studies\textsuperscript{2-12} make possible a calculation of the total number of each type of hemic cells\textsuperscript{*} in the body, and their distribution in three compartments—the hematopoietic organs, the blood, neither of these sites. The calculations are given for standard man, the 70 Kg. human male. Values per Kg. may be obtained by dividing the figures given by 70, and values for other age and sex groups and for other species may be calculated by the same principles.

Since physiologic variations in the figures used in these calculations are of the order of ±50 per cent, most of the values computed from them are subject to errors of this order of magnitude and have been rounded. This does not in any way change the fundamental conclusion that seems inescapable from the data to be presented that leukocytes are really not blood cells. In other words, only a very small proportion of those leukocytes outside the hematopoietic organs are present in the blood at any one time.

Since most of the pertinent literature is familiar to readers of this journal, and these references are extremely numerous, no attempt has been made to cite all articles which have a bearing on the content of this article. The articles cited in the references included should be read by anyone wishing to follow through any point in detail.

Basis for the Calculations

The calculations to be presented depend on certain facts. Each series of hemic cells reaches a stage of differentiation beyond which cell division does not occur. This necessitates a type of cell division which leads to an arithmetic\textsuperscript{13, 14} not logarithmic, production of cells. When one cell, capable of division, divides, one of the resultant cells must differentiate; the other must remain immature to divide again. If both cells remain capable of division, there is no cell to differentiate. If both cells differentiate, there is no cell left to divide again (fig. 1).\textsuperscript{13} In the steady state the total number of cells present in the body will be the product of the number of cells capable of division and the number of divisions in one life span of the cell series. The number of cell divisions per unit time interval will exactly equal the number of cells dying in the same time interval, and an equal number of cells will cross the dividing line between each stage of differ-


From the Division of Experimental Medicine, University of Oregon Medical School Portland, Oregon.

Submitted March 1, 1954; accepted for publication April 6, 1954.


From www.bloodjournal.org by guest on September 14, 2017. For personal use only.
entiation in the same time interval. This leads to a direct proportion between the length of time a cell spends in one stage of differentiation expressed as a proportion of the total life span and the number of cells in that stage of differentiation expressed as a proportion of the total number of differentiating cells in that series. Since the total life span of differentiating cells of the erythrocytic series is well known\textsuperscript{14-17} and nucleated erythrocytes occur only in the marrow, the numbers of nucleated erythrocytes in the marrow may be calculated. Their ratio to the stages of other series which occur exclusively in the marrow permits calculation of the number of exclusively marrow cells of these other series. From data on the life spans of these other series,\textsuperscript{6, 8, 9, 11, 12} the ratio of the marrow stages to the extramedullary cells may be calculated.

Mathematically expressed,\textsuperscript{*} $A, B, C, \ldots$ represents the number of cells in successive differentiating stages of a cell series, $N =$ the sum of all these stages, $a =$ cells capable of division and $t_A, t_B, t_C, \ldots =$ the time spent in each stage of differentiation, the sum of which is equal to the total life span, $T$. Then $A/t_A = B/t_B = \ldots = N/T = a$ constant, which is 1 if $A, B, \ldots$ are expressed as a proportion of the total number of cells $N$ in the body and time $t$ as proportion of total life span $T$. If $I$ is equal to the average intermitotic interval and $x = T/I = N/a$ the number of mitoses per $a$ cell in one life span, then in the steady state, $N$ is equal to $ax$. The total number of cells of a series in the body, $S = axt/T + a$ in the steady state. This is a straight line arithmetic equation with $a$ equal to the intercept on the ordinant and $axt/T =$ to the slope of the line defining the number of new cells produced in time $t$; $-axt/T =$ slope of line defining the number of cells disappearing in time $t$.

**Results**

The Erythrocytic Series

The total life span of the erythrocytic series in the blood is well established as 120 days.\textsuperscript{15-17} The total number of erythrocytes in the bloodstream in standard man is $5.4 \times 10^8 \times 10^8 \times 5 \times 10^4 = 27 \times 10^{12}$. In the healthy human male

\* The figures given in this paper do not include the probability functions\textsuperscript{17} nor the time during which dead but incompletely autolysed, disintegrated cells persist in the blood stream. In marrow cultures the disintegrated cells of the granulocytic series persist for about eighteen hours and the disintegrated cells of the lymphocytic series about nine days. The time is probably shorter in the body because of removal by the spleen and reticuloendothelial tissue. The dead erythrocyte is indistinguishable morphologically from the living and its time of survival in the bloodstream and in the culture has not been determined. The presence of such cells is, however, clearly indicated by the acute early drop in transfusion of labeled bank blood.\textsuperscript{17}

This type of cell division and differentiation requires a different mathematical analysis of the DNA uptake of $P^{32}$ from that in current use, since the DNA uptake curve must include the disintegrating cells present in the blood stream, plus 1 intermitotic interval, plus the allowance for the unlabeled DNA in the cells initially present. The equations for correct mathematical analysis of DNA uptake curves of $P^{32}$ have been calculated by Dr. Demetrios Rigas, my associate, and are to be published elsewhere.

In the steady state the number of cells capable of division does not change. In disease it may change, but usually only at long intervals. The time of this change may be recognized because it will always lead to a logarithmic change in cell numbers; however, random cell death may also lead to a logarithmic change in numbers, as may the logarithmic action of internally administered isotopes.
all of these cells are present in the bloodstream. There are, therefore, produced per day and entering the bloodstream per day \((27 \times 10^{12})/120 = 2.25 \times 10^{11}\) cells per day. The number of reticulocytes averages 1.5 per cent, and 1.5 per cent of 120 days is 1.8 days or forty-three hours, and 1.5 per cent of 27 \(\times\) 10\(^{12}\) is 4 \(\times\) 10\(^{11}\). If reticulocyte numbers are plotted when there is a sudden change in rate of cell division, the erythrocyte peak is found on the fourth day and the intercept with the base line reticulocyte count of this line projected backwards is at one and one-half to two days. (See figs. 4 and 5 in Sturgis.) Furthermore, nucleated erythrocytes have been observed to disappear in hypoplasia, or PA type nucleated erythrocytes to disappear in twenty-four to forty-eight hours, from which it can be concluded that \(t_A + t_B \ldots\) to \(t_H\), the total time of differentiating nucleated erythrocytes, is of the order of thirty-six to forty-eight hours. Figure 1 shows the calculation of the number of nucleated

---

**Fig. 1.**—In this and subsequent figures the cells below the lowest horizontal line represent all cells capable of division, \(a\), in the mathematical model. The cells below the heavy horizontal line represent all cells in the hematopoietic organs, the marrow in this instance. The ascending diagonal line defines the time course of the single differentiating cell resulting from the first division after 0 time, and sums below it the total number of new cells produced since 0 time, \(t_A\). The area above this line indicates the rate of decrease of old cells present at time \(t_A\). The break in the chart indicates the omission of that part of the chart between 100 hours and 122 days. The value of \(I\), intermitotic interval, may be read directly where the ascending line crosses 3 \(\times\) 10\(^{11}\) cells, which is twice the value of 1.5 \(\times\) 10\(^{11}\), the number of dividing cells, and is in this case 16 hours or two-thirds of a day. The value of \(x\) is 122 divided by \(\frac{3}{2} = 366/2\) which is 183. The diagonal ascending line would intercept the vertical line at 122 days at 183 \(\times\) 1.5 \(\times\) 10\(^{11}\) + 1.5 \(\times\) 10\(^{12}\) or 27.6 \(\times\) 10\(^{12}\) cells when all cells present would be new cells and none of the old cells initially present would be left.
NUMBER AND DISTRIBUTION OF HUMAN HEMIC CELLS

NUMBER AND DISTRIBUTION OF NEUTROPHILS OF THE GRANULOCYTIC SERIES

<table>
<thead>
<tr>
<th>Class</th>
<th>Total</th>
<th>Number of Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(gm.)</td>
<td>(gm.)</td>
</tr>
<tr>
<td>108</td>
<td>30</td>
<td>3 x 10^14</td>
</tr>
<tr>
<td>72</td>
<td>27</td>
<td>2 x 10^14</td>
</tr>
<tr>
<td>36</td>
<td>18</td>
<td>1 x 10^14</td>
</tr>
<tr>
<td>24</td>
<td>12</td>
<td>6 x 10^13</td>
</tr>
<tr>
<td>12</td>
<td>6</td>
<td>3 x 10^13</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>1.5 x 10^13</td>
</tr>
<tr>
<td>3</td>
<td>1.5</td>
<td>7.5 x 10^12</td>
</tr>
<tr>
<td>1.5</td>
<td>0.75</td>
<td>3.75 x 10^12</td>
</tr>
<tr>
<td>0.75</td>
<td>0.375</td>
<td>1.875 x 10^12</td>
</tr>
<tr>
<td>0.375</td>
<td>0.1875</td>
<td>0.9375 x 10^12</td>
</tr>
</tbody>
</table>

FIG. 2.—See legend to figure 1. In this figure a = 3 × 10^4 and includes all cells of the granulocytic series with nucleoli. I = 12 hours and T = 108 hours so x = 108/12 = 9 and S = 27 × 10^11 + 3 × 10^11 or 3 × 10^12.

NUMBER AND DISTRIBUTION OF CELLS OF THE LYMPHOCYTIC SERIES

<table>
<thead>
<tr>
<th>Class</th>
<th>Total</th>
<th>Number of Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(gm.)</td>
<td>(gm.)</td>
</tr>
<tr>
<td>105</td>
<td>20</td>
<td>2 x 10^11</td>
</tr>
<tr>
<td>90</td>
<td>18</td>
<td>1.8 x 10^11</td>
</tr>
<tr>
<td>75</td>
<td>15</td>
<td>1.5 x 10^11</td>
</tr>
<tr>
<td>60</td>
<td>12</td>
<td>1.2 x 10^11</td>
</tr>
<tr>
<td>45</td>
<td>9</td>
<td>9 x 10^10</td>
</tr>
<tr>
<td>30</td>
<td>6</td>
<td>6 x 10^10</td>
</tr>
<tr>
<td>15</td>
<td>3</td>
<td>3 x 10^10</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>2 x 10^10</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>1 x 10^10</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>0.5 x 10^10</td>
</tr>
<tr>
<td>1.5</td>
<td>0.25</td>
<td>0.25 x 10^10</td>
</tr>
</tbody>
</table>

FIG. 3.—See legends to figures 1 and 2. In this graph a = 2 × 10^11 and I = 24 hours. T = 30 days and x = 30.
cells of the erythrocytic series in the marrow on the basis of the assumption that \( t_n \), the time in the marrow, is forty-eight hours and that one-fourth of the nucleated erythrocytes contain nucleoli and are capable of division. Note that for each day of increase or decrease in this time the number of nucleated erythrocytes in the marrow would be changed by \( 2.25 \times 10^{11} \) or 50 per cent, with a corresponding change in all other cells present in the marrow which, as will be pointed out later, would change the total mass of hemic cells in the marrow from approximately 1300 Gm. to 1900 Gm. or 700 Gm. so that the correct value cannot be very far from two days. Furthermore, the assumption of forty-eight hours for the nucleated erythrocytes in the marrow leads to an intermitotic interval of sixteen hours, a very reasonable figure. The intermitotic interval may be read at a glance from figures 1 to 3 because it is equal to the time which it takes to produce new cells equal in number to the cells capable of division, in other words, for each cell capable of division to divide once.

Neutrophilic Cells of the Granulocytic Series

The eosinophils and basophils are discussed in the section of this paper on “other hemic cells.” Studies by the marrow culture technics have shown the total life span of the granulocytic series through the segmented neutrophils to be 108 hours, divided approximately as follows: myelocytes plus metamyelocytes, twenty-four hours; band neutrophils, thirty-six hours; and segmented neutrophils, forty-eight hours. Whether calculated from our own data or from that reviewed in table 60 of Standard Values in Blood, the ratio of nucleated erythrocytes in the marrow to total neutrophilic cells of the granulocytic series through the band cell is 1:3. Since there were \( 6 \times 10^{11} \) nucleated erythrocytic cells calculated to be in the marrow, there should be three times as many, or \( 18 \times 10^{11} \), cells of the granulocytic series in the true marrow, undiluted by blood, and these should be subdivided in the ratios of their proportions in the normal marrow differential count which is also the ratio of the relative time spent in each stage. Figure 2 shows graphically the calculated total number of neutrophils in the body and their distribution. The results are given both in numbers and grams of cells, since our determination of the volume of the cells of the granulocytic series makes this possible. Approximately two billion cells of the granulocytic series equals 1 Gm. irrespective of whether they are mature or immature. Note that this calculation leads to a value of 600 Gm. of segmented neutrophils outside the marrow, whereas there are only about 10 Gm. present in the circulating blood at any one moment of time. If we use the figures of Kline and Clifton based on DNA uptake of \( 32 \) as if they applied to neutrophils alone, the number of neutrophils outside the marrow would have to be more than double the value given in figure 3.

The Lymphocytic Series

Studies of lymphocytic volume have shown that approximately four billion lymphocytes equal 1 Gm. Studies of DNA \( P_{31} \) in lymph nodes and spleen have shown that the total number of cells of the lymphocytic series in lymph
NUMBER AND DISTRIBUTION OF HUMAN HEMIC CELLS

# Table 1: Hemic Cells in Extramedullary Hematopoietic Tissue

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Total Grams</th>
<th>Lymphocytic Series</th>
<th>Other Hemic Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cells $\times 10^{11}$</td>
<td>Grams</td>
<td>No. of Cells $\times 10^{11}$</td>
</tr>
<tr>
<td>Spleen</td>
<td>160</td>
<td>1.6</td>
<td>40</td>
</tr>
<tr>
<td>Lymph Nodes</td>
<td>140</td>
<td>1.6</td>
<td>40</td>
</tr>
<tr>
<td>Thymus, tonsils, Peyer's patches</td>
<td>100</td>
<td>0.8</td>
<td>20</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>400</strong></td>
<td><strong>4</strong></td>
<td><strong>100</strong></td>
</tr>
<tr>
<td>+ Marrow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total in hematopoietic organs</strong></td>
<td><strong>8</strong></td>
<td><strong>200</strong></td>
<td></td>
</tr>
</tbody>
</table>

* Includes Kupffer cells of liver.
† Includes histiocytic foci in areolar tissue.

The weight of the lymph nodes, Peyer's patches, thymus, tonsils, and adenoid tissue has been estimated to be one-half to one per cent of the body weight. From the DNA uptake of $^{32}$P it has been shown that the life span of the lymphocytic series in chronic leukemic lymphocytic leukemias is at least thirty days and there is much to suggest that it is even longer in the normal. From the uptake of $^{32}$P in lymph nodes and in acute lymphocytic leukemias and from the proportion of prolymphocytes and younger cells to total lymphocytes in chronic leukemias, it is estimated that the time spent in lymphatic tissue is of the order of one-tenth of the life span of the cells. From these figures, the data in table 1 for these tissues have been calculated, and by the ratio of lymphocytes in the marrow to the nucleated erythrocytes, the marrow values have been calculated. From these totals and the ratio of one to ten, the distribution of the lymphocytic series between the hematopoietic organs and the body outside these organs has been calculated as shown in figure 3. While admittedly these are only very approximate values, the total number of lymphocytes in the blood is only of the order of 3 Gm. so that the conclusion seems inescapable that, at any one time, the great majority of the lymphocytes outside the hematopoietic organs are not in the blood stream.

**Other Hemic Cells**

The great majority of these belong to the monocytic or histiocytic series. In cultures of blood from patients with monocytic leukemias, acute or chronic, the promonocytes have much material to phagocytose and they become morphologically indistinguishable from the tissue cells of the histiocytic series. Therefore, along with many others, I believe the tissue histiocytes and the cells of the monocytic series to be one series of cells, which also includes the tissue macrophages, Kupffer cells of the liver, and the microglial cells. In cultures of acute monocytic leukemic blood, the various giant cells with multiple nuclei described by Reubuck develop. From their percentages in the marrow in relation to the
EDWIN E. OSGOOD

Table 2.—Other Hemic Cells in Marrow

<table>
<thead>
<tr>
<th>Hemic Series</th>
<th>No. of Cells</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monocytic Series</td>
<td>$0.5 \times 10^{11}$</td>
<td>1.4</td>
</tr>
<tr>
<td>Plasmocytic Series</td>
<td>$0.2 \times 10^{11}$</td>
<td>0.6</td>
</tr>
<tr>
<td>Thrombocytic Series*</td>
<td>$0.1 \times 10^{11}$</td>
<td>0.2</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>$1.0 \times 10^{11}$</td>
<td>3</td>
</tr>
<tr>
<td>Basophils</td>
<td>$0.1 \times 10^{11}$</td>
<td>0.2</td>
</tr>
<tr>
<td>Disintegrated Cells</td>
<td>$3.0 \times 10^{11}$</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$4.9 \times 10^{11}$</td>
<td>15.4</td>
</tr>
</tbody>
</table>

* Nucleated cells only.
† These values are more accurate than those in Table 3, which before rounding off would show slightly lower values for lymphocytes and neutrophils than those obtained by rounding the figures.

number of nucleated erythrocytes in the marrow the total numbers of cells of the monocytic, plasmocytic, nucleated thrombocytic, eosinophilic, and basophilic series may be calculated, as well as the numbers of disintegrated cells. The monocytic and plasmocytic cells of other hematopoietic organs were included in table 1. The values which are summarized in table 2 for the other hemic cells in the marrow were calculated on the basis of the following data: The numbers of the exclusively marrow cells of each series were calculated from their ratio to nucleated erythrocytes. The percentages of the total cells in the true marrow undiluted by blood were then computed from these numbers. The monocytic and plasmocytic series have life spans and ratios of life spans in and out of the hematopoietic organs similar to those of the granulocytic series.24 The life spans outside the marrow for eosinophils and basophils are eight to twelve days,6 and the time in the marrow for the eosinophils and basophils is similar to that of the immature neutrophils. The life span of the thrombocytes in the blood is five days.27 A method has been developed by which the number of nucleated cells of the thrombocytic series28 and their ratio to the nucleated erythrocytes was determined. If we assume, as seems probable, that all the thrombocytes outside the marrow are present in the blood, one can calculate that approximately 1000 to 2000 will bud from each megakaryocyte per day and that the great majority of all other cells in this group must be outside the hematopoietic organs and blood.

Total Hemic Cells in the Body and their Distribution

The data from all these calculations are summarized in table 3 and the percentage distribution of these cells in undiluted marrow calculated from this data is also given. These agree well with the values in table 611 which is based on study of 750 adults and includes the grand mean of twenty-one authors' means. The ratio of cells in the bloodstream to the total cells outside the hematopoietic organs is shown in table 3. The ratio for eosinophils and basophils is probably about 1 to 100, similar to that for the neutrophils, whereas the ratio of the monocytic and plasmocytic series, which constitute the great majority of the "other hemic cells," is of the order of 1 to 400, as given in table 3.
### Table 3: Number and Distribution of Human Hemic Cells

<table>
<thead>
<tr>
<th>Cell Series</th>
<th>Hemic Cells in Hematopoietic Organs</th>
<th>Hemic Cells Outside Hematopoietic Organs</th>
<th>Total Hemic Cells in Body</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Marrow</td>
<td>Lymphocytic Tissue and Spleen</td>
<td>Blood</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>No. of Cells X 10^11</td>
<td>Grams</td>
</tr>
<tr>
<td>Erythrocytic</td>
<td>19</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Granulocytic</td>
<td>56</td>
<td>18</td>
<td>900</td>
</tr>
<tr>
<td>Lymphocytic</td>
<td>12.5</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>Other Hemic Cells*</td>
<td>12.5</td>
<td>4</td>
<td>200</td>
</tr>
<tr>
<td>Total Leukocytes</td>
<td>81</td>
<td>26</td>
<td>1200</td>
</tr>
<tr>
<td>Fat, Blood Connective</td>
<td>1700</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue</td>
<td>WBC/comm.</td>
<td>3000</td>
<td>700</td>
</tr>
</tbody>
</table>

* Monocytic, plasmocytic, eosinophilic, basophilic, thromboctye series and disintegrated cells.
The total value for marrow tissue agrees well with the figure of 4.6 per cent (range 3.4 to 5.9) of body weight given by Mechanik.29

Intermitotic Intervals

From the data given in figures 1, 2, and 3, the corresponding intermitotic intervals are readily calculated as the time elapsed until the total number of cells capable of division is equaled by differentiating cells, in other words, when each cell has on the average undergone one mitosis. These times are: for the erythrocytic series, sixteen hours; granulocytic series, twelve hours; and lymphocytic series, twenty-four hours, all very reasonable figures. If one takes the values given by Japa30 for numbers of mitoses present at any one moment of time in the marrow, the duration of mitoses for these series comes out about one hour, also a very reasonable value.

Discussion

At first sight the values given in table 3 seemed very surprising, even to the author, but careful thinking through of the implications of these results explains many otherwise very perplexing observations. The values for the erythrocytic series do not require any budding such as that described by Clemmeson and Plum,31 which, with a great deal of experience in marrow cultures, we have never observed. They account for the straight line arithmetic increase and disappearance rate of erythrocytes that is observed when there is no evidence of erythrocyte destruction.16, 17 The values for leukocytes similarly account for the straight line arithmetic decrease and increase after a single massive dose of irradiation (figs. 1, 4, and 514) and for the straight line arithmetic increases and decreases observed in these cells in marrow cultures8, 9, 11, 12 and in patients receiving x-ray irradiation.32-34 There will, of course, be logarithmic changes when isotope therapy with a logarithmic decay is used, where there are logarithmic effects on cell division. The number of neutrophils outside the blood-forming organs and blood could easily account for the rapid appearance of these cells in the blood stream after adrenalin35 or adrenocortical activity;28 the accumulation of hundreds of grams of these cells in a very short time in pneumonic consolidations, peritonitis, empyemas, or abscesses; and for the inability to raise the leukocyte level by transfusing leukocytes.37 The very rapid disappearance of neutrophils in allergic reaction could also be accounted for by an increased rate of migration out of the blood stream. The relatively enormous numbers of eosinophils promptly appearing in any area of allergic reaction long before there is any increase in the eosinophils in the blood and the rapid disappearance of eosinophils after adrenalin28 or adrenocortical action24 could be explained by a simple redistribution between blood and tissue.

Perhaps the most surprising values of all are those for the lymphocytic series. They are also probably the values subject to the greatest error in these calculations. But when one stops to think of the frequency with which "small round cell" infiltrations are seen about capillaries in tissue sections and when one looks carefully in the tissue sections for such cells under the oil immersion objective, especially in areolar tissues of the body, and considers that there are 7,000 oil immersion fields in one square cm. of section, about 1 × 10¹ such
sections 6 to 8 μ thick in the entire body,* and that from the thoracic duct alone about 4 × 10^{-9} or 1 to 8 times the total number of lymphocytes in the blood stream enter the blood every twenty-four hours,

and that diverting this flow in man has little effect on the lymphocyte count, these values seem much more reasonable. It is true that some have observed decreases in the lymphocyte count in the blood on diverting thoracic lymph in animals but at that time the effect of adrenocortical stimulation and adrenalin production were not taken into consideration. Furthermore, most of these experiments were done on animals and no factor is known for converting cell life span data from one species to another.

The monocytic, histiocytic, and plasmocytic series are observed by every pathologist and histologist to be very widespread in body tissues generally, particularly in areolar tissue.

These observations would account for the rapid appearance of relatively large numbers of cells on the cover slips in the experiments done by Rehuck. They would account for the rapid disappearance of leukocytes from the blood stream after massive transfusions of leukocytes, or in parabiosis or cross circulation experiments, and make it unnecessary to postulate the short life spans, which are totally incompatible with the DNA uptake of these cells. These "life spans" merely represent mean time in the blood stream on one trip for cells which may enter the blood stream several times in their true life span. The figures given would account for the relatively large numbers of these cells which are lost from the body each day into the gastrointestinal tract. It seems probable that a considerable number of the lymphocytes formed may never enter the bloodstream but may be lost into the gastrointestinal tract directly from the Peyer's patches where they are formed.

The figures of table 3 would account for the observations which have been made by those who have studied the capillaries during life that leukocytes are seen migrating through the capillary walls, and when one compares the area of capillaries observed with the total area of capillary bed in the body, one finds it not unreasonable that the large numbers of leukocytes necessitated by these calculations enter and leave the blood stream per unit of time.

The importance of the marrow as a source of lymphocytes, while often overlooked, has previously been pointed out by Yoffey. The leukocytes in the blood stream must indeed be regarded as en route to another destination as has been pointed out by Drinker and Yoffey, and, since this article was in semifinal draft, by White.

So many leukocytes are present in the body outside the blood stream and hematopoietic organs, where are they? The evidence provided by Bierman and his co-workers, and in the references he cites, suggests that large numbers of these are present in the lungs. This is the largest capillary bed in the body, and the only one through which the entire blood volume passes in any one circulation. In view of the ratios shown, it is not surprising that the majority of leukocytes disappear from the blood stream in one circulation through the

* This would give an average of 10 or 12 leukocytes per oil immersion field. only 1 or 2 of which would be segmented neutrophils.
lungs. It would seem most reasonable, therefore, to postulate that the leukocytes constitute a motile army constantly shifting to the sites where they are needed most, and that the numbers of leukocytes will vary greatly in different locations according to the proportion of the total capillary bed open in that area at a particular time. While few leukocytes disappeared in the lower extremities, it must be recalled that these studies by Bierman were made on patients who were and had been at bed rest and that the number disappearing in the capillary bed might be vastly different if many capillaries were open due to active exercise of these areas. There are probably great shifts of leukocytes occurring in relation to digestive processes and other visceral activity, as well as the well-known response to acute or chronic inflammation or allergic reaction. Fichtelius has demonstrated DNA labeled lymphocytes in all tissues investigated many hours after intravenous injection of such lymphocytes.

The type of cell division described accounts for the marrow appearance usually described as maturation arrest on the basis of early cell death, a decreased rate of cell division or beginning regeneration after a period of hypoplasia and also for the "hiatus leukemicus."

**SUMMARY**

1. Methods are described which make possible the calculation of the number and distribution of the hemic cells of the body.
2. The numbers of these cells in the various blood-forming organs, in the blood outside these areas, and in the total body are summarized in table 3, together with the ratios of the number in the blood to the number outside the hematopoietic organs for the standard 70 Kg. human male. Dividing these figures by 70 will give the values per Kg.
3. By similar methods the values for other age and sex groups in man and for other species may be calculated.
4. Leukocytes apparently are not primarily blood cells but are merely en route in the blood to the defense of body tissue generally. Only 1/40 to 1/400 of the total leukocytes outside the hematopoietic organs are present in the blood stream at any one time.
5. These somewhat surprising figures account for many previously made observations which were hitherto hard to explain.

**SUMMARIO IN INTERLINGUA**

1. Es describite methodos que permette le calculation del numero e distribuccion del cellulas sanguinee in le corpore.
2. Le numero de tal cellulas in le varie organos hematopoietic, in le sanguine foras de iste areas, e in le corpore total es summarisate in forma tabular insimul con le proportion del numeros in le sanguine in relation al numeros foras del organos hematopoietic, con omne datos calculate pro le masculo human del peso standard de 70 kg. Le division del datos per 70 resulta in valores per kg.
3. Simile methodos pote esser usate pro calcular datos pro altere gruppos human secundo sexo e etate e etiam pro altere species.
4. Il pare que leucocytos non es in principio cellulas sanguinee sed se trova
simplemente in route intra le sanguine pro le defensa del textos corporee in general. Solo 1/400 a 1/40 del leucocytos total foras del organos hematopoietic es presente a un date tempore intra le fluxo del sanguine.

(5) Iste datos es alique surprendente sed illos presenta un explication de multe phenomenos que usque nune essave difficile a explicar.

REFERENCES

1 ALBRITTON, E. C., Editor: Standard Values in Blood, prepared under the direction of the Committee on the Handbook of Biological Data, American Institute of Biological Sciences, The National Research Council, United States Air Force, Wright Air Development Center, Wright-Patterson Air Force Base, Dayton, Ohio. AF Technical Report No. 6039, July, 1951. (Tables 37, 49, 60, 61, and references cited)


9 —: Is the action of roentgen rays direct or indirect? An investigation of this question by the method of human marrow culture. Am. J. Roentgenol. 48: 214, 1942.


12 — AND KRIPPAEHNE, M. L.: Evidence for shorter life span of neutrophils from chronic granulocytic leukemia than from non-leukemic marrow. (In preparation.)


EDWIN E. OSGOOD


NUMBER AND DISTRIBUTION OF HUMAN HEMIC CELLS

Number and Distribution of Human Hemic Cells

EDWIN E. OSGOOD