On the Essential Nature of the Hematopoietic Function of Bone Marrow


By

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It has been discussed in previous report (Report 71) that the neutrophils play the leading role in the field of cell-bacterium reaction while the lymphocytes play the leading role in the field of antibody-antigen reaction, acting as antagonists to each other; and it has been also stated that the neutropoietic system in the bone marrow which forms neutrophils acts as antagonist to the lymphatic system which forms lymphocytes.

This report concerns a functional observation on such subordinate reaction cells, as monocytes, endothel cells, eosinophils, basophils and plasma cells, from the standpoint of the hematopoietic phases of the bone marrow and the blood reaction fields.2-30


According to the observation of cells of subordinate defense reaction viewed from the defense reaction fields of blood, monocytes and endothel cells act as cells of defense reaction subordinate to the neutrophils, the cells of main defense reaction in the field of cell-bacterium reaction, while eosinophils, basophils and plasma cells act as cells of defense reaction subordinate to lymphocytes, the cells of main defense reaction in the field of antibody-antigen reaction.

1) Monocytes

Monocytes, in the 3 basal forms of reaction of leucocytes, as shown in the previous report\textsuperscript{11} Fig. 1, act later than neutrophils, increase in the fever-abating stage, act in the field of cell-bacterium reaction by means of phagocytosis and play a subordinate role to the leading actor of the neutrophils. Monocytes, when compared with neutrophils, are by far larger-sized in body, inferior in mobility, but by far more powerful in the ability of phagocytosis. They phagocytize pathogenic agents, and even erythrocytes as often observed common. Wintrobe\textsuperscript{11} called monocytes “scavengers”. Monocytes dispose of waste products which are produced in host-parasite struggles, and other material ingredients.

They appear last in the field of cell-bacterium reaction and keep it clean and orderly. Monocytes contain nuclease, proteinase, carbohydrazide, as do neutrophils, but they differ from neutrophils in that they are rich in lipase. This presumably enables them to digest bacteria with lipoid capsule and explains the well-recognized role of monocytes in tuberculosis and leprosy.

Monocytes increase also in viral diseases, such as varicella, rubeola, mumps and primary atypical pneumonia, in spirochetoses, such as relapsing fever and lues, and in protozoal diseases, such as kala-azar, trypanosomiasis and malaria.

The behavior of monocytes in tuberculosis requires attention. It is generally accepted that in a tuberculous patient monocytosis and neutrophilia are an unfavorable sign and lymphocytosis and eosinophilia a favorable sign.

In following the course of patients with tuberculosis, considerable attention is given by Medlar\textsuperscript{12} to the ratio of monocytes to lymphocytes, for the latter varies inversely with the former in this disease and lymphocytosis occurs when a tuberculous lesion is healing. The normal average M: L ratio is 943: 2,805, that is, an index of 2.9. A very unfavorable ratio would be 3,469: 2,799 (index 0.8); a favorable one is 854:3,047 (index 3.6). In the same way, the monocytic increase can be seen when leprosy has taken a turn for the worse.

The M: L ratio shows the arena where the main host-parasite battle takes place; the arena of main defense reaction shifts to the 1st region when the ratio is small, and to the IIIrd region when the ratio is large.

2) Endothel Cells

Endothel cells are thought to be reticulo-endothelial cells originated from the intima or the endocardium, but they are included in monocytes by American and European authors.

Endothel cells act in the field of cell-bacterium reaction, appear frequently in the peripheral blood in acute infections, especially in endocarditis lenta and phagocytize pathogenic microbes, pigments and foreign bodies.
1) Eosinophils

Eosinophils occupy 1–3% of the normal leucocytes, decrease or disappear from the peripheral blood at the acme stage, reappear in the fever-abating stage and increase in the convalescence in infectious diseases, showing post-infectious eosinophilia. They increase remarkably from the beginning of acute exanthema and appear largely in the peripheral blood at the time of allergic phenomenon to neutralize poison (antigen).

Eosinophils, according to Schlecht,33) make antigen of allergy harmless. Heilmeyer34) insists that the granules of eosinophils are released for this purpose to the surrounding eosinophils. Schlecht33,35,36) observed eosinophilic infiltration in lungs and bronchi of animals, which had been previously sensitized by intraperitoneal injection of heterogeneous serum, by inhalation of the same serum.

Code and McDonald37) reported that eosinophils seem to be particularly rich in histamine; that is, the increase of histamine is always observed in the locus of allergic reaction and it seems to arise from the eosinophilic increase. Dalton38) considered eosinophils as the providers of histamine against the local congestion of sensitized tissue.

Though there are various opinions about the role of eosinophils, it is obvious that eosinophils perform antitoxic function in the field of antibody-antigen reaction, neutralizing, detoxicating and eliminating toxins, foreign proteins and decomposed heterogeneous proteins.

The Charcot-leyden’s crystals, so regularly found in the bronchi or the intestinal tract wherever eosinophils are being abundantly broken down, are thought to be crystalline protein derived from the nucleous of eosinophils.

Most of acute exanthematic diseases are caused by viruses, and in allergic reaction viruses have characteristics analogous to toxine, so that the relation between acute exanthemata and eosinophils, as shown later on, is to be easily

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<th>Day or week of illness</th>
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<td>Endocarditis lenta</td>
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<td>Weil’s disease</td>
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<td>Bacillary dysentery</td>
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<td>Japanese encephalitis</td>
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understood by the detoxicating action of eosinophils.

2) Basophils occupy 0.2-0.6% of normal leucocytes, as shown in Table I, decrease or disappear at the peak stage of infectious diseases, reappear in the fever-abating stage, increase in the convalescence more or less later than the increase of eosinophils and show post-infectious basophilia. The increase is usually at most 1-2%, as shown in Table I, and never exceeds 5%.

Basophils are very numerous in the blood of many of the amphibia and it has been suggested, therefore, that, in man, they may represent evolutionary rests.

The role of basophils, according to Schlecht, is related to the formation of heparin or its preservation. It seems plausible, according to Thoma and Wiercinski, that they function in inflammation by delivering anticoagulants, heparin, to facilitate absorption or to prevent clotting of blood and lymph.

It is now widely confirmed that basophils form heparin. Amano says that heparin most effectively facilitates the formation of striated fibers (striated at 650Å). It precedes chondroitin sulfate in effectiveness. Fibers are said to develop gradually by the function of heparin from a solution through subtle fibers, microscopically visible fibers and fine argent-affine fibers to thick collagenous fibers.

This process of fiber formation was therapeutically proved in a completely reverse process. Hypophyseal-adrenocortical hormones, such as adrenocorticotropic hormone (ACTH), cortisone, prednisone, prednisolone, etc. cause decrease of lymphocytes, eosinophils and basophils, and so restrain the antibody-antigen reaction.

Fibers formed in collagen diseases, therefore, decrease or disappear by giving hypophyseal-adrenocortical hormone. This process is testified in roentgenograms and in recovery from general symptoms of bronchial asthma. Thus the

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<th>of Basophils (%)</th>
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<tr>
<td>0.09</td>
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<td>0.4</td>
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<td>0.1</td>
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mechanism of fiber formation has been inductively interpreted.

Further, it can be easily understood that the basophilia of amphibia is of great importance in adaptation to the internal environment, as heparin prevents clotting of blood and lymph. The activity of leucocytes of a frog stops, according to Ueki,\textsuperscript{42}) at 2°-5°C. Keeping blood and lymph in normal condition is essential for cold-blooded animals, whose temperature changes according to outside temperature.

About 0.4% of basophils in man (warm-blooded creature) means an evolutionary rest, while 8-38% in cold-blooded animals, as shown in Table II by Klieneberger,\textsuperscript{43}) means the necessity for the adaptation to outside temperature.

According to recent examinations, basophils seem to form serotonin decarboxylase and histamine in addition to heparin.

In short, the role of basophils is thought to be the formation of heparin, thereby preventing clotting of blood and lymph and restoring tissue by fiber formation through heparin as its adjuvant. For this purpose the basophils increase in number in the last stage of inflammation and infection and play in the field of antibody-antigen reaction.

3) Plasma Cells

Plasma cells in the peripheral blood were formerly divided into two kinds, namely, Marschalko type and Zürk type. The former is nowadays identified as Rohr's myeloic plasma cells\textsuperscript{44}) and the latter as Moeschlin's lymphatic plasma

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<thead>
<tr>
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<tbody>
<tr>
<td>Mouse</td>
<td>789 - 1,172</td>
<td>13,200 arterial blood 3,960</td>
<td>8 - 45.1/2</td>
</tr>
<tr>
<td>Guinea pig</td>
<td>443 - 615</td>
<td>6,900 - 13,400</td>
<td>9 - 48</td>
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<tr>
<td>Rabbit</td>
<td>433 - 638</td>
<td>3,450 - 12,050</td>
<td>8.1/4 - 50.3/4</td>
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<tr>
<td>Cat</td>
<td>661 - 948</td>
<td>10,400 - 29,000</td>
<td>45 - 87</td>
</tr>
<tr>
<td>Dog</td>
<td>600 - 976</td>
<td>5,700 - 11,100</td>
<td>49 - 68</td>
</tr>
<tr>
<td>Monkey</td>
<td>504 - 591</td>
<td>3,700 - 27,140</td>
<td>16 1/3 - 43</td>
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<tr>
<td>Sheep</td>
<td>674 - 1,632</td>
<td>4,200 - 9,000</td>
<td>28 1/3 - 38 2/3</td>
</tr>
<tr>
<td>Fowl</td>
<td>344 - 391</td>
<td>13,000 - 36,500</td>
<td>18 2/3 - 33 1/2</td>
</tr>
<tr>
<td>Pigen</td>
<td>284 - 390</td>
<td>13,000 - 28,600</td>
<td>40 - 64 1/2</td>
</tr>
<tr>
<td>Frog</td>
<td>47 - 46</td>
<td>3,575 - 6,900</td>
<td>34 - 76</td>
</tr>
</tbody>
</table>
cells. Moeschlin’s plasma cells are at present identified as atypical lymphocytes, which derived from lymphatic tissue and play the same roles as that of the lymphocytes above.

Myeloic plasma cells as named by Rohr will be discussed here.

(1) Formation of plasma cells

About the origin of plasma cells there are 3 theories, namely, the theory of myeloblastic origination by Naegeli, the theory of reticuloendothelial origination in the bone marrow by Rohr and the theory of adventitial origination by Amano.

Amano’s theory, which is recently gaining ground, is judged to be cogent, especially when viewed from the author’s theory of defense reaction fields.

Rohr’s plasma cells in the bone marrow, according to Amano’s close observation, are dismasked as nothing but adventitial cells of the blood vessels in the bone marrow.

Plasma cells, as shown in Table III, appear in the peripheral blood at the acme stage of infection, increase in the fever-abating stage and disappear from the blood in the reconvalescence. They act as forerunner in the field of antibody-antigen reaction, preceding lymphocytes.

(2) Function of plasma cells

Markoff’s suggestion on the formation of serum protein by plasma cells has been confirmed by Bing and Christensen, Bing, Fagraeus and Thorell.
TABLE III. Appearance

<table>
<thead>
<tr>
<th>Day (week) of the illness</th>
<th>Day</th>
<th>1</th>
<th>2</th>
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<th>4</th>
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<tbody>
<tr>
<td>Scarlet fever</td>
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<td>0</td>
<td>0.35</td>
<td>1.16</td>
<td>1.61</td>
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<tr>
<td>Typhoid fever</td>
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<td>0.6</td>
<td>0.7</td>
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<td>1.0</td>
<td>1.3</td>
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<td>Epidemic nephritis</td>
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<td>0.4</td>
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<tr>
<td>Bacillary dysentery</td>
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<td>3.5</td>
<td>8.7</td>
<td>13.5</td>
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<td>11.8</td>
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<td>Erysipelas</td>
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<td>Inumi-fever</td>
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Cf.; ( ) shows the percentage

Bjørneboe and Gormsen,51) Amano,47) Bloom and Wislocki42) and Heilmeyer and Begemann,53) Heilmeyer and Begemann53) observed a case of multiple myeloma which had serum protein of 15%. Since combination of antibody with globulin is proved by electrophoresis, it has been generally confirmed that the plasma cells participate in the formation of antibodies. Bjørneboe and Gormsen57) reported that hyperimmunization in rabbits causes marked proliferation of plasma cells in the spleen and other organs, and Fagraeus54) reported that antibody is formed in tissue cultures of spleen of rabbits previously injected with typhoid bacilli. He found that the red pulp, which contains abundant plasma cells, formed larger amounts of antibody than the white pulp which consists of lymph follicles. Amano47) reported the formation of gamma-globulin of serum protein by plasma cells and from his experimental results he concluded that the antibody is formed by plasma cells.

Undritz55) thinks that the plasma cells are phylogenetically the oldest cells, basing on his findings on comparative anatomy, and that these cells participate in the formation of the protein in animals of low evolution. Plasma cells do not, therefore, appear in the normal man, but appear only in infectious diseases in a percentage less than 1–3%.

That plasma cells are the cells which form antibodies is evidently induced from 1) the abundance of RNA in their body, 2) protein secretion from a highly differentiated fine structure in the cells inferred in electron microscopic study, 3) no phagocytosis (cell-bacterium reaction) and 4) correspondence of their reaction stage to that of antibody-antigen reaction.

Though the lymphocyte theory has been opposed to the plasma cell theory about the formation of antibodies, it is evident that both the lymphocytes and the plasma cells form antibodies and act in the field of antibody-antigen reaction.
of Plasma Cells (\%) 

<table>
<thead>
<tr>
<th>Week</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
<th>VII</th>
<th>VIII</th>
<th>IX</th>
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<td>0.88</td>
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<td>8.7</td>
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<tr>
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When viewed from the fields of defense reaction and the kinds of antibodies which are formed in infectious diseases are numerous, antibodies are presumably not formed from one kind of cells alone, since we recall the most suitable adaptation to the environment by the highly differentiated functions of various cells.

Mutual Relation of Leucocytes and its Biological Significance

There is a certain order in the activity of various leucocytes in the reaction in infectious diseases, showing a close mutual relation.

1. Leucocytes playing in the field of cell-bacterium reaction.

Leucocyte reaction in infection and inflammation is performed according to 3 basal forms, namely, leucocytotic, normo-leucocytotic and leucopenic types of reaction.

It begins first by unspecific cell-bacterium reaction.

1) Neutrophils

The cells in the front of reaction in infection and inflammation must be (1) unspecific reaction cells which counteract all sorts of pathogenic agents, (2) numerous enough to fight the huge number of bacilli, (3) quick in mobility, (4) small in size to be able to pass through tissues, (5) able to digest promptly the microbes with enzymes.

Neutrophils, which occupy 55-65\% of leucocytes in the normal blood, with many reserved cells in the bone marrow, have these properties. They are formed in the first-phase reaction of neutropoietic system in the bone marrow in leucocytotic diseases, increase more and more, perform powerful phagocytosis and form the main force of defense reaction.

2) Monocytes

Monocytes come into the field of cell-bacterium reaction next to neutrophils.
They phagocytize waste products and other materials by their relatively huge bodies and strong phagocytosis. They contain lipase in abundance and become the scavengers in the field of cell-bacterium reaction, though their mobility is inferior to neutrophils.

3) Endothel Cells

Endothel cells are thought of as sort of tissue cells which appear separately in the peripheral blood in infection and inflammation. They appear especially in the fever-rising stage and at the peak stage of endocarditis lenta, and actively engage in phagocytosis.

2. Leucocytes playing in the field of antibody-antigen reaction.

Leucocytes forming specific biochemical substances according to the characteristics of pathogenic agents, act indirectly against them. They do not increase during the first few days of a disease, and rather decrease or disappear at the sensitization (initial stage) and increase later than the cells of cell-bacterium reaction.

1) Lymphocytes

Lymphocytes come into action next to neutrophils, and play the leading role in the field of antibody-antigen reaction. In leucopenic diseases they perform the main defense reaction, increasing relatively and then absolutely at the peak. In typhoid fever, the percentage of lymphocytes is proportional to titer of agglutinin, and antagonistically proportional to number of bacilli. Therefore, the lymphocytes are very closely correlated to production of agglutinin, and as seen in Table IV, the rate of finding bacilli in the blood was the highest (92.5%).

<table>
<thead>
<tr>
<th>Day of the illness</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Sum</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. in which culture was made</td>
<td>1</td>
<td>9</td>
<td>12</td>
<td>14</td>
<td>22</td>
<td>53</td>
<td>111</td>
<td></td>
</tr>
<tr>
<td>Bone marrow</td>
<td>100</td>
<td>100</td>
<td>83.3</td>
<td>92.9</td>
<td>90.8</td>
<td>92.5</td>
<td>91.9</td>
<td></td>
</tr>
<tr>
<td>Venous blood</td>
<td>0</td>
<td>77.8</td>
<td>75.0</td>
<td>92.9</td>
<td>77.3</td>
<td>73.6</td>
<td>76.6</td>
<td></td>
</tr>
<tr>
<td>Stool</td>
<td>0</td>
<td>11.1</td>
<td>33.3</td>
<td>21.4</td>
<td>31.8</td>
<td>35.9</td>
<td>30.6</td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td>0</td>
<td>11.1</td>
<td>0</td>
<td>7.1</td>
<td>4.5</td>
<td>5.7</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>Pharyngeal mucus</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.9</td>
<td>0</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Agglutination titer (more than 200)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>34</td>
<td>52</td>
<td>72</td>
<td>72</td>
<td></td>
</tr>
</tbody>
</table>

on the 5th day of illness, when agglutinin in the blood could be definitely proved. Thereafter, the number of bacilli gradually decreased and the titer of agglutination gradually increased.

2) Eosinophils

Eosinophils increase later than lymphocytes, form antitoxic antibodies
(antibodies against foreign protein), transform the products of decompositions or
disintegrations and foreign protein and detoxicate toxins in the field of antibody-
antigen reaction in the host-parasite struggle. They increase from the beginning
of diseases, such as acute exanthemata and allergy, and neutralize the antigen.

3) Basophils

Basophils are the last to enter the field of antibody-antigen reaction, prevent-
ing clotting of blood and lymph by formation of heparin as well as repairing the
defective tissue in infection or inflammation by fiber formation.

4) Plasma cells

Plasma cells perform antibody-antigen reaction chiefly forming antibody, and
appear in the peripheral blood at the acme or fever-abating stage of infection or
inflammation.

About the Correspondence of the Fields of Defense Reaction of Blood
with the Phases of Hematopoietic Function of Bone Marrow,
Viewed from the Function of Leucocytes.

In Reports 1–7,1–7) it has been stated that, as far as the bone marrow function
is not insufficient, the leucopoietic function of the bone marrow shows diphasic
formation, that the fields of leucocyte reaction comprise the 2 fields of cell-bacterium
reaction and antibody-antigen reaction enacted under antagonistic-constant rela-
tion, and that the phases of leucopoietic function of the bone marrow are in
Correspondence with the fields of leucocyte reaction and represent a picture of
purposeful adaptation to the internal environment.

When viewed from the angle of the function of leucocytes, we know still more
clearly that the phases of hematopoietic function of the bone marrow are in very
close correlation to the demands of time and fields of defense reaction.

Neutrophils and lymphocytes, as shown in Table V, occupy 93%, the largest
majority of leucocytes in the normal blood, forming the main force of defense
reaction of blood under an antagonistic-constant relation.

Neutropoiesis in the bone marrow shows, therefore, diphasic formation in
accordance with the reaction fields.

The subordinate reaction cells, comprising monocytes, eosinophils and
basophils, represent only 7% of leucocytes. Eosinophils are of diphasic forma-
tion, monocytes and basophils are of monophasic formation.

Eosinophils decrease or disappear in the struggle stage in infection, reappear
and then increase in convalescence and in allergic phenomenon. The eruption
in acute exanthemata appears in adequate quantitative relation between antibody
and antigen. For the detoxication of antigen (toxine), there is an increase of
eosinophils from the beginning of a disease. The demand for eosinophils varies
with the existence or non-existence of allergic phenomenon owing to the
TABLE V. Relationships Between Hematopoietic Phases and Reaction Fields of Leucocytes.

<table>
<thead>
<tr>
<th>Leucocytes</th>
<th>Normal W.B.C.</th>
<th>Forming Tissues</th>
<th>Hematopoietic Phases</th>
<th>Reaction fields of leucocytes</th>
<th>Appearance in the Peripheral Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>5.5</td>
<td>Bone-Marrow</td>
<td>Rise of Eosinophils in the Bone-Marrow</td>
<td>Eosinopenia</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>18</td>
<td>Lymphoid Tissues</td>
<td>Diphasic rise of Eosinophils</td>
<td>Leucophaophilia</td>
<td></td>
</tr>
<tr>
<td>Monocytes</td>
<td>5</td>
<td>Bone-Marrow</td>
<td>Monophasic rise of Neutrophils</td>
<td>Increase in the Lymphocytic reaction</td>
<td></td>
</tr>
<tr>
<td>Eosinophils</td>
<td>2</td>
<td>Skin and Tissue</td>
<td>Diphasic rise of Basophils</td>
<td>Allergy, Inflammation, Basophilia</td>
<td></td>
</tr>
<tr>
<td>Basophils</td>
<td>0.2</td>
<td>Bone-Marrow</td>
<td>Monophasic rise of Basophils</td>
<td>Fever Stage</td>
<td></td>
</tr>
<tr>
<td>Endothelial cells</td>
<td>0</td>
<td>Intima</td>
<td>Monophasic rise of Neutrophils</td>
<td>Fever Stage</td>
<td>Fever Stage</td>
</tr>
<tr>
<td>Plasma cells</td>
<td>0</td>
<td>Adventitia</td>
<td>Monophasic rise of Basophils</td>
<td>Fever Stage</td>
<td>Fever Stage</td>
</tr>
</tbody>
</table>

characteristics of the pathogenic agents.

The two phases of rising and falling of eosinophil formation in the bone marrow arise from the demand for eosinophils in the struggle stage (that is the exigency of time); the diphasic formation and one-field reaction of eosinophils are realized.

Monocytes and basophils appear as the last reactors in the field of cell-bacterium reaction and in the field of antibody-antigen reaction, to complete the work in the respective fields of reaction by one-field reaction, corresponding to which the hematopoietic function in the bone marrow is of monophasic type.

The origination of leucocytes, in my opinion, is inferred to be as follows (Table V).

Neutrophils and lymphocytes, which perform the main defense reaction, act antagonistically to each other, and the bone marrow and the lymphatic tissue which form these reaction cells, show an antagonistic relation. On the contrary, the cells of a subordinate defense reaction, as monocytes, eosinophils and basophils, are formed in the bone marrow as well as extramedullarily. Extramedullary formation of monocytes and basophils has been generally accepted. Basophils formed in the bone marrow and mast cells formed in the tissue are deemed to be identical. It is, accordingly, no wonder that eosinophils arise from tissue, too. The grounds to affirm the eosinophilic formation in tissue, especially, in the skin and mucous membrane consist in fact of the increase of eosinophils in the peripheral blood from the early stage of disease preceding the rise of eosinopoietic function of bone marrow in allergy and acute exanthemata, and of the increase of the cells in mucous membrane of bronchi in bronchial asthma and in the skin in allergy.

As the skin and mucous membrane covering the surface of body are the first entrance for pathogenic agent (antigen) to touch or to invade the body, it is most
desirable for the environmental adaptation of living organism to form eosinophils in the skin and mucous membrane.

Allergic phenomenon appear most sensitively in the skin and mucous membrane. Hypophyseal-adrenocortical hormones, as ACTH, cortisone, prednisone and prednisolone, which are most effective for most of the diseases of skin and mucous membrane, are administered generally in department of opthalmology, oto-laryngology and dermatology. The above facts support the formation of eosinophils in the skin and mucous membrane.

Plasma cells and endothel cells do not appear in normal blood, they appear in the peripheral blood as a phenomenon of angio-mesenchymal tissue reaction in infection and inflammation. The position of plasma cells in the field of antibody-antigen reaction corresponds to the position of endothel cells in the field of cell-bacterium reaction. These two kinds of cells originate from blood vessels, namely, as shown in Table V, plasma cells arise from the adventitia of the blood vessels and endothel cells from the intima and the former performs antibody-antigen reaction, the latter cell-bacterium reaction, both appearing in the peripheral blood in a percentage less than 1–3% at the peak stage.

From the observation of formation of blood cells and their function in the defense mechanism of the body, as described above, it is clear that the hematopoietic phases in the bone marrow, under antagonistic-constant relation of the bone marrow to the lymphatic tissues, correspond to the fields of defense reaction and form a strong, fine defense net-work to secure the safety of body with cooperation of the defense reaction of tissue.

CONCLUSION

The results of the functional observation on monocytes, endothel cells, eosinophils, basophils and plasma cells from the standpoint of the hematopoietic phases of the bone marrow and the fields of defense reaction of the blood are as follows.

Monocytes, as cavengers, clean up the field of cell-bacterium reaction by appearance in the field later than neutrophils, playing a subordinate role to the latter, by performing the role of phagocytosis.

Endothel cells appear at the acme of infection and perform cell-bacterium reaction.

Eosinophils play a subordinate role in the field of antibody-antigen reaction and perform the reaction by detoxication in the reconvalescent stage of infection, in allergy and acute exanthemata.

Basophils are the last player in the field of antibody-antigen reaction, keep the constitution of blood and lymph normal, restore the tissues by fiber formation and complete the field of antibody-antigen reaction.

Plasma cells appear in the peripheral blood at the acme and in the fever-
abating stage of infection and inflammation, act indirectly upon pathogenic agents by antibody formation and play the main role of antibody formation in tissues.

As the reaction takes place in two dimensions of time and space, the hematopoietic phases of the bone marrow corresponds, strictly speaking, to the time and space of the reaction.

Neutrophils and lymphocytes perform, therefore, cell-bacterium reaction (one-field reaction) and antibody-antigen reaction (one-field reaction) respectively in response to the demand of space (field) under antagonistic-constant relation of the two, and neutrophilic series in the bone marrow show diphasic formation. Monocytes and basophils show monophasic formation in the bone marrow, corresponding to the one field reaction. Eosinophils show diphasic formation in response to the demand of time of antibody-antigen reaction and perform one-field reaction.

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