On the Essential Nature of the Hematopoietic Function of Bone Marrow

Report 12. Clinical Observation of Infectious Diseases from the Standpoint of Hematopoietic Phases of the Bone Marrow and the Blood Reaction Fields, with Special Reference to the Causative Mechanism of Sepsis and Bacillema

By

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PREFACE

It has been clearly shown in Reports I–II^{11}) that the hematopoietic phases in the bone marrow correspond to the stages and fields of blood reaction and are reflections of the most rational and purposeful adaptation of the body to internal environments.

Since biological reactions occur on the 2 dimensions of time and space, like physico-chemical reactions, the essential nature of these reactions cannot be realized without an idea of time and space.

In natural science, especially physics and engineering, the idea of space has been developed and the electric field, magnetic field and electro-magnetic field were discovered. Thus, the essential nature of objects cannot be now discussed without the theory of electro-magnetic field. In nuclear physics which has been surprisingly developed in recent years, an elementary particle cannot be discussed without the quantum theory of the wave field.

In the past, only the one dimension of time has been considered in biological reactions and the dimension of space has not been brought into consideration in medicine and biology.

In order to clarify the essential nature of the hematopoietic function of the bone marrow, the author has applied the idea of the dimension of space to biological reactions. Furthermore, he has found the hematopoietic phases in the bone marrow, and has made it clear that the hematopoietic phases in the bone
marrow originate from the 2 dimensions of time and space in biological reactions. The 2 dimensions of time and space are directly related with phases, and thus hematopoietic diphasis and the 2 dimensions of time and space are not redundant concepts.

The defense reaction of life, which functions to preserve life, consists of 2 substantially different reactions—cell-stimulant factor (cell-bacterium) reaction and antibody-antigen reaction—in the broader sense, and the intensities of the 2 reactions are antagonistic and the fields of cell-stimulant factor reaction and of antibody-antigen reaction are substantially different.

The signs and symptoms of diseases have been not systematically but independently discussed in the parts of medicine, since the idea of space has not been considered. The development of clinical pictures in a disease is no more than the observation of biological reactions from clinical medical aspect. The development of a series of clinical pictures, such as onset, course, recovery, post-infectious immunity and prognosis of a disease, therefore, is related to the body defense reaction. It can be also regarded as various interactions between the cell-stimulant factor reaction and antibody-antigen reaction, and thus the body reaction is uniformly understood.12–46)

Development of Clinical Picture Observed from the Standpoint of the Field of Body Defense Reaction

The body defense reaction consists of 2 substantially different reactions—cell-bacterium reaction and antibody-antigen reaction. The intensities of these 2 reactions differ depending upon the specificity of pathogenic factors, and are antagonistic to each other as the one becomes stronger, the other becomes that much weaker, as shown in Fig. 1. And the fields of these reactions are divided into 3 regions depending on the intensities of the 2 reactions.

That is, 1) the cell-bacterium reaction is superior in this region, 2) the cell-bacterium reaction and the antibody-antigen reaction are equal in intensity in this region and 3) the antibody-antigen reaction is superior in this region.

These are named as I region, II region and III region. These regions overlap I region, II region and III region of the blood reaction and the 3 regions of the latter consist of a part of the 3 regions of the former.

Leucocytosis appears in I region, where the cell-bacterium reaction is the main defense reaction, normo-leucocytosis appears in II region, where the cell-bacterium reaction and antibody-antigen reaction are equal and leucopenia does in III region, where the antibody-antigen reaction is the main defense reaction.

Infectious diseases are, thus, divided to 3 groups depending on the field where the main body defense reaction takes place. The first group includes diseases in which the main defense reaction takes place in I region and the second group correspondingly includes diseases in which the main defense reaction takes
Field of cell-bacterium reaction | Field of antibody-antigen reaction
---|---
**I region** | **II region** | **III region**

### Strength of reaction

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Cell-bacterium reaction</th>
<th>Antibody-antigen reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st group</td>
<td>2nd group</td>
<td>3rd group</td>
</tr>
<tr>
<td>Coccal infections, purulent and hemorrhagic diseases, spasmodic diseases and dysentery.</td>
<td>A group of bacillary infections, tuberculosis and leprosy.</td>
<td>Bacillary, rickettsial and viral infections.</td>
</tr>
</tbody>
</table>

#### Defense reaction of blood

<table>
<thead>
<tr>
<th>Defense force</th>
<th>Defense force of blood cells</th>
<th>Defense force of blood serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>(#)</td>
<td>(+)</td>
<td>(-)</td>
</tr>
</tbody>
</table>

#### Leucocyte reaction

| Leucocyte reaction | Leucocytosis | Normo-leucocytosis | Leucopenia |

#### Main reaction cells

<table>
<thead>
<tr>
<th>Main reaction cells</th>
<th>Monocytes</th>
<th>Plasma cells</th>
<th>Eosinophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Subordinate reaction cells

<table>
<thead>
<tr>
<th>Subordinate reaction cells</th>
<th>Basophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monocytes</td>
<td></td>
</tr>
<tr>
<td>Plasma cells</td>
<td></td>
</tr>
<tr>
<td>Eosinophils</td>
<td></td>
</tr>
</tbody>
</table>

#### Reinfaction

<table>
<thead>
<tr>
<th>Reinfaction</th>
<th>Frequent</th>
<th>Less frequent</th>
<th>Rare</th>
</tr>
</thead>
</table>

#### Super-infection

<table>
<thead>
<tr>
<th>Super-infection</th>
<th>Frequent</th>
<th>Less frequent</th>
<th>Rare</th>
</tr>
</thead>
</table>

#### Relapse

<table>
<thead>
<tr>
<th>Relapse</th>
<th>Frequent</th>
<th>Less frequent</th>
<th>Rare</th>
</tr>
</thead>
</table>

#### Revival

<table>
<thead>
<tr>
<th>Revival</th>
<th>Frequent</th>
<th>Less frequent</th>
<th>Rare</th>
</tr>
</thead>
</table>

#### Production of post-infectious antibodies

<table>
<thead>
<tr>
<th>Production of post-infectious antibodies</th>
<th>Weak. Infection cannot be prohibited.</th>
<th>Stronger</th>
<th>Strongest</th>
</tr>
</thead>
</table>

#### By invading of pathogenic agents into circulating blood

<table>
<thead>
<tr>
<th>By invading of pathogenic agents into circulating blood</th>
<th>Sepsis</th>
<th>Intermediate type</th>
<th>Bacillemia</th>
</tr>
</thead>
</table>

#### Efficacy of vaccine

<table>
<thead>
<tr>
<th>Efficacy of vaccine</th>
<th>Not effective</th>
<th>Effective</th>
<th>Very effective</th>
</tr>
</thead>
</table>

Fig. 1. Fields of body defense reaction and development of clinical pictures in infectious diseases.
place in II region as does the third group in III region.
1) The first group: infectious diseases in I region
   Infectious diseases due to staphylococci, streptococci and diplococci, etc.,
   purulent, hemorrhagic and spasmodic diseases, dysentery and other local
diseases.
2) The second group: infectious diseases in II region
   A part of bacillary infections, acid bacilli infections such as various
tuberculous infections, leprosy.
3) The third group: infectious diseases in III region
   Bacillary infections such as typhoid and paratyphoid fever, salmonelloses,
   Malta-fever, Bang's fever, rickettsioses and viral diseases.

In these infectious diseases the arenas in which the main defense reactions
occur are determined by the specificity of pathogenic microbes. Pathogenic
microbes causing diseases in the first group belong to the first-phase factor, the
ones in the third group to the second-phase factor, and the ones in the second
group to the intermediate factor.

When the development of clinical pictures in infectious diseases is viewed from
the standpoint of the field of body defense reaction, there are quite systematic
differences between the first, the second and the third groups, and the differences
are to be noted to shift in between the 3 groups with regular order. These
differences are regarded as expressions of the body adapting most rationally and
purposefully to internal environments.

1. Onset of infectious diseases

There are no specific differences in the onset of infectious diseases between the
3 groups. The balance in the host-parasite relationship is different, however.
Pathogenic microbes in the first group are balanced parasites, the ones in the
third group unbalanced parasites and the ones in the second group an intermediate
type. This balance is related to the degree of intimacy of parasitism of pathogenic
microbes. The more intimate parasitism has the more unbalanced pathogenic
microbes, and the less intimate parasitism has the more balanced pathogenic
microbes. The pathogenic microbes in the first group, therefore, are not much
influenced by environmental alterations, while the ones in the third group are
markedly influenced and end up in an adaptive insufficiency to the environment
and vanish. For example, destinies of bacillary dysentery (the first group) and
typhoid or paratyphoid fever (the third group) before and after the Second World
War clearly indicate the differences in the balance.

2. Reinfection

Reinfection frequently occurs in diseases due to pathogenic microbes in the
first group, especially in pneumonia, bacillary dysentery and coecal infections.
Table I. Reinfection in one Family — 3 Repeated Family Infections by Dysentery during 3 Years and 8 Months.

<table>
<thead>
<tr>
<th>Infection</th>
<th>Onset</th>
<th>Interval</th>
<th>Type of bacilli</th>
<th>Father, 58 years old</th>
<th>Elder brother, 16 years old</th>
<th>Younger brother, 14 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>First infection</td>
<td>Aug. 1951</td>
<td>2 years</td>
<td>Shigella Fl. 2a</td>
<td>Mild. Diarrhea for 2 days.</td>
<td>Moderate. Mucous bloody diarrhea. Isolated and treated during 38 days.</td>
<td>Mild. Diarrhea for 3 days.</td>
</tr>
<tr>
<td>Second infection</td>
<td>Aug. 1953</td>
<td>1 year and 8 months</td>
<td>Shigella days. 2</td>
<td>Normal</td>
<td>Severe. Pure mucous bloody diarrhea. Isolated and treated for 37 days.</td>
<td>Moderate. Pure mucous bloody diarrhea. Relapsed. Isolated for 28 days.</td>
</tr>
</tbody>
</table>

Table I shows one example of reinfection in one family — 3 repeated family infections with dysentery during 3 years and 8 months. In the first group, the formation of antibody and development of immunity is so little that reinfection is not prevented. Reinfection in the second group is less frequent than the first group, and the least in the third group. Reinfection, particularly in rickettsioses and viral diseases, never occurs sole 2–3 exceptions.

Thus, incidence of reinfection becomes lower in order of the first, second and
third groups. The difference in incidence of reinfection is inversely related to the intensity of immunity produced in a host by the first infection, although the opportunities of invasion of pathogenic microbes are equal in each group. Sub clinical infection is frequent in the third group. The antibody is unperceivably formed, especially in viral diseases, by the first infection and prevents reinfection.

It should be realized that the reinfection, viewed from the standpoint of the field of body defense reaction, is most frequent in I region (the first group), less in II region (the second group) and the least in III region (the third group), and thus it is noted that a systematic difference exists.

Reinfection often occurs in influenza. It may be attributed to the fact that influenza viruses cause their variation and then the antibodies do not agree with the altered antigen. Reinfection finally occurs since the antibodies have species specificity.

3. Superinfection

Superinfection is frequent in the first group, less in the second group and seldom in the third group. Superinfection in the first group diseases such as dysentery and coccal infections is quite frequent. For example, patients with Shigellosis become frequently infected by other kinds of Shigella from new admission, and then superinfection by more than 2 kinds of Shigella occurs. In order to prevent superinfection, it has been urged separate isolation wards are to be made depending upon a type of Shigella.

4. Aggravation

Aggravation, which is often called relapse or revival, occurs often during the course of an infectious disease.

1) Relapse

Relapse occurs more frequently in diseases which have the main body defense reaction in the field of cell-bacterium reaction, and less frequently in diseases which have the main body defense reaction in the field of antibody-antigen reaction.

Relapse, therefore, occurs most frequently in the first group, less frequently in the second group and seldom in the third group. For example, coccal infections (the first group) cause often repeated relapses and result in a chronic form and sometimes in death.

Relapse usually occurs in 18% of Shigellosis patients, in 4-6% (average 5%) of typhoid fever patients, less in rickettsioses and rarely (less than 1.0%) in viral diseases (Fig. 2). Antibiotics and chemotherapy cause rapid disappearance of antigen even in bacillary infections such as typhoid and paratyphoid fever and Japanese river fever (the third group).

Then the production of antibody is interrupted and the incidence of relapse
Fig. 2. Relapse of typhoid fever treated with CP, 60 years old, ♀.
increases. Table II shows that relapse occurred more frequently in patients with typhoid and paratyphoid fever treated with Chloramphenicol than in cases untreated. The earlier in the course of the diseases was Chloramphenicol therapy begun, the more frequently relapse occurred. The reason for this high incidence in relapse is that Chloramphenicol eradicates the bacilli in a short period, and then the production of antibody is prohibited. Some of the bacilli, however, barely survive and are kept in some foci for sometime under control of the main defense power of the body without any symptoms. As shown in Fig. 2, multiplication of bacilli, controlled once, becomes again dominant after discontinuance of Chloramphenicol, and 5-7 days after lysis and relapse occurs. The number of bacilli in this stage is not yet sufficient to be detected from arterial blood, venous

Table II. Relationships between Relapse and Weeks in Chloramphenicol Therapy
(Dosis: Chloramphenicol 250 mg 6-8 Tablets in a Day, 4-8 Days).

<table>
<thead>
<tr>
<th>Disease</th>
<th>Week of disease in CP therapy</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
<th>VII</th>
<th>Sum</th>
<th>Cases in natural course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typhoid fever</td>
<td>No. of cases with Cp therapy</td>
<td>7</td>
<td>8</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td></td>
<td>31</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>No. of relapse cases</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Rate of relapse (%)</td>
<td>42.9</td>
<td>37.5</td>
<td>28.7</td>
<td>20.0</td>
<td></td>
<td></td>
<td>29.0</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>Paratyphoid A</td>
<td>No. of cases with CP therapy</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>No. of relapse cases</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Rate of relapse (%)</td>
<td>60.0</td>
<td>33.3</td>
<td>20.0</td>
<td></td>
<td></td>
<td></td>
<td>38.5</td>
<td>5.6</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 3. Staphylococcal sepsis, 42 years old, ❋.
blood, stool, urine or pharyngeal mucus except from the bone marrow. This is an abortive form of relapse. Thereafter, fever of 37.1°-37.2°C appears intermittently for 8 days and typical relapse with 40.2°C appears. The bacilli are found from the bone marrow on the first day and in addition from the arterial blood, venous blood and stool on the third day. This causative mechanism in relapse in treatment of typhoid fever by Chloramphenicol is clearly realized in the host-parasite relationship.

Thus, relapse is closely related to the antibody-antigen reactions in the host-parasite relationship.

2) Revival

Revival is pathophysiologically a subtype of relapse. In revival, fever declines and does not return to the normal level but rebounds again. General symptoms are those of aggravation after remission. When relapses and revivals occur, the courses of diseases become chronic with irregular fever.

In coccal infections, particularly sepsis, as shown in Fig. 3, revivals occur and the course is prolonged and the prognosis is often grave.

Revival is most frequent in the first group, less frequent in the second group (commonly seen in “Schub” in tuberculous diseases and the reactional phases of leprosy), and rare in the third group (rickettsioses, viral diseases) as in Fig. 4.

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Fig. 4. Bacillemia.
5. Causative mechanism of sepsis and bacillemia from the standpoint of the field of body defense reaction

Pathogenic microbes spread often through hematogenous dissemination, resulting in bacteremia. The reactions of the body in bacteremia are different depending on the kinds of pathogenic microbes, and following this, sepsis or bacillemia clinically occurs.

Schottmuller\(^47\) (1914) defined sepsis as a disease in which foci appear in the body and the bacilli go into the circulating blood intermittently or continuously from the foci and then subjective and objective symptoms occur. This definition, however, is given to clinical symptoms, originating from circulating pathogenic microbes through the blood, and it is not concerned with the causative mechanism of sepsis and bacillemia.

In 1845, Vichow\(^48\) applied a term of “pyemia” to a state with abnormal increase of white blood cells. In 1882, Gussenbauer\(^49\) differentiated sepsis from pyemia by the presence of metastasis. Later, Martius\(^50\) placed great importance on the fact that bacterial toxine flowed out into the blood causing toxemia and general symptoms, and defined sepsis as purulent disease regardless of the presence of foci. Furthermore, Linck\(^51\) regarded sepsis as a state which results from the spread of pathogenic microbes and their metabolic products into the circulating blood by the lowering of the defense force against infection.

Thus, there have been various theories regarding sepsis, pyemia, toxemia and septicopyemia. These names are only histopathological ones and are of no pathophysiological significance.

Up to date, the causative mechanism and essential nature of sepsis and bacillemia have never been clarified yet. In general, bacillemia has been thought empirically as a state, in which, although bacilli are present in the blood, toxic symptoms do not appear because of bacteriocidal force of the blood, and bacillemia has been thus differentiated from sepsis. Its causative mechanism and essential nature, however, are still obscure.

It is now evident that there is a clear-cut difference between sepsis and bacillemia when the causative mechanism and essential nature are considered from the standpoint of the field of body defense reaction in the adaptation of the body to internal environments.

Streptococci and staphylococci are the most common causes of sepsis. Streptococcus hemolyticus and Streptococcus pyogenes cause 3/4 of all sepsis, and then Streptococcus virdans, Staphylococcus albus and aureus, pneumococcus, meningococcus and gonococcus follow. Furthermore, in children and aged people, Bac. pyogenes and E. coli sometimes cause sepsis. Bacillemia is caused by typhoid bacilli, paratyphoid A, B, K (Salmonella Sendai) and C bacilli, Salmonella group, rickettsia group and virus group. Rickettsemia and viremia
are also belonging to bacillema in broader sense.

The pathogenic microbes causing sepsis, therefore, are belonging to the first group and ones causing bacillema to the third group. The pathogenic microbes in the first group cause the main battle between host and parasite in the field of cell-bacterium reaction, and the ones in the third group cause the same in the field of antibody-antigen reaction, respectively.

From the clinical aspects, therefore, since the main arena of host-parasite battle in the first group is in the field of cell-bacterium reaction, relapse and revival reoccur and courses of the diseases become prolonged. In sepsis, depending on characteristics of pathogenic microbes and individual differences of the host, pathogenic microbes invade the blood vessel system and symptoms such as fever and chill occur. Relapse or revival reoccurs and the fever form is unstable and irregular. Microbes intermittently or continuously flow out into the blood stream and foci are formed in every part of the body. Thus, as in Fig. 3, sepsis shows a characteristically prolonged fever form and 50–90% of all sepsis were fatal before advent of antibiotics.

On the contrary, bacillema is caused by pathogenic microbes of the third group such as the Salmonella, rickettsia and virus groups. The main arena of host-parasite battle is in the field of antibody-antigen reaction, and pathogenic microbes spread through hematogenous dissemination causing bacillema, rickettsemia or viremia which patho-physiologically are all included in bacillema in a broader sense. The pathogenic microbes in the third group have a strong affinity with the host, and form foci in the affinitive organs. As already mentioned, the pathogenic microbes in this group cause less frequently relapse or revival and production of antibodies gradually increases. Then fever and other symptoms subside and the disease becomes cured. The fever form is regular and characteristic for the pathogenic microbe and the course is usually short, and a strong immunity is acquired afterward.

The fever form in lobar pneumonia needs some attention. Lobar pneumonia caused by Diplococcus pneumoniae begins with onset of fever and often chills, and it progresses with continued fever for 7–9 days, and then fever rapidly declines with a crisis. This fever form is quite similar to the one in rickettsioses or viral diseases. The fever, as in Fig. 5, rises 1) in the stages of engorgement of the lung and 2) the stage of hepatisation (stages of red hepatisation and gray hepatisation) and declines with crisis lysis 3) in the stage of resolution. Thus, the fever form of lobar pneumonia by Diplococcus pneumoniae, as with disease in the third group, is regular because of localized pulmonary lesions. When the cocci enter the blood vessel system, sepsis with otitis, peritonitis, endocarditis or meningitis occurs.

As in Fig. 6, the fever form becomes irregular and the course becomes chronic with repeated relapse or revival. Before the advent of chemotherapy and anti-
biotics, pneumococci-sepsis occupied 10% of all sepsis and its mortality rate was 50%. Although Diplococcus pneumoniae usually causes a similar fever pattern to rickettsioses and viral diseases, it shows the characteristics of the pathogenic agent (cocci) of the first-phase factor when it goes into the bloodstream, and causes sepsis with irregular fever pattern and symptoms.

Typhoid fever, which belongs to the third group, as stated in Report 8, sometimes results in sepsis in infants. The lymphoid tissues of infants are underdeveloped and typhoid fever is usually mild with remittent fever, and some severe cases develop sepsislike symptoms without remarkable elevation of antibody as in Fig. 7. These facts suggest that the lymphoid tissue plays an important role in the causative mechanism of sepsis and bacillemia and that the causative mechanism of sepsis and bacillemia depends upon whether the cell-bacterium reaction or antibody-antigen reaction occurs as the main defense reaction against invading pathogenic microbes.

The disease in the second group, for example, tuberculosis, causes often repeated hematogenous dissemination or symptoms of miliary tuberculosis, and has an intermediate form between sepsis and bacillemia. In the reactional phase of leprosy, leprous bacilli are found in the circulating blood. These are generally called bacillemia but are intermediate forms between sepsis and bacillemia.

Mentioned above, the essential difference between sepsis and bacillemia is based upon the characteristics of the main defense reaction chosen by the characteristics of pathogenic microbes. The causative mechanism of sepsis and bacillemia, therefore, is related to the main body defense reaction of host and cannot be realized without this idea.

6. Development of post-infectious immunity

Immunity usually develops after infection. The intensity of post-infectious immunity depends on the characteristics of pathogenic microbes. Development
Fig. 6. Pneumococcal sepsis, 36 years old, ♀.
Fig. 7. Typhoid fever (one year and 5 months old, 5, followed by family infection of 4 members, associated with hemorrhagic tendency and cerebral symptoms.

of post-infectious immunity is weak in diseases of the first group, in which the main defense reaction occurs in the field of cell-bacterium reaction. Production of antimicrobial antibodies is weak, but the antitoxic antibodies are produced according to the production of toxine.

Scarlet fever is associated with acute exanthema which is an allergic phenomenon of infection by Streptococcus hemolyticus, and the Dick test becomes negative with the production of antitoxic antibodies afterwards. Reinfection by the same cocci no longer causes exanthema because of the completion of toxine immunity but it causes repeatedly tonsillitis and adenitis submaxillaris, and it is considered that it leads to rheumatism and collagen disease.

On the contrary, the diseases of the third group develop strong post-infectious immunity, which is usually life-long.

Diseases of the second group are intermediate forms.

7. Prognosis of infectious diseases and the development of collagen disease.

Prognosis of infectious diseases is unique in each causative pathogenic microbe and its mortality rate is not related to the field of body defense reaction but to its severity.

The development of collagen diseases, here, is important. It is noteworthy that development of collagen disease, which is related to the body defense reaction, especially allergy, is high in the first group, less in the second group and rare in the third group.

Fanconi & Wallgren\textsuperscript{52}) in 1958, as in Fig. 8, made a schematic diagram of the spectrum of each type of infectious diseases from toxicity of the pathogenic microbe and the strength of body defense. Since the defense strength of the
host and the toxicity of the pathogenic microbe are in inverse correlation in host-parasite relationship, the sepsis, pyemia, endocarditis lenta and cellular form, serous form, exudative form and rheumatic form of collagen disease and its immunity are arranged in order as in Fig. 8. Salicyclic acid preparations, ACTH, Cortisone, Prednisone and Prednisolone are effective from 10° to 80°, and antibiotics and chemical drugs are effective from 90° to 180°. This schema shows an attitude of defense reaction of the host in the diseases of the first group but does not correspond to the attitude of defense reaction of the host in diseases in the second and third groups. The production of the antimicrobial antibodies is low in diseases of the first group and allergic reaction results from toxine of pathogenetic microbes. Some of them often turn into collagen disease due to unbalanced functions of the autonomic nervous system of the host and progress chronically before completion of immunity. The schema of Fanconi & Wallgren, therefore, corresponds only to the spectrum in diseases of the first group from the standpoint of body defense reaction.

On the contrary, the diseases of the third group such as bacillary infections (typhoid and paratyphoid fever), rickettsial diseases and viral diseases, acquire strong post-infectious immunity and seldom turn into collagen disease. The diseases of the second group are of an intermediate type.

Furthermore, some diseases of the third group such as encephalitis japonica and poliomyelitis anterior acuta cause organic sequelae, which usually subside gradually and do not turn into collagen disease. And several years after typhoid fever, Bernhard’s paresthesia around the N. cut. femoris lateralis sometimes occurs. This may be due to degeneration of tissue the same as falling out of
hair after the course of typhoid fever. The spectrum of diseases of the third group (Figs. 9, 2), therefore, is more simplified than that in diseases of the first group shown in (Figs. 9, 1). The diseases of the second group are of the intermediate form.

CONCLUSION

The body defense reaction of the host in infectious diseases consists of the cell-bacterium reaction and antibody-antigen reaction and the development of clinical picture in infectious diseases is only clinical observation of variously intricated interplay of the strengths of the two reactions.

These two reactions are in antagonistic relation and the field of cell-bacterium reaction and of the antibody-antigen reaction are essentially different. Which one is the main arena in host-parasite battle is determined by the characteristics of pathogenic microbes. Infectious diseases are classified into the first, the second and the third groups by the fields, where the main defense reaction occurs, and there are clinically systematic differences between the 3 groups.

In the diseases of the first group, reinfection, superinfection, relapse and revival often occur. Most of them cause irregular fever forms because of repeated relapse and revival and become chronic. When the pathogenic microbes go into the circulating blood, sepsis occurs. The diseases of this group cause leucocytosis but development of post-infectious immunity is weak. Some
of them turn to collagen disease from toxine produced by the pathogenic microbes.

On the contrary, in the diseases of the third group, reinfection and superinfection are rare and relapse or revival is less frequent. The pathogenic microbes in this group go into the circulating blood and cause bacillemia (including rickettsemia and viremia). Most of this group show regular fever forms and typical clinical courses and the courses are rather short. Leucopenia occurs and the production of antibodies is elevated and strong post-infectious immunity is acquired. Collagen disease seldom results.

Thus, from the standpoint of the field of defense reaction, development of clinical pictures in infectious diseases is systematically regarded as variously intertraced interplay of the cell-bacterium reaction and antibody-antigen reaction, and the essential nature of infectious diseases can be well realized pathophysiologicaly.

References

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