Protein metabolism is disturbed in various diseases and the serum protein is subjected to this disturbed metabolism in the organism\(^1\). Although many serum reactions were devised to detect the disturbed protein metabolism, a quantitative determination of serum globulin has not been accomplished. Rowe\(^2\) fractionated the serum protein by salting-out with ammonium sulfate but a quantitative determination of the fractions was hindered by the presence of nitrogen in ammonium sulfate\(^3\). Subsequently, sodium sulfate was used by Howe\(^4\) and sodium sulfate by Saito and Yoshikawa\(^5\) instead of ammonium sulfate. However, the serum protein was denatured by all of these methods and the results by these methods were not constant. Since the improvement of an electrophoretic apparatus by Tiselius\(^6\) in 1937, the investigation of the serum protein by electrophoresis made a great progress, taking the place of Howe's complicate salting-out method with sodium sulfate.

As clinical application of the serum electrophoresis prevailed, introductive descriptions on the serum electrophoresis were published by Wuhrmann\(^7\), Antweiler\(^8\), Wall\(^9\), Tomita\(^10\), Miyoshi\(^11\) and Fujita\(^12\). Many authors reported on the electrophoretic patterns of the serum protein in individual cardiac disorders but Tomita\(^13\) was the first to report on the characteristic serum electrophoretic patterns in cardiac diseases in general.

Electrophoretic study on the serum protein fractions was performed on 5,300 cases in total and one fourth of them with cardiac diseases were selected for this investigation.

Materials and Methods

1) Four hundred seventy patients with cardiac diseases who entered Maekawa Clinic since 1950 were selected for this investigation.

2) About 8 cc of the blood was obtained early in the morning before breakfast, with a view to avoiding the dietary influence and hourly fluctuation,\(^14\) from the cubital vein, kept for 40 minutes in a thermostat regulated at 37°C and centrifugated. Then, the total protein of the supernatant serum was measured before the serum was diluted up to 1.4 g/dl with phosphate buffer. The diluted serum was dialysed against phosphate buffer for 24 hours at room-temperature in winter and at 6°C~10°C in summer in a cellophane bag and filtered for electrophoresis.

3) The total protein was measured with a Hitachi refratometer.

4) The electrophoretic apparatus used for this study was of the mode of Schlieren-Diagonal made in Hitachi Company. The buffer solution of pH 8.03 consisted of 163.5 cc of M/5 NaH\(_2\)PO\(_4\)12H\(_2\)O, 10 cc of M/5 NaH\(_2\)PO\(_4\)2H\(_2\)O and 826.5 cc of distilled water. The procedures in serum electrophoresis was the same as those postulated in the Japanese Electrophoretic Society Regulations\(^16\). Namely, the electrophoresis was performed with the voltage of 150 to 200 V and amperage of 10 to 14 mA in a thermostatic bath kept at 4 to 10°C. Photographs were taken 60 minutes after the start of electrophoresis, regulating the slit distance and slit angle to obtain a proper electrophoretic pattern. For the determination of the percentage and amount of serum protein fractions, the electrophoretic picture was enlarged five times the original size. By planimetry of the descending electrophoretic pattern, the percentage of serum protein fractions was first determined. Then, the amount of the respective fractions was calculated in relation to the total protein.
RESULTS

I. Normal range of serum protein fractions

The serum electrophoretic patterns obtained from 5 healthy adult males and 5 healthy adult females were considered to be normal and the respective values are shown in Table I.

<table>
<thead>
<tr>
<th>Table I</th>
<th>Normal Range in Serum Protein Fraction (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.P.</td>
<td>8.15</td>
</tr>
<tr>
<td>Al</td>
<td>7.21</td>
</tr>
</tbody>
</table>

T.P. : Total Protein  
Al : Albumin  
α-Gl : α-Globulin  
β-Gl : β-Globulin  
γ-Gl : γ-Globulin  
A/G : Albumin/Globulin

II. Serum protein fractions in cardiac diseases

Electrophoretic patterns of the serum protein were determined in patients with mitral insufficiency, mitral stenosis, mitral stenoinficiency, aortic insufficiency, aortic stenosis, combined valvular disease, coronary insufficiency, myocardial infarction, endocarditis, pericarditis, and decompensated hypertension which were classified according to the most predominant symptoms of the disease. Although rheumatism, syphilis, and hereditary predisposition should be taken into consideration as an etiological factor in subdividing valvular diseases, the factors which influence the serum electrophoretic pattern were not the etiology of the disease but that whether the disease is well compensated or not. Therefore, each valvular disease was further divided into the compensated and the decompensated.

<table>
<thead>
<tr>
<th>Table II</th>
<th>Relationship between Serum α-Globulin and Patient Temperature in Bacterial Endocarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temp.</td>
<td>57.5°C (Below)</td>
</tr>
<tr>
<td>α-Gl</td>
<td>3</td>
</tr>
</tbody>
</table>

Fig. 1. Serum protein fraction mitral insufficiency 26 cases.

b) Mitral stenosis (Fig. 2)

In a compensated mitral stenosis, the total protein remained unaltered or slightly decreased and albumin decreased. The decrease of albumin was more marked in mitral stenosis than in mitral insufficiency and mitral stenoinficiency. α-globulin increased, β-globulin remained normal or occasionally slightly increased and γ-globulin tended to increase more.
than in other mitral valvular diseases. In the
decompensated, alteration of the total protein
was nearly the same as that in the compensated.
Decrease in albumin was not so marked as in
other mitral valvular diseases. The differences
of serum electrophoretic patterns between in
the compensated and in the decompensated
were the slightest of all other mitral valvular
diseases. α- and β-globulin tended to increase
more than in the compensated and the increase
of γ-globulin was most marked of all other
mitral valvular diseases.

d) Aortic insufficiency (Fig. 4)
In the compensated, the total protein re-
ained normal or decreased and albumin de-
creased moderately. α-globulin increased,
β-globulin increased in more than 1/2 of the
cases and γ-globulin remained normal or slightly
decreased in some cases. In the decompensated,
c) Mitral stenoininsufficiency (Fig. 3)
In compensated cases, the decrease of the
total protein and albumin was more than in
mitral insufficiency but less than in mitral
stenosis. α-globulin tended to increase and
β- and γ-globulin remained normal. In the
decompensated, the amount of total protein
was nearly the same as that in the compensated.
Decrease in albumin was less than in mitral
insufficiency and slightly more than in mitral
stenosis. α- and β-globulin tended to increase
in comparison to those in the compensated and
alteration of γ-globulin was more than in mitral
insufficiency but slightly less than in mitral
stenosis.
alteration in the total protein was less than in the compensated and albumin decreased markedly. α-globulin tended to increase, β-globulin remained unaltered and γ-globulin tended to increase in comparison with those in the compensated.

e) Aortic stenosis (Fig. 5)

The number of the cases was not large enough to refer to the characteristic tendency of electrophoretic pattern in the aortic stenosis. In the compensated, albumin decreased, α-globulin increased and γ-globulin remained normal. In the decompensated, albumin decreased and α-and γ-globulin increased.

\[\text{Fig. 5. Serum protein fraction aortic stenosis 8 cases.}\]

g) Congenital heart disease (Fig. 7)

Patients with congenital heart diseases of many kinds under the age of 15 were selected for this investigation. In the compensated, the total protein remained normal or decreased and albumin decreased moderately. α-globulin increased but β-globulin remained normal. In

\[\text{Fig. 7. Serum protein fraction congenital heart disease 38 cases.}\]

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the decompensated, alteration in the total protein was not uniform. Decrease in albumin was less than in the compensated. $\beta$-globulin was unaltered but $\gamma$-globulin increased moderately.

**h) Coronary insufficiency (Fig. 8)**

Patients with characteristic electrocardiographic pattern of coronary insufficiency and cardiac discomfort were selected. The total protein remained normal or slightly decreased and albumin decreased moderately. $\alpha$-globulin increased moderately, $\beta$-globulin increased in more than 1/2 of the cases tested and $\gamma$-globulin generally remained normal. Increase in $\beta$-globulin was proportional to that in the serum cholesterol and the patients with increased $\beta$-globulin were frequently diabetic.

![Graph](image)

**Fig. 8.** Serum protein fraction coronary insufficiency and sclerosis 33 cases.

**i) Myocardial infarction (Fig. 9)**

Blood was obtained immediately after hospitalization from the patients with complaints of chest pain, substernal oppression and cardiac asthma. The total protein remained normal or decreased moderately. Albumin decreased moderately but markedly in those cases whose total protein was decreased. Increase in $\alpha$-globulin was detected 5 days after the onset of heart attack, most marked in the 2nd to 3rd week and returned to the premordial level about 60 to 90 days after the attack. In those cases which deteriorated progressively or recurred, $\alpha$-globulin did not decrease and increased in some cases. Increase in $\beta$-globulin was detected 10 to 15 days after stroke and returned to the premordial level in the 3rd to 4th month. $\gamma$-globulin remained within a normal range. Even in the decompensated cases an increase in $\gamma$-globulin was, not marked.

![Graph](image)

**Fig. 9.** Serum protein fraction myocardial infarction 40 cases.

**j) Endocarditis**

Endocarditis has been classified according to the etiology. In the present study, however, endocarditis was subdivided into bacterial and rheumatic. Serum electrophoretic patterns on admission are shown in Fig. 10.

(a) Bacterial endocarditis (Fig. 11)

The total protein varied markedly according to the cases. An increase in the total protein was accompanied with that in $\gamma$-globulin and a decrease in the total protein seemed to be due to the decrease in albumin. $\alpha$-globulin tended to increase in most cases, $\beta$-globulin remained unaltered and $\gamma$-globulin increased markedly in most cases. As indicated in Figs. 13, 14, 15 and 16, there was no relation between the variations in albumin and $\gamma$-globulin and those in erythrocyte sedimentation rate, leukocyte count and the size of the liver. However, significant relations were observed.
both between \(\alpha\)-globulin and fever and between \(\gamma\)-globulin and plasma cell count in the bone marrow.

(b) Rheumatic endocarditis (Fig. 12)

The total protein remained normal but albumin decreased markedly in 1/5 cases. \(\alpha\)-globulin increased in many cases, \(\beta\)-globulin remained normal and \(\gamma\)-globulin increased moderately in 1/2 cases. Those cases with a marked decrease in albumin and marked increase in \(\alpha\)- and \(\gamma\)-globulins were accompanied by complications such as rheumatic polyarthritis.

Fig. 14. Relationship between serum γ-globulin and erythrocyte sedimentation rate in bacterial endocarditis 23 cases.

Fig. 15. Relationship between serum albumin and leucocytosis in bacterial endocarditis 22 cases.

Fig. 16. Relationship between serum γ-globulin and leucocytosis in bacterial endocarditis 22 cases.

Fig. 17. Serum protein fraction myocarditis 23 cases.

k) Myocarditis (Fig. 17)

The diagnosis of myocarditis was made clinically in 32 cases. Alterations in serum electrophoretic patterns were slight: the total protein was normal or slightly decreased, albumin decreased moderately, β-globulin remained unaltered and γ-globulin increased in 1/2 cases.

l) Pericarditis (Fig. 18)

The serum electrophoretic patterns in pericarditis varied markedly according to the stage of the disease. Accordingly, pericarditis was subdivided into acute, subacute and chronic stages.
decrease in albumin and a marked increase in α-globulin were observed in all the cases. β-globulin was mostly normal, 7-globulin tended to increase slightly in most cases but a marked increase in cases with complications such as polyarthritis, pleuritis and peritonitis, α- and 7-globulins increased markedly.

(b) Subacute stage (Fig. 20)

Variations in the serum electrophoretic pattern in improved cases were different from those in chronically progressed cases. In improved cases, the total protein remained normal or increased slightly and albumin was decreased moderately but less than in acute stage. α-globulin was increased but less than in acute stage, β-globulin was normal or slightly increased but more than in acute stage and 7-globulin increased more than in acute stage. In chronically progressed cases, albumin remained markedly decreased or only slightly increased, α-globulin was increased but less than in acute stage, β-globulin remained unaltered and 7-globulin increased but the degree of increase was less than in acute stage.

(c) Chronic stage (Fig. 21)

Alteration in the serum electrophoretic patterns of pericarditis in chronic stage was

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as marked as those in nephrotic syndromes. The total protein, albumin and α-globulin decreased markedly, β-globulin tended to increase and γ-globulin decreased slightly. In the improved cases, albumin and γ-globulin increased gradually but in the chronically progressed cases, they decreased gradually.

(d) Pericarditis due to a malignant tumor (Fig. 22)

The number of the cases was not large enough to make conclusion but there was a tendency that the total protein decreases due to a marked decrease in albumin, α-globulin increased markedly, β- and γ-globulins remained mostly normal.

m) Decompensated essential hypertension

Variations of electrophoretic patterns in decompensated cases of essential hypertension were shown in Fig. 23. Total protein was normal or moderately decreased in the cases with a marked decrease in albumin. Albumin was moderately to markedly decreased. The prognosis of the cases with albumin of less than 3.25 g/l was poor. β-globulin was increased in 1/2 of the cases tested. In the cases with an increase in β-globulin, serum cholesterol was also proportionally increased. In improved cases, albumin increased, α-globulin decreased, and γ-globulin returned to normal within 1 to 2 months.

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DISCUSSION

A. Cardiac valvular disease

The major factor which affects the serum electrophoretic pattern in cardiac valvular disease is whether the heart is decompensated or not. According to Wuhrmann and Watanabe, the serum protein is not affected in a compensated stage, while, Yamada and Oji reported the increase in 7-globulin. Fujita observed a decrease in albumin and increase in β- and 7-globulins and stated that the variation in serum electrophoretic pattern is less in a compensated stage than in a decompensated but the same tendency was present. In a decompensated stage, Wuhrmann, Evans, Watanabe and Saito observed a decrease in albumin and an increase in 7-globulin and Fujita and Kinugasa a decrease in albumin and an increase in β- globulins. In the present study, albumin was decreased markedly and α-, β- and 7-globulins were increased. Among the globulins, an increase in 7-globulin was most marked. However, it is a well known fact that the influences of cardiac valvular disease upon the organism is different in each valvular disease.

The variations in the electrophoretic pattern in cardiac valvular disease have been found to be different in various valvular disease. Tomita was the first to discuss the characteristic alteration in the serum electrophoretic pattern in separate cardiac valvular disease. In the present study, discussion will be made on each cardiac valvular disease classifying into a compensated and a decompensated.

1) Mitral insufficiency

It has been said that mitral insufficiency can be compensated longer than other valvular disease, but once decompensated it is difficult to be compensated. Tomita stated that it was of interest that 7-globulin is normal or decreased in a compensated stage but when decompensated albumin decreases and 7-globulin increases moderately, which is in agreement with the author's observation. The author considers it is natural that the decompensated mitral insufficiency in which a decrease in albumin is most marked is difficult to be compensated. The facts that 7-globulin is normal or slightly decreased in a compensated stage and that an increase in 7-globulin in a decompensated stage is lowest of all the mitral valvular disease can be explained by author's analysis which will be described in Part II.

2) Mitral stenosis

In comparison to mitral insufficiency, mitral stenosis is easily decompensated but can be compensated relatively easily by rest and treatment. The decrease in albumin in a compensated stage was most marked among the mitral valvular disease. The slightest decrease in albumin in a compensated mitral stenosis can be interpreted in the same way as in mitral insufficiency. 7-globulin was increased moderately even in compensated stage. The marked increase in 7-globulin in a decompensated stage was considered to be due to the secondary infections in congested lungs which occur more frequency than in mitral insufficiency.

3) Mitral steno-insufficiency

Variations both in a compensated and decompensated mitral steno-insufficiency were nearly an intermediate of mitral insufficiency and mitral stenosis. But the facts that they were more similar to those in mitral stenosis than to those in mitral insufficiency can be interpreted in the same way as in mitral stenosis and insufficiency.

4) Aortic insufficiency

Aortic insufficiency can be classified, syphilitic, rheumatic, bacterial and functional (left ventricular hypertrophy) but etiological difference was not observed. Variations in a compensated cases were nearly the same as in other compensated valvular disease but in the case with arteriosclerosis, β-globulin was increased in many cases. As Tomita pointed out, it is of interest that 7-globulin is decreased in some cases as in mitral insufficiency. Variations in a decompensated stage were similar to those in other decompensated valvular disease.

5) Aortic stenosis

On account of the number of cases being small, discussion is deferred.

6) Combined valvular disease

It may be natural that variation of electrophoretic patterns in combined valvular disease in which the number of injured valves and severity of valvular damage are various showed

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no definite tendency. In a compensated stage, 7-globulin was increased in some cases but remained normal or slightly decreased in others. Variations in a decompensated stage occurred also in a wider range and had no definite tendency.

7) Congenital heart disease

Although a statistical study on variations of serum electrophoretic pattern in congenital heart disease in which various types of irregularity are included seemed meaningless, there was a definite tendency in them. As pointed out by Kawana39 and Hashimoto26, changes in various organs in congenital heart disease in the young are different from those in the elderly persons. It is of interest that changes in albumin in a decompensated stage was nearly the same as in a compensated stage.

8) Coronary insufficiency

Wuhrmann37 stated that simple arteriosclerosis without any complications showed no changes in blood chemistry. However, the number of arteriosclerosis without complications being small, the cases with cardiac discomfort and abnormal electrocardiograms were employed as the subjects. An increase in a-globulin in coronary insufficiency was slighter than that in myocardial infarction. An increase in 8-globulin was proportional to that in serum cholesterol, and arteriosclerosis was found in many of the cases with an increase in 8-globulin.

9) Myocardial infarction

Acceleration of erythrocyte sedimentation rate in myocardial infarction25,27,29 is well known, and Riseman20 stated that myocardial infarction can be differentiated from angina pectoris by erythrocyte sedimentation rate since erythrocyte sedimentation is accelerated 2 to 3 hours after attack for several weeks in myocardial infarction. According to Friedberg30, acceleration of erythrocyte sedimentation rate is due to an absorption of necrotic materials of a myocardial infarct into the blood. Sinke23 and Greenspan20 observed an increase in serum mucoprotein and stated that its detection is valuable for the differential diagnosis of myocardial infarction from other coronary diseases in which changes in electrocardiograms are not marked. Observing an increase in plasma fibrinogen in myocardial infarction, Lasner24 stated that its continuous determination is useful for the judgement of prognosis of myocardial infarction. The determination of serum S.G.-O.T. has been reported43,45,49 to be valuable for the diagnosis and prognosis of myocardial infarction by some investigators. Recently, Bing et al43,44 investigated myocardial infarction by the use of coronary vein catheterisation. By them a substance of small molecular weight was found to exude from the myocardium in early stage of coronary artery occlusion and a substance of high molecular weight in late stage (myocardial infarction). Kroop40 reported that an increase in C.R.P. in myocardial infarction can be utilized for the differentiation from coronary insufficiency. James40 observed cryoglobulin in a case of myocardial infarction. The author40 also observed a slight increase in cryoglobulin in a patient of 7-g-multiple myeloma with a marked hyperproteinemia and transient coronary insufficiency in electrocardiograms. Beaumont40 observed an increase in blood coagulability in myocardial infarction and analysed it in relation to prothrombin time, plasma fibrinogen and heparin tolerance test. Murakami et al40 ascribed an increase in blood coagulability to adrenocortical hyperfunction.

In spite of these various reports on alterations in blood chemistry in myocardial infarction, investigations into the serum electrophoretic patterns were relatively few. In the present study, albumin decreased moderately to markedly, a-globulin increased markedly, 8-globulin increased moderately and 7-globulin remained nearly unaltered. Leinward47 observed an increase in a-globulin. Tomita35 stated that a-globulin increases markedly early in myocardial infarction, remains high for more than 1 month and returns to the original value after 2 month and a half after the onset of myocardial infarction.

Tomita reported that both C.R.P. and a-globulin were increased in myocardial infarction. The author also observed the increase of a-globulin on the fourth or fifth day after the onset of infarct, and the maximum increase after 7 to 10 days followed by gradual decrease to the normal value in two to three months. It seems that the prognosis is bad in the cases
whose $\alpha$-globulin increases markedly or does not decrease with the course of the disease. In the cases with repeated recidivation, the increase of $\alpha$-globulin is observed at the time of recidivation. Therefore, a follow up measurement of $\alpha$-globulin may be helpful for the diagnosis and judgement of the course and prognosis of myocardial infarction. It is interesting that mucoprotein shows a similar electrophoretic fluctuation as that of $\alpha$-globulin. $\beta$-globulin tends to increase from the beginning of the infarction. The increase and decrease correspond to the course of the illness and it takes about 3 to 6 months to return to the original level. Zajcev also observed the increase of $\beta$-globulin. Although some scholars reported that $\gamma$-globulin increases with the severity or the course of infarction, the author observed the decrease in some cases. As Tomita pointed out, in cases of myocardial infarction no such increase of $\gamma$-globulin occurs as seen in cases of ordinary inflammatory diseases and no significant increase occurs even when it is combined with decompensation, while other cardiac cases in decompensation show the increase.

10) Endocarditis

Wuhrmann states that the increase of $\alpha$, $\beta$-globulins occurs in acute inflammatory heart disease and the increase of $\gamma$-globulin is observed along with the course of the illness. Fujita et al. reported the increase of $\gamma$-globulin at a relatively early stage of endocarditis. Tomita observed the marked increase of $\gamma$-globulin. He reported the increase of $\alpha$-globulin and decrease of albumin in cases accompanying high fever. The total protein, however, is normal due to the marked increase of $\gamma$-globulin. The author too obtained the same results as Tomita's, i.e. a marked increase in $\gamma$-globulin and a marked decrease in albumin. There was no correlation between albumin or $\gamma$-globulin and leukocytes count or erythrocyte sedimentation rate, although Fujita et al. reported a correlation between sedimentation rate and albumin or $\gamma$-globulin. Regarding the correlation between $\alpha$-globulin and fever, Tomita and the author also observed a parallel correlation as is shown in Table II. The increase of $\alpha$-globulin may be due to accentuated metabolism during febrile period, as Schedlowskii explained. The normalization of protein pattern occurred within one month by $\gamma$-globulin therapy in the effective cases, according to Fujita, and continued even after the discontinuance of the therapy, while in the ineffective cases normalization did not occur. Ito et al. reported that $\gamma$-globulin was found to be significantly increased in the patients who died, while in the patients who survived it was normal or slightly increased or it was normalized after the treatment even if it was markedly increased prior to the treatment.

The author observed that it takes 3 to 6 months after the therapy to see the normalization of $\gamma$-globulin, albumin or $\alpha$-globulin. In cases of bad prognosis the variation of albumin and $\gamma$-globulin was slight and $\alpha$-globulin tended to increase. Regarding the correlation between myelohistiocytes and $\gamma$-globulin, there are reports by Fujita and Kumatani. The author also noted some correlation between them, but the number of the cases is not enough to make a definite conclusion.

B. Rheumatic endocarditis

Tomita reported that this disease does not cause any specific change in electrophoretic pattern except only a slight decrease of albumin which is commonly found in general inflammation. The author obtained the same results as Tomita's with a few exceptional cases which showed a marked decrease in albumin and a moderate increase in $\gamma$-globulin. These changes are probably the reflection of the inflammation of other parts of the body (e.g. rheumatoid arthritis).

11) Myocarditis

According to Wuhrmann, the electrophoretic changes are slight in myocarditis with an isolated lesion but the inflammatory pattern in shown in diffuse myocarditis. Tomita too noted a slight inflammatory pattern, i.e. normal total protein content, a decrease in albumin, normal or a slight increase in $\gamma$-globulin, no change in $\beta$-globulin, normal or a slight increase in $\gamma$-globulin.

Wachi, based on the Maekawa's theory for allergy, succeeded to produce myocarditis in rabbits by means of Tomita's method, and
he found the increase of total protein and \( \gamma \)-globulin.

Besides the Tomita's results, the author found that \( \alpha \)- and \( \beta \)-globulins were markedly increased in the cases with slight inflammation in other parts of the body than the heart. 12) *Pericarditis*

This disease is interesting as far as the electrophoretic pattern is concerned. When this disease is classified into three stages, acute, subacute and chronic, and also good prognosis cases and bad prognosis cases, the electrophoretic patterns in those stages and cases are quite similar to those in nephritis in a period from the acute to chronic stage.

According to Wuhrmann, in acute pericarditis there was observed the increase of \( \alpha \)- and \( \beta \)-globulins which corresponds to the findings in pleurisy or peritonitis. Thus pericarditis has specific electrophoretic changes. However, there has been no valuable report except by Tomita. According to Tomita, the early stage of exudative pericarditis showed the increase of \( \alpha \)- and \( \beta \)-globulins consequently hypo-albuminemia. In addition to the same results as Tomita's, the author found a marked increase of \( \gamma \)-globulin in the cases combining with such significant inflammation as polyarthritis, pleurisy and peritonitis etc.. The cause for the decrease of albumin may be explained by the analysis of the decrease of albumin in cardiac failure which will be described by the author in the next report Part II (Hypofunction in albumin production of the liver due to increased venous pressure).

Subacute phase: the characteristic change in curable patients at this phase is a relative increase in albumin and \( \gamma \)-globulin. It is understood that the increase of albumin is due to a relative decrease of venous pressure and the increase of \( \gamma \)-globulin due to continued inflammation.

The change of albumin is less in the cases developing into the chronic phase than in the acute phase, i.e. the marked decrease of albumin and slight increase of \( \gamma \)-globulin. It is assumed by the author that the decrease of albumin is due to the continued high venous pressure and the slight increase of \( \gamma \)-globulin is due to both the continued inflammation as well as the decrease of albumin caused by decreased production of total albumin as stated by Tomita\(^6\). In cases with chronic pericarditis especially constrictive pericarditis was observed a marked decrease of total protein and albumin, a moderate decrease of \( \gamma \)-globulin and an increase of \( \alpha \)-globulin.

McQuarrie\(^5\) reported that hypoproteinemia is attributable to the loss of protein into ascites and the decrease of liver function.

Tomita et al also presume that hypoproteinemia is due to the decreased ability to produce serum protein, because, in spite of marked hypoproteinemia, erythrocyte count and hemoglobin contents are normal or rather increased and serum electrolytes and urine are normal, moreover, if the increased venous pressure is attributable \( \gamma \)-globulin should increase makedly as seen in the cardiac cases due to metabolic diseases.

Because of the decrease of not only albumin but \( \gamma \)-globulin, the author also feels that these electrophoretic abnormalities are due to impaired ability to produce total serum protein.

In the cases facing toward the recovery at this stage, the increase of albumin first occurs, besides, in some cases \( \gamma \)-globulin increase above the normal range and then return to the normal value. Regarding the pericarditis due to malignant tumor, Antweiler\(^9\) reported a most frequent fluctuation on \( \alpha \)-globulin and \( \psi \) peak, and also no significance on the change of \( \gamma \)-globulin. The author obtained the same results as Antweiler did. The author presumes that the marked decrease of albumin is due to the primary decrease by this illness as well as the secondary decrease by the increased venous pressure.

13) *Decompensated hypertension*

The true cause for essential hypertension is still unknown despite the various studies on it's pathogenesis by many investigators, e.g. there have been renal, neurogenic and endocrine theories. Prof. Maekawa sought the pathogenesis in the disturbance of ATP-ATPase system in the cardiovascular system.

When essential hypertension is reviewed from the stand point of serum protein pattern, hypertensinogen is included in a range from \( \alpha_2 \) to \( \beta \), globulin\(^8\), as Tomita\(^5\) reported, and

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the change of serum protein pattern is unexpectedly little, e.g. only the slight decrease of albumin and increase of β-globulin. In a decompensated condition, however, the moderate decrease of albumin, increase of α- and β-globulins and marked increase of γ-globulin.

It is interesting to note that the increase of β-globulin is related in some extent with the level of serum cholesterol, and that Lewis and Page's report\(^{61,62}\) that β-globulin is increased in hypertensive patients with severe vascular damage.

**CONCLUSION**

1) Electrophoretic determinations by means of the Tiselius apparatus were done on 924 sera of 470 cardiac patients, and the specific protein patterns due to various diseases were studied.

Valvular heart diseases were classified for the study into two phases; compensated and decompensated.

2) Decompensated heart failures: the decrease of albumin and increase of α-, β- and γ-globulins especially γ-globulin were observed.

3) Compensated mitral valvular diseases: the change of protein pattern was most slight in mitral insufficiency and most marked in mitral stenosis.

 Decompensated mitral valvular diseases: the decrease of albumin was slight in the stenosis and marked in the insufficiency, whereas the increase of γ-globulin was slight in the insufficiency and marked in the stenosis.

 Decompensated phase of aortic insufficiency: the changes of protein pattern were similar to those of other valvular diseases. However, it was noted that many of the cases showing the increase of β-globulin were combined with arteriosclerosis.

 The combined valvular disease also shows similar pattern as other valvular diseases do. However, alteration of the patterns is most marked in this disease.

4) Congenital heart diseases: the decrease of albumin was not marked either in the decompensated or decompensated phase.

5) Coronary insufficiency: the decrease of albumin and increase of α- and β-globulin were observed.

6) Myocardial infarction: the decrease of albumin and marked increase of α-globulin and moderate increase of β-globulin. α-globulin is increased from the beginning of the disease and returns to the normal range after 2 to 3 months.

7) Endocarditis: In bacterial endocarditis were observed a marked decrease in albumin, a moderate increase in α-globulin and a marked increase in γ-globulin. In rheumatic endocarditis were observed a decrease in albumin, a moderate increase in α-globulin and a slight increase in γ-globulin.

8) Myocarditis: the decrease of albumin and slight increase of α-globulin and in a half of the cases the increase of γ-globulin.

9) Pericarditis: the changes of protein patterns varies at each phase of this disease. In general, however, the specific feature is the marked decrease of albumin. The increase of γ-globulin occurs at the acute phase and its decrease at the chronic phase. The increase of albumin is observed in the cases facing toward recovery. However, there was observed a further decrease of albumin in patients progressively worse, and the decrease remains same in patients being stable.

10) Decompensated hypertension: the protein patterns are almost same as those in other cardiac valvular diseases. However, arteriosclerosis was often combined in the patients with increase in β-globulin.

**Acknowledgement**

The author wishes to express his deep appreciation and greatfulness to Prof. M. Maekawa for his guidance and advise for this study. The author is also deeply indebted to Assist. Prof. Tomita of the Central Laboratory of Kyoto University Hospital for his constant guidance and interest. Thanks are due to Drs. H. Kato, K. Nakajima, H. Honda and U. Suzuki for their cooperation.

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