SERUM CHOLESTEROL LEVEL OF VISCOSE RAYON WORKERS

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The rayon industry in Japan, first enterprised in 1916, had been one of the most important light-industries until the beginning of the World War II. As the demand of production was so quickly expanded in the early period, that relatively severe form of CS₂ poisoning and toxic hazard in factories were often noticed particularly from 1923 to 1933(1). The high level of CS₂ concentration and subsequent health hazard gradually became a great matter of concern particularly from the administrative standpoint of health protection for the workers, and, in this connection, many clinical as well as laboratory studies as to toxicologic effects of CS₂ and practical preventive measures in the industry were made.

In 1949 a research committee of industrial medicine was organized in Japan Synthetic Textile Association in order to reexamine occupational hazards of the industry as thoroughly as possible. The standard measuring method of CS₂ concentration in the air was worked out to be recommended to factories, and actual physical conditions of workers were also periodically examined. Consequently, concentration of the toxic gas in working places has been lowered to a safety level, and the incidence of acute and severe poisoning is now practically zero. Consideration to a latent or chronic poisoning caused by repeated exposure to a low concentration has then been taken up by the Committee, applying hematological, neurological, biochemical and epidemiological techniques to the inplant health service.

As a part of the committee's contributions, this study on serum cholesterol and ester-ratio levels in viscose rayon workers was done. For a comparative purpose, a similar study by animal experiment using rabbits which were exposed to CS₂ for a relatively long period is discussed in the comment of this paper. The value for the clinical test of this blood constituents has been evaluated by Johnstone(2) and von Oettingen(3) as a sign of chronic CS₂ poisoning.

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RESULTS

Subjects: The subjects were selected from spinning and acid cutting or refining male workers who were regularly exposed to CS₂ for eight hours daily. Four viscose rayon factories located in a rural district of the country were chosen as representative in terms of the scale and size of production and facility, and the communities to which these workers belonged were of approximately the same social level. The factories were classified into two groups according to the average concentration of CS₂ in the working place; the A group consisted of two factories of artificial silk and staple fibre, where average CS₂ concentration was relatively low, i.e. 5-19 ppm, and the B group comprised two factories of staple fibre, where average concentration was rather high, i.e. 15-65 ppm. CS₂ concentration in air was measured by McKee's Diethylamine-copper acetate Method with use of two glass-filtered bubbling samplers and a photoelectric colorimeter.

One hundred and thirty-four male workers supposed to be exposed to CS₂, in both groups of factories were selected randomly, of which 64 were from the A group and 70 were from the B group; their ages were from 19 to 40 years, and the history of employment varied from 1 to 10 years. Most of the workers in the A group did not present any noticeable subjective symptoms at the time of the study. Among the B group workers, however, there were some complaints; 12 slight headache, 5 fatigue during their shift-hours, 6 irritability, 8 impaired appetite, 10 sleeplessness and 5 pains in legs. The amount of CS₂ excreted in the urine was 2 to 20 micrograms per hour in the A group and 5 to 40 micrograms per hour in the B group during eight hours of a day shift. As the control group, some male workers were selected randomly from the clerical department of each factory where CS₂ workers were examined. Since there was no significant difference in values of blood cholesterol and its constituents among control persons of each factory, total of these amounting to 48 was taken as the whole control group for comparison with the CS₂ exposed group. Their age was ranging from 19 to 40 years. Although the factories examined in this study located in different places, these localities were situated in one district of the country, and it was feasible to assume that the workers belonged to the social class of the same type and their dietary custom was of the same Japanese rural form.

Method: Total, free and combined (esterified) cholesterol of the serum were determined by Yanagisawa's Method based on Kingsley's and Zuckerman's principles. The percentage of the esterified cholesterol to the total cholesterol
(ester-ratio) was then calculated. The serum was separated from the blood drawn out of the cubital vein of the subjects at the end of a day shift.

To ascertain if there was any significant diurnal change in the serum cholesterol, some of CS₂ workers were examined twice a day before and after their shifts at the early period of the study. Thus the average total serum cholesterol level of 60 workers chosen from different plants was shown to be 188.1 mg percent (standard error, 4.7 mg percent) for the value before and

![Graph showing serum total cholesterol level](image)

**Fig. 1.** Serum total cholesterol level.
A: group of low CS₂ concentration  
B: group of high CS₂ concentration  
C: control group
188.0 mg percent (standard error, 5.0 mg percent) for the value after the shift. It was also shown that the average of ester-ratio of 57 cut of the 60 workers was 57.5 percent (standard error, 1.3 percent) before and 57.5 percent (standard error, 1.4 percent) after the shift. As there were no significant differences between these results, the values obtained after the shift alone were given in the following description.

The Total Cholesterol in the Serum: The serum total cholesterol values in the A group which was exposed to a relatively low concentration of CS$_2$ as stated above are shown in A of Figure 1 and those for the B group workers exposed to a high concentration are shown in B of the same figure along with those of the control workers indicated by C. The mean of 64 workers in the A group was 157.5 mg percent (standard deviation, 23.5 mg percent and standard error, 3.0 mg percent), and that of the B group consisting of 70 workers was 212.6 mg percent (standard deviation, 34.3 mg percent and standard error, 4.1 mg percent), whereas the mean of 48 control workers showed 154.0 mg percent (standard deviation, 23.5 mg percent and standard error, 3.4 mg percent). There was no significant difference between the means of the A and the control group, and both of them fell within the normal range of the rural people of Japan\(^\text{(8)}\). However, there was a significant difference between the B and the control group, probability was found to be less than 0.01 by-the “Student’s t-test.” Seven workers out of 70 of the B group showed more than 250 mg percent of the total cholesterol and one among them showed even over 300 mg percent.

Special care was taken in considering whether or not the serum cholesterol amount of CS$_2$ exposed workers was different from that of a general Japanese inhabitants. From our own experience, it may be seen that the serum cholesterol level of a normal Japanese is generally lower than that of the normal people of the Western World. This may probably be due to the fact that consumption of lipid by the Japanese is generally nearly half of that by Western people. Two of the authors (T. and S.)\(^\text{(8)}\) have also found that the serum total cholesterol of urban people was distinctly higher than that of rural people. In their study 45 healthy male students and clerical workers were tested as a urban group and their average total cholesterol was 206.3 mg percent (standard deviation, 42.6 mg percent). And 78 healthy rural inhabitants and farmers selected as a rural group showed 162.7 mg percent (standard deviation, 27.1 mg percent) for average total cholesterol; this value was significantly lower than the former. It should be also noted that the age distribution of the both groups was almost the same, ranging 19 to 40 years and ester-ratio of the two groups
were of no significant difference.

Thus, in order to avoid the error derived from the geographical factor and the social condition, the control subjects in this study were carefully chosen from the clerical workers in each factory investigated.

The Cholesterol Ester and the Ester-ratio: The fraction cholesterol ester of the CS₂ workers and the control was shown in Figure 2. The mean of CS₂ workers in the A group was 95.0 mg percent (standard deviation, 18.1 mg percent and standard error, 2.3 mg percent), that of the B group was 111.4 mg

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**Fig. 2.** Serum cholesterol ester level.
A: group of low CS₂ concentration
B: group of high CS₂ concentration
C: control group
percent (standard deviation, 29.5 mg percent and standard error, 3.5 mg percent), and that of the control group was 96.1 mg percent (standard deviation, 17.8 mg percent and standard error, 2.6 mg percent). There was no significant difference between the A and the control groups, whereas the esterified fraction in the B group was significantly larger than that in the control (P<0.01).

The ratios of esterified to total cholesterol (ester-ratio) were, as shown in Figure 3, 60.4 percent (standard deviation, 7.9 percent and standard error, 1.0 percent) for the A group, 52.8 percent (standard deviation, 12.6 percent

![Figure 3. Serum ester-ratio.](image)

A: group of low CS₂ concentration
B: group of high CS₂ concentration
C: control group
and standard error, 1.5 percent) for the B group and 62.2 percent (standard deviation, 7.8 percent and standard error, 1.1 percent) for the control group. Between the means of the A and the control groups no significant difference was found. On the other hand, the ester-ratio of the B group showed a remarkable decrease compared with the control group, and a significant difference was found between the two means; (P<0.001). In 13 subjects of the B group (18.5%), ester-ratio was less than 40 percent, which was considered to be lower than normal.

The elevated serum total cholesterol level and the lowered ester-ratio were considered in this study to be due to an effect of CS₂. The affirmative evaluation, however, may require further intensive toxicological investigation.

**COMMENT**

It has been stated that as a secondary sign of the toxicologic effect, the serum cholesterol value will increase and the ester-ratio will decrease in case of absorption of various industrial solvents or toxic materials such as chloroform, phosphorus and carbon tetrachloride which mainly cause damage to the liver function(9)(10). Lewey(11) has reported that 54 CS₂ workers showed 34% higher mean value of serum total cholesterol and lower cholesterol ester-ratio than control workers. He also stated that any correlation between these changes and retinal or peripheral arteriosclerosis was not found, and these changes could be regarded as an indication of disturbance of systemic metabolism possibly caused by a toxic disorder of the liver function partly correlating with deficiency of vitamin B₃. Recently Vigliani(12) has reported that in his studies on chronic CS₂ encephalopathy, an increase of the serum β/α lipoprotein ratio in connection with high cholesterolemia was found in CS₂ patients.

On the other hand, a report by Rubin et al(13) stated that serum cholesterol level of 30 shift workers in a low grade exposure of less than 10 ppm of average CS₂ concentration, was all within the range of the normal value (between 160 and 230 mg per 100 ml), the mean value of 30 workers being 218.07 mg per 100 ml of the serum, and that no one presented any definite symptoms of CS₂ intoxication.

Judging from our present results and those by the above-mentioned investigators, this blood chemical change can be recognized as one of the signs of chronic CS₂ poisoning. However, it may be difficult to decide whether this sign is a primary direct effect by CS₂ or its secondary metabolic change. We may also conclude that with the comparison of the concentration of CS₂ in the two groups in relating to the serum cholesterol level, 20 ppm for the threshold limit
value of CS₂ which adopted by the A.C.G.I.H. in U.S.A. is agreeable.

A similar result of the serum cholesterol change was achieved in our experiment on rabbits. Details of this experiment is described by one of the authors (S.T.) in another periodical. In this study, as shown in Table 1,

<table>
<thead>
<tr>
<th>Rabbit</th>
<th>Total cholesterol (T. C.) (mg%) and Ester-Ratio (E. R.) (%)</th>
<th>Control (Before exposure)</th>
<th>Days of exposure to CS₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T. C. 67</td>
<td>100 108 128* 127</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. R. 63</td>
<td>67 67 52* 52</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>T. C. 56</td>
<td>80 84 132* 132</td>
<td></td>
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<tr>
<td></td>
<td>E. R. 77</td>
<td>59 61 39* 39</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>T. C. 42</td>
<td>42 51 56 63  70</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. R. 67</td>
<td>67 55 50 44  40</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>T. C. 42</td>
<td>42 47 47 75  84</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. R. 55</td>
<td>60 60 37 33</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>T. C. 66</td>
<td>80 112 115 115 119 120</td>
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<tr>
<td></td>
<td>E. R. 68</td>
<td>56 43 39 39  40 38</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>T. C. 33</td>
<td>33 45 50 54  97 105</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. R. 61</td>
<td>61 53 48 44  25 23</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>T. C. 45</td>
<td>50 54 76 98  117 122</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. R. 76</td>
<td>74 69 49 40  33 28</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>T. C. 62</td>
<td>73 84 96 107 107 114</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. R. 58</td>
<td>50 39 38 34  31 26</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>T. C. 62</td>
<td>70 89 91 94  107 115</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. R. 58</td>
<td>56 51 50 48  37 33</td>
<td></td>
</tr>
</tbody>
</table>

* Asterisk indicates interruption of exposure to CS₂.

nine male rabbits were exposed to a regulated concentration of from 150 to 180 ppm in a gas chamber for three hours daily, six days a week during a period of almost 200 days. In the first 10 days, a slight elevation of serum total cholesterol level and a decrease of ester-ratio began, and the progression of the changes became gradually distinct in the following days. After about ninety experimental days the exposure to two rabbits (No. 1 and 4) was discontinued and, nevertheless, the high cholesterol level was kept for the following sixty days. All the animals did not show any other noticeable signs of intoxication except a secondary anemia with slight loss of body weight. The results of this experiment and the serum cholesterol behavior of workers in relatively high CS₂ exposure may be caused by an identical toxicologic process.
In the routine periodic physical examination of CS₂ workers, the serum cholesterol test seems to be worthwhile for early detection of the poisoning particularly in evaluating the intensity of exposure to CS₂ in the plant. However, for the purpose of diagnosing an individual CS₂ chronic poisoning, other clinical tests, for instance, ophthalmological, psychiatric, neurological, and others would be more to be relied upon, because the normal range of the serum cholesterol is rather wide. On the other hand, the relatively narrow range of the normal cholesterol ester-ratio can be used as an indicator for diagnosis of chronic CS₂ poisoning. In this case, however, other liver diseases, chronic alcohol poisoning, and similar diseases should be differentiated.

SUMMARY

The level of serum total and esterified cholesterol was estimated and the ratio of esterified to total cholesterol was calculated in the total of 134 CS₂ workers and 48 controls in four representative viscose rayon plants in a rural district of Japan. The four plants were grouped into two categories according to CS₂ concentration in the air of working places: the A group consisted of two plants where CS₂ concentration was ranging from 5 to 19 ppm and the number of subjects was 64, and the B group comprised two plants where CS₂ concentration was from 15 to 65 ppm and 70 subjects were selected randomly.

In the A group the average values of total cholesterol, esterified cholesterol and ratio of esterified to total cholesterol in the serum were 157.5 mg percent, 95.0 mg percent and 60.4 percent, respectively. There was no statistical significant difference between these average values in the CS₂ exposed workers and the controls, whose total cholesterol, esterified cholesterol and ester ratio were measured as 154.0 mg percent, 96.1 mg percent and 62.2 percent respectively.

In the B group the average values of total cholesterol, esterified cholesterol and ratio were 212.6 mg percent, 111.4 mg percent and 52.8 percent respectively. The significant differences were ascertained statistically in total cholesterol, esterified cholesterol and ratio of esterified to total cholesterol of the CS₂ workers from the controls. The serum total and esterified cholesterol appeared to be higher and the ester ratio was lower in the subjects of the B group which was exposed to a relatively high concentration of CS₂ than in the A group which was exposed to a lower concentration. Among 70 subjects of the B group, 12 persons had a slight headache, 5 fatigue during their shift, 6 irritability, 8 impaired appetite, 10 sleeplessness and 5 pains in legs.

The blood change of the same type was assured by an experiment of
rabbits which were exposed to 150 to 180 ppm of CS$_2$ for 200 days.

We would like to conclude that the change of the serum cholesterol level can be taken for one of the early signs of chronic CS$_2$ poisoning.

REFERENCE