FURTHER OBSERVATIONS ON THE MECHANICAL FRAGILITY OF THE RED CELL IN LEAD POISONING

BY

A. J. DE KRETSER and H. A. WALDRON

From the Medical Department, Vauxhall Motors Ltd., Dunstable and Luton

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Further experiments on the effects of lead on the mechanical fragility of the red cell confirm previous findings, that lead does not increase the mechanical fragility index of the red cell at the blood lead levels found in clinical plumbism.

Above these levels lead does increase the mechanical fragility index, reaching its maximum effect at about 50 μg. of lead/ml. blood.

The present investigations were undertaken in view of the apparent contradiction between the results of our previous work (de Kretser and Waldron, 1963; Waldron, 1964) and those of the classic experiments of Aub, Reznikoff, and Smith (1924). Aub et al. considered that an increase in the mechanical fragility of the red cell was a significant factor in the pathogenesis of the anaemia of lead poisoning. Our present experiments have confirmed that lead has an effect on the red cells above a concentration of 10 μg. lead/ml. blood, but at or below this figure there is no increase in the mechanical fragility.

Lead, as lead acetate, was added to whole blood in vitro to give final concentrations of 10 to 100 μg. lead/ml. whole blood, and the mechanical fragility index (M.F.I.) of the red cells was determined at each concentration. A group of nine workers who had shown an apparent undue susceptibility to absorb lead as compared with their co-workers were also studied to see if lead had a greater effect on the M.F.I. of their red cells than on normal cells.

Workers were defined as being unduly sensitive to lead if they showed a very marked increase in urinary coproporphyrin excretion after being exposed to lead for a short time, compared with workers having the same degree and length of exposure. After being taken off work involving contact with lead the urinary coproporphyrin excretion of all the men in the susceptible group quickly fell to normal only to become markedly raised on further exposure to lead. Of all the records of the lead workers examined for this investigation, some 500 to 600, only the nine chosen satisfied our criteria of selection. At the time of the experiment they were on work away from contact with lead.

Methods

The techniques for leading the red cells and estimating the M.F.I. were carried out as described in a previous paper (de Kretser and Waldron, 1963). Heparinized blood was used in all experiments. The red cells were exposed to concentrations of lead from 10 to 100 μg./ml. in increments of 10 μg./ml. Ten values were obtained for each group including a control group.

The following investigations were carried out on the nine lead workers studied, using standard techniques: haemoglobin, reticulocyte count, E.S.R., serum bilirubin, semi-quantitative urinary coproporphyrin, and urinary urobilinogen. In those workers with a serum bilirubin above 0·8 mg./100 ml., an electrophoresis of serum proteins and liver function tests were performed.

Results

At a concentration of 10 μg. lead/ml. blood there was a slight fall in the mean M.F.I. as compared with that found in the control group. Above this level, increasing concentrations of lead caused a parallel increase in the mean M.F.I. reaching a maximum effect between 40 and 50 μg. lead/ml. blood (Table 1; Figure).

No increase in the M.F.I. was found in the apparently lead-susceptible group of workers.
increased susceptibility to absorb lead as compared with their co-workers would have shown an increase in the M.F.I. at low concentrations of lead. Using concentrations of 10 and 40 μg. lead/ml. blood, however, no increase in the M.F.I. was found (Table 2).

### Table 2

**Mechanical fragility indices obtained from incubating blood from presumed lead susceptibles with lead in vitro**

<table>
<thead>
<tr>
<th>Case</th>
<th>M.F.I.10</th>
<th>M.F.I.15</th>
<th>M.F.I.40</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.12</td>
<td>7.12</td>
<td>17.20</td>
</tr>
<tr>
<td>2</td>
<td>7.56</td>
<td>7.86</td>
<td>15.71</td>
</tr>
<tr>
<td>3</td>
<td>7.86</td>
<td>7.86</td>
<td>15.71</td>
</tr>
<tr>
<td>4</td>
<td>8.00</td>
<td>8.36</td>
<td>15.71</td>
</tr>
<tr>
<td>5</td>
<td>7.66</td>
<td>7.66</td>
<td>15.71</td>
</tr>
<tr>
<td>6</td>
<td>6.86</td>
<td>6.86</td>
<td>15.71</td>
</tr>
<tr>
<td>7</td>
<td>8.20</td>
<td>7.86</td>
<td>15.71</td>
</tr>
<tr>
<td>8</td>
<td>6.32</td>
<td>7.59</td>
<td>15.71</td>
</tr>
<tr>
<td>9</td>
<td>9.29</td>
<td>8.42</td>
<td>15.71</td>
</tr>
<tr>
<td>Mean</td>
<td>7.45</td>
<td>7.73</td>
<td>11.58</td>
</tr>
</tbody>
</table>

M.F.I.10 = control; M.F.I.15 = 10 μg. lead/ml. blood; M.F.I.40 = 40 μg. lead/ml. blood.

The conclusion is forced upon us by the results presented in this paper and by our previous work that alterations in the mechanical fragility of the red cell envelope play little, if any, part in the production of the anaemia of lead poisoning.

Our thanks are due to Dr. G. A. Matthews for performing the serum electrophoresis and liver function tests. We are grateful to Dr. A. R. Thompson and the Management of Vauxhall Motors Limited for permission to publish this paper.

### References


### Discussion

The mechanism of the production of anaemia in lead poisoning is still open to question. Lead may produce its effect by affecting the maturation of the red cell or it may act directly on the cell. The protagonists of the theory that lead produces its effect on the red cell primarily by increasing the mechanical fragility of the cell base their arguments mainly on the work of Aub *et al.* (1924). These authors showed that concentrations of 0·01 mg. lead/ml. of washed red cells increased the mechanical fragility of the erythrocyte *in vitro*. The results presented in this paper confirm this, although at levels which are far in excess of those which one would expect to find in cases of lead poisoning. At the levels that one would expect in plumbism, or even at levels up to 10 μg./ml. blood, lead has no detectable effect on the M.F.I. *in vitro*.

It was hoped that observations on the red cells from the group of nine workers who had shown an
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