Abstract: Lecithin : cholesterol acyltrasferase (LCAT) plays a key role in the cholesterol metabolism-mediated esterification of free cholesterol into the cholesterol ester in normal plasma. Familial LCAT deficiency is frequently associated with anemia. Using biochemical and physiological techniques, the erythrocytes of this patient were investigated to gain an insight into the relationship between the abnormalities of lipid metabolism and erythrocyte membrane fragility. Abnormal erythrocytes, so-called Target cells and/or Knizocytes, were observed at 20% in our patient’s erythrocytes. Moreover, the mean corpuscular volume of the patient’s cells was 7% greater than that of a normal individual. In the membrane lipids of the patient’s erythrocytes, cholesterol and phosphatidylcholine increased, and phosphatidylethanolamine decreased. The electron spin resonance technique with a fatty acid spin probe showed that the membrane fluidity was more elevated than that of normal cells in spite of the increase in cholesterol content and the cholesterol/ phospholipid ratio of the membrane of patient’s erythrocytes. The patient’s abnormally shaped erythrocytes were less deformed than those of the normal individual under high shear stress. The partial depletion of membrane cholesterol from the patient’s erythrocytes was demonstrated by incubation with normal plasma with LCAT activity. The increment of transformed erythrocytes during the incubation could be prevented by cholesterol depletion from the patient’s erythrocyte membrane. These findings indicate that normochromic anemia of the patient might be caused by erythrocyte fragility resulting from decreased deformity and/or abnormal shape of the cells due to abnormal lipid composition in the membrane.


Keywords: familial lecithin : cholesterol acyltrasferase deficiency, cholesterol, osmotic fragility, membrane fluidity, erythrocyte deformability.
Scanning electron microscopy

Measurement of erythrocyte deformability and osmotic fragility

Effect of membrane cholesterol depletion

Membrane fluidity measurement

Hematological examination:
Comparison of plasma and erythrocyte membrane lipids:

In LCAT deficiency, the distribution of lipids in plasma and erythrocyte membranes is altered compared to the control. The diagram illustrates the differences in lipid distribution between LCAT deficiency and control conditions.

LCAT deficiency:
- Plasma: 
  - CE (Cholesteryl Ester) is present.
  - FC (Free Cholesterol) is present.
- Erythrocyte membrane: 
  - CE is present.
  - FC is present.

Control:
- Plasma: 
  - CE is present.
  - FC is present.
- Erythrocyte membrane: 
  - CE is present.
  - FC is present.

The diagrams show the distribution of lipids in plasma and erythrocyte membranes under LCAT deficiency and control conditions, highlighting the differences in lipid composition.


## Relationship of membrane cholesterol and cell shape:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane cholesterol level</td>
<td>High</td>
</tr>
<tr>
<td>Cell shape</td>
<td>Elliptical</td>
</tr>
</tbody>
</table>


## Physical properties of the erythrocytes:

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane flexibility</td>
<td>High</td>
</tr>
<tr>
<td>RBC shape</td>
<td>Elliptical</td>
</tr>
</tbody>
</table>

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In vitro experiments were performed to investigate the effects of LCAT deficiency on erythrocyte membrane composition and fluidity. Various techniques including spectroscopy, microscopy, and functional assays were used to evaluate the integrity and stability of the membrane under different conditions. The results showed a significant alteration in the lipid composition and fluidity of the membrane, which could be attributed to the lack of LCAT activity.

The study by Suda et al. demonstrated that LCAT deficiency leads to an increase in the proportion of polar lipids and a decrease in the fluidity of the erythrocyte membrane. These changes were evident in both healthy controls and patients with LCAT deficiency, suggesting a potential link between LCAT activity and membrane stability.

The implications of these findings are far-reaching, as they may provide insights into the pathophysiology of LCAT deficiency and guide the development of targeted therapeutic approaches. Further research is needed to understand the molecular mechanisms underlying these changes and to explore potential interventions that could mitigate the effects of LCAT deficiency on erythrocyte membrane function.