Effect of Low Molecular Weight Dextran on Red Blood Cell Charge During Clinical Extracorporeal Circulation

By Eugene F. Bernstein, M.D., Fred G. Emmings, D.D.S., Robert L. Evans, Ph.D., Aldo Castaneda, M.D., and Richard L. Varco, M.D., Ph.D.

RED BLOOD CELL sludging, or aggregation, has been demonstrated to accompany prolonged extracorporeal circulation, and has been implicated as a serious cause of morbidity, and occasionally even of death, following such perfusions. This red blood cell aggregation is characterized by slow blood flow in small vessels, clumping of red blood cells with plugging of capillaries and venules, the appearance of hyperchromatic cells, plasma skimming, and the absence of vasoconstriction. Low molecular weight dextran (LmDx) has been shown to delay the onset of, prevent, or markedly diminish aggregation under these and other circumstances.

The largest forces mutually attracting red blood cells include chemical bonding, ion pair and triplet formation, and surface or interfacial tension. Those forces which appear to be large and capable of causing cellular repulsion include electrical charge and those steric forces which hinder chemical or ionic bonding. Of these, electrical charge appears to be a large factor, and one which may be measured simply. In these studies, performed on 50 patients undergoing open-heart operations, samples of blood were taken for analysis before and after the pump-oxygenator run, in an effort to determine the effect of extracorporeal circulation on red blood cell charge, and the effect of low molecular weight dextran upon this factor during clinical extracorporeal circulation.

Methods

Thirty-ml. blood samples were obtained from the femoral arterial cannula of patients about to undergo total cardiopulmonary bypass for the correction of acquired and congenital cardiac lesions. The samples were obtained during anesthesia, following heparinization, but before bypass was instituted. Similar samples were obtained at the end of cardiopulmonary bypass, prior to the administration of heparin antagonists. These blood samples were analyzed for sedimentation rate, hematocrit, whole blood viscosity, plasma viscosity, plasma hemoglobin, and red blood cell charge.

Red blood cell charge was determined in a microelectrophoresis apparatus modified from that originally described by Northrup and Kunitz and later modified by Abramson et al. An electric potential was placed across the glass chamber by means of a zine-zine sulfate electrode system and NaCl agar bridges. A potential gradient of approximately 10 volts/cm. was employed, involving a current flow of 8 to 10 ma. The voltage across the chamber was measured through two platinum electrodes connected to an RCA Volt-ohmyst vacuum tube voltmeter. Dark-field microscopy was employed because of the combined advantages of better contrast of the unstained cells and the relative absence of heating within the chamber. A diluted sample of red blood cells in their own plasma was permitted to enter the chamber. The voltage was applied, and the velocity of the cells measured with the aid of a stop watch and a calibrated micrometer eyepiece disc. Each determination consisted of the mean of 10 separate cell velocity measurements. The formula employed for the calculation of red blood cell charge is:

\[ Q = \frac{6 \pi r \eta v}{E_x} \]

where \( Q \) equals charge in coulombs, \( r \) is the radius of the red blood cell (cm.), \( \eta \) is the viscosity of the plasma (poise), \( v \) is the velocity of the red cell (cm./sec.), and \( E_x \) is the potential gradient employed (volts/cm.).

Red blood cell diameters were measured directly by placing a drop of the suspension on a microscope slide and observing the individual blood cells, at a magnification of 980 diameters, with...
Table 1

Distribution of Lesions at Operation

<table>
<thead>
<tr>
<th>Lesion</th>
<th>LmDx + blood primed</th>
<th>5 per cent dextrose primed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interaltrial septal defect</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Interventricular septal defect</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Rheumatic valvular disease</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Congenital aortic stenosis</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Atrioventricular canal</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Left ventricular-right atrial shunt</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cor trilocularis</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Results

Perfusions Primed with Low Molecular Weight Dextran and Blood

The distribution of lesions in 37 patients undergoing heart operations in which the pump-oxygenator system was primed with blood and low molecular weight dextran, usually in the ratio of 2:1, is indicated in Table 1. As shown in Figure 1, in 36 of these 37 patients, samples of blood taken at the end of perfusion demonstrated more highly charged red blood cells (more electronegative) than control samples taken from the same patients prior to perfusion. The one patient whose red cells did not become more negative in this group expired in the operating room shortly after the end of the perfusion.

Perfusions Primed with Five Per Cent Dextrose in Water

In 13 patients, extracorporeal bypass was carried out using the Zuhdi technique with 5 per cent dextrose as the priming agent. The distribution of lesions in these patients is also listed in Table 1. In these patients, samples taken at the end of perfusion revealed red blood cells with greater electrical charge (more electronegative) in only six instances, while in the other seven instances the charge was less negative. In no instance was the change in charge striking (Fig. 2). The mean change in charge in these patients was from 1.14 to 1.10 \times 10^{-8} \text{ coulombs/cell}. This contrasts sharply with the mean change in charge in the first group of patients, in which low molecular weight dextran was included in the perfusing medium, where the mean electrical charge at the end of perfusion was 1.46 \times 10^{-8} \text{ coulombs/cell}, in contrast with a mean control charge of 1.23 \times 10^{-8} \text{ coulombs/cell}.

Discussion

The results of these studies confirm the results of earlier studies performed both in vitro and in the experimental animal laboratory. In these, it has been shown that pumping and oxygenating whole blood in an in vitro system does not appear to affect red blood cell charge. This is also true when an animal is added to the circuit. Such studies are comparable to the clinical studies reported here, in which dextrose in water was used as the priming agent.
solution. Similar results were obtained in the animal laboratory when whole blood alone was used as a priming vehicle.

However, in in vitro studies, the addition of low molecular weight dextran to whole blood results in a progressive stepwise increase in electronegative charge. This increase has been confirmed in experimental animal studies involving both partial and total body perfusion in which LmDx is used to prime the system. The results reported here from patients perfused with low molecular weight dextran as a part of the priming volume of the pump-oxygenator system confirm the previously reported results from the experimental animal laboratory. While electric charge of the blood cells is not the only force involved in the aggregation process, and does not appear to be altered by extracorporeal circulation alone, the protective action of low molecular weight dextran appears to include an increase in red blood cellular electronegativity, consistent with an increase in the total forces of repulsion between cells. In experimental studies, this increase in red blood cell electronegativity is accompanied by a decrease in the red blood cell aggregation normally seen during prolonged extracorporeal circulation. While red blood cell aggregation during extracorporeal circulation is not normally associated with changes in red blood cell charge, the effect of dextran appears to include its ability to counter an increase in the forces of attraction with an increase in the total forces of repulsion between cells. This appears to be of considerable value in improving perfusion in small blood vessels and, therefore, also of vital organs and tissues.

The role of other attractive forces such as surface or interfacial tension, protein denaturation, and chemical bonding, as well as the role of pH, ionic strength, and the concentration of polyvalent salts, remains to be investigated and explained. These factors all probably involve the red blood cell membrane in some way, as demonstrated in electron microscopic studies by the groups of Bloch, Lee, and Katchalsky. It may be that priming the extracorporeal circuit with low molecular weight dextran results in coating the circulating red blood cells with dextran, increasing their electronegativity, and preventing the subsequent coating of these cells with some other substances (which produce aggregation).

Summary

Low molecular weight dextran, when included in the priming mixture of a pump oxygenator for clinical extracorporeal circulation, almost uniformly increased the electric charge of red blood cells. In perfusions in which 5 per cent dextrose and water were used as the priming vehicle, there appeared to be no change in red blood cell charge. The increase in red blood cell electronegativity, associated with the presence of low molecular weight dextran, appeared to decrease red blood cell aggregation and permit improved tissue perfusion.
References


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