Effects of intracoronary infusion of arterial blood or Fluosol-DA 20% on regional myocardial metabolism and function during brief coronary artery occlusions

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ABSTRACT  Effects of intracoronary infusion (50 ml/min) of arterial blood, oxygenated or unoxygenated Fluosol, or Plasmalyte A on hemodynamics, electrocardiogram, regional myocardial function, and lactate metabolism were studied in six closed-chest dogs during 2 min occlusions of the left anterior descending coronary artery followed by 10 min of reperfusion. Normal hemodynamics were maintained with infusion of arterial blood and oxygenated Fluosol, whereas unoxygenated Fluosol and Plasmalyte A resulted in hemodynamic deterioration similar to that noted with no treatment. Ischemic zone systolic fractional area change, an index of systolic function measured by two-dimensional echocardiography, remained normal during the occlusion supplemented with intracoronary arterial blood (49 ± 7%), was moderately hypokinetic with oxygenated Fluosol (31 ± 10%), and became severely hypokinetic with unoxygenated Fluosol (14 ± 14%), with Plasmalyte A (2 ± 13%), and in the absence of treatment (5 ± 9%). Only infusion of arterial blood resulted in no ST segment elevation or lactate production. Thus intracoronary infusion of arterial blood during brief coronary occlusion maintained normal myocardial function and aerobic metabolism. Infusion of oxygenated Fluosol resulted in amelioration of the decline in regional function after coronary occlusion, but not complete protection.


PERCUTANEOUS transluminal coronary angioplasty is now an accepted clinical method for the treatment of patients with severe coronary artery stenosis.1 The primary success rate is 80% to 90%, but there remains a significant restenosis rate of approximately 25% after 18 months.2 It has been suggested that prolonged balloon inflation might reduce the incidence of restenosis; however, even during the very short occlusion times of 30 to 60 sec used today, percutaneous transluminal coronary angioplasty procedures are frequently complicated by chest pain, electrocardiographic ST segment elevation, and significant regional and global dysfunction.3−4 This is analogous to the rapid contractile, metabolic, and electrophysiologic derangements caused by single or multiple brief coronary artery occlusions in the experimental animal. To avoid these short-term ischemic derangements and to permit prolongation of the occlusion, it is necessary to protect the jeopardized myocardium during the ischemic period.

The perfluorochemical emulsion Fluosol-DA 20% (Fluosol, Alpha Therapeutic Corp.) features a high oxygen carrying capacity and a low viscosity, properties that could be useful in providing an alternative nutritive perfusate.5,6 Preliminary experience with infusion of Fluosol into the distal coronary artery during percutaneous transluminal coronary angioplasty has been reported recently,7 as has distal intracoronary infusion of arterial blood.8 However, the consequent functional and metabolic changes have not been systematically investigated. The purpose of this experimental investigation was therefore to evaluate the ef-
fects of intracoronary infusion of Fluosol or arterial blood on ischemic myocardial dysfunction and associated metabolic derangements during 2 min of occlusion of the left anterior descending artery in the dog. A 2 min coronary occlusion was chosen because, unlike occlusions of 5 min or greater, recovery of systolic function after a 2 min occlusion is rapid and therefore permits testing of multiple treatments.\textsuperscript{9, 10}

\textbf{Methods}

\textbf{Experimental preparation.} Six healthy dogs of both sexes weighing 18 to 35 kg were premedicated with intramuscular morphine sulfate (2 mg/kg) and anesthetized with intravenous sodium thiopental (20 mg/kg). After endotracheal intubation, anesthesia was maintained with enflurane. Respiration was controlled with a Harvard ventilator to maintain arterial blood gas within the following ranges: pH 7.35 to 7.45, Pa\textsubscript{O\textsubscript{2}} 80 to 150 mm Hg, and Pa\textsubscript{CO\textsubscript{2}} 35 to 45 mm Hg. Heparin (300 IU/kg) was administered intravenously before instrumentation, supplemented by 1000 IU every 2 hr. Saline was infused at a rate of 100 to 150 ml/hr. A No. 4F intracoronary double-lumen catheter (American Edwards Laboratories) was inserted under fluoroscopic control into the left anterior descending coronary artery proximal to the first diagonal branch.\textsuperscript{11} A No. 7F catheter was inserted into the great cardiac vein for blood sampling. Simultaneous arterial blood samples were also withdrawn from a catheter placed in the aortic root. Ascending aortic and left ventricular pressures were measured with Mikro-Tip catheter pressure transducers (Millar Instruments, Inc.), and left ventricular dp/dt was obtained by electronic differentiation. A single precordial lead electrocardiogram was monitored continuously.

\textbf{Two-dimensional echocardiography.} Two-dimensional echocardiography was used to assess regional systolic left ventricular wall function. A midpapillary left ventricular short-axis cross-section was subdivided into eight segments in a standardized manner, using the epicardial center of gravity and an internal reference system as previously described.\textsuperscript{11} Fractional area change (FAC) was computed for each of the eight segments to assess systolic function in the ischemic and the nonischemic zones with the formula:

\[
\text{FAC\%} = \frac{\text{EDA} - \text{ESA}}{\text{EDA}}
\]

where EDA = end-diastolic area and ESA = end-systolic area.

It has been demonstrated previously that the fractional area change at the midpapillary level in an anesthetized animal before any intervention is 51 \pm 8\% for anterior segments and 58 \pm 6\% for posterior segments.\textsuperscript{12} Normal regional function was defined as a fractional area change within 2 SDs of the mean, hypokinesis as a fractional area change less than 2 SDs below the mean, akinesis as a fractional area change of zero, and dyskinesis as a negative fractional area change.

\textbf{Lactate metabolism.} Lactate was determined enzymatically (Diagnostic Kit of Lactate, Sigma Chemical Co.). Blood samples were taken from the aorta and the great cardiac vein and the lactate extraction ratio was calculated as [(aortic - great cardiac vein lactate)/aortic lactate] \times 100.

\textbf{Experimental protocol.} The left anterior descending coronary artery balloon catheter was inflated for 2 min, followed by balloon deflation and reperfusion lasting at least 10 min to allow regional left ventricular function to return to baseline. This 2 min occlusion-reperfusion cycle was repeated five times, either without treatment or with one of the following intracoronary infusions given in random order (table 1): arterial blood, oxygenated Fluosol, unoxygenated Fluosol, and an unoxygenated electrolyte solution, Plasmalyte A (Travenol Laboratories, Inc.). The composition of Fluosol and Plasmalyte A is provided in table 2. Each of the treatment solutions was administered at a rate of 50 ml/min for the 2 min occlusion period through the central lumen of the intracoronary balloon catheter by means of an angiographic injector (Mark IV) with a 130 ml reusable syringe. A warming jacket was used to maintain the solutions at body temperature. Arterial blood was obtained from the left femoral artery. Oxygenated Fluosol was obtained by gently bubbling 95% O\textsubscript{2}/5% CO\textsubscript{2} through the Fluosol for 1 hr before its administration, yielding a Pa\textsubscript{O\textsubscript{2}} of greater than 600 mm Hg. Sequential hemodynamics and two-dimensional echocardiographic measurements were recorded during the experiment. Lactate was measured before occlusion of the left anterior descending coronary artery and again 20 sec after reperfusion following each of the occlusions.

\textbf{Statistical analysis.} Unless otherwise indicated, all data are presented as mean \pm SD. When the data were seen to assume a normal distribution (as determined by the Shapiro and Wilks W statistic for normalcy), a parametric two-way repeated-measures analysis of variance was performed. If the distribution was skewed or the groups had nonequivalent variances, a nonparametric analysis of variance (Friedman’s test) was used to compare the effects of each treatment over time and to study the effects at specific time points across treatments. Whenever significant time or treatment effects were detected, a Newman-Keul multiple comparison test was used for further analysis. The alpha level for each of these tests was set at .05. All p values were derived from two-tailed tests.

\textbf{Results}

\textbf{Hemodynamics (table 3).} There were no significant differences in the preocclusion heart rate among the

\begin{table}[h]
\centering
\caption{Sequence of untreated and treated occlusions for each of the dogs}
\label{table:occlusions}
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Dog} & \textbf{Untreated} & \textbf{Blood} & \textbf{FL-O\textsubscript{2}} & \textbf{FL-UN} & \textbf{Electrolyte} \\
\hline
1 & 1 & 5 & 4 & 2 & 3 \\
2 & 5 & 1 & 3 & 4 & 2 \\
3 & 5 & 3 & 4 & 3 & 5 \\
4 & 2 & 1 & 4 & 3 & 5 \\
5 & 3 & 2 & 1 & 4 & 5 \\
6 & 3 & 4 & 5 & 1 & 2 \\
\hline
\textbf{Total} & 19 & 16 & 21 & 16 & 18 \\
\hline
\end{tabular}
\end{table}

\begin{table}[h]
\centering
\caption{Sequence of untreated and treated occlusions for each of the dogs}
\label{table:occlusions}
\begin{tabular}{|c|c|c|c|c|c|}
\hline
\textbf{Dog} & \textbf{Untreated} & \textbf{Blood} & \textbf{FL-O\textsubscript{2}} & \textbf{FL-UN} & \textbf{Electrolyte} \\
\hline
1 & 1 & 5 & 4 & 2 & 3 \\
2 & 5 & 1 & 3 & 4 & 2 \\
3 & 5 & 3 & 4 & 3 & 5 \\
4 & 2 & 1 & 4 & 3 & 5 \\
5 & 3 & 2 & 1 & 4 & 5 \\
6 & 3 & 4 & 5 & 1 & 2 \\
\hline
\textbf{Total} & 19 & 16 & 21 & 16 & 18 \\
\hline
\end{tabular}
\end{table}

\begin{table}
\centering
\caption{Composition and physical properties of Fluosol and Plasmalyte A}
\label{table:composition}
\begin{tabular}{|c|c|c|}
\hline
\textbf{Parameter} & \textbf{Fluosol} & \textbf{Plasmalyte A} \\
\hline
Na (meq/l) & 128 & 140 \\
K (meq/l) & 4.6 & 5.0 \\
Ca (mg/dl) & 10.0 & 0 \\
HCO\textsubscript{3} (meq/l) & 25.0 & 0 \\
Acetate (meq/l) & 0 & 27.0 \\
Glucose (meq/l) & 180 & 0 \\
Osmolarity (mOsm/l) & 449 & 294 \\
\textbf{pH} & 7.4 & 7.4(approx.) \\
\hline
\end{tabular}
\end{table}
TABLE 3
Hemodynamic data

<table>
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<tr>
<th></th>
<th>Preocclusion</th>
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<th>2 min occl.</th>
<th>1 min reperfusion</th>
<th>3 min reperfusion</th>
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<tr>
<td>Untreated</td>
<td>125 ± 16</td>
<td>122 ± 15</td>
<td>119 ± 17</td>
<td>122 ± 17</td>
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<td>Arterial blood</td>
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<td>119 ± 18</td>
<td>117 ± 19</td>
<td>119 ± 23</td>
<td>126 ± 20</td>
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<td>FL-O₂</td>
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<td>121 ± 15</td>
<td>119 ± 19</td>
<td>117 ± 16</td>
<td>126 ± 21</td>
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<td>114 ± 15</td>
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<td>112 ± 17</td>
<td>118 ± 13</td>
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<td>94 ± 20</td>
<td>103 ± 20</td>
<td>104 ± 23</td>
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<td>107 ± 22</td>
<td>111 ± 25</td>
<td>110 ± 26</td>
<td>109 ± 29</td>
</tr>
<tr>
<td>FL-O₂</td>
<td>104 ± 25</td>
<td>104 ± 20</td>
<td>106 ± 21</td>
<td>103 ± 20</td>
<td>104 ± 22</td>
</tr>
<tr>
<td>FL-UN</td>
<td>102 ± 14</td>
<td>102 ± 17</td>
<td>102 ± 19</td>
<td>102 ± 17</td>
<td>103 ± 18</td>
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<tr>
<td>Electrolyte</td>
<td>105 ± 17</td>
<td>82 ± 8, ³</td>
<td>75 ± 8, ³</td>
<td>83 ± 6, ³</td>
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<td>LVEDP (mm Hg)</td>
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<td>Untreated</td>
<td>4.2 ± 1.2</td>
<td>6.8 ± 1.7³</td>
<td>7.7 ± 2.0³</td>
<td>4.5 ± 1.4</td>
<td>4.5 ± 1.6</td>
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<tr>
<td>Arterial blood</td>
<td>4.8 ± 1.2</td>
<td>5.7 ± 1.8³</td>
<td>6.5 ± 1.9³</td>
<td>5.3 ± 1.9</td>
<td>5.0 ± 2.0</td>
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<tr>
<td>FL-O₂</td>
<td>4.2 ± 1.2</td>
<td>5.3 ± 1.0³</td>
<td>7.3 ± 2.1³</td>
<td>5.2 ± 1.5</td>
<td>4.7 ± 1.0</td>
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<tr>
<td>FL-UN</td>
<td>4.0 ± 1.3</td>
<td>7.5 ± 2.2³</td>
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<td>5.7 ± 2.5</td>
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<td>Electrolyte</td>
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<td>9.0 ± 1.3³, ²</td>
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<td>6.8 ± 2.1</td>
<td>4.3 ± 1.5</td>
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<td>Positive dP/dt (mm Hg/sec)</td>
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<td></td>
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<tr>
<td>Untreated</td>
<td>1664 ± 220</td>
<td>1265 ± 248³</td>
<td>1259 ± 261³</td>
<td>1648 ± 210</td>
<td>1646 ± 207</td>
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<tr>
<td>Arterial blood</td>
<td>1631 ± 166</td>
<td>1609 ± 278³</td>
<td>1535 ± 227³</td>
<td>1704 ± 297</td>
<td>1693 ± 209</td>
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<tr>
<td>FL-O₂</td>
<td>1580 ± 259</td>
<td>1553 ± 194³</td>
<td>1523 ± 250³</td>
<td>1585 ± 289</td>
<td>1611 ± 276</td>
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<tr>
<td>FL-UN</td>
<td>1690 ± 240</td>
<td>1404 ± 197³</td>
<td>1413 ± 274³</td>
<td>1628 ± 285</td>
<td>1663 ± 207</td>
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<tr>
<td>Electrolyte</td>
<td>1595 ± 189</td>
<td>1150 ± 240³</td>
<td>956 ± 211³, ²</td>
<td>1223 ± 216³</td>
<td>1500 ± 269</td>
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<td>Negative dP/dt (mm Hg/sec)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Untreated</td>
<td>1193 ± 208</td>
<td>864 ± 197³</td>
<td>909 ± 226³</td>
<td>1111 ± 178³</td>
<td>1154 ± 201</td>
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<tr>
<td>Arterial blood</td>
<td>1140 ± 214</td>
<td>1159 ± 206³</td>
<td>1207 ± 226³</td>
<td>1167 ± 199</td>
<td>1176 ± 219</td>
</tr>
<tr>
<td>FL-O₂</td>
<td>1182 ± 235</td>
<td>967 ± 209</td>
<td>1077 ± 226³</td>
<td>1176 ± 198</td>
<td>1183 ± 212</td>
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<tr>
<td>FL-UN</td>
<td>1192 ± 176</td>
<td>911 ± 235³, ²</td>
<td>991 ± 227³, ²</td>
<td>1150 ± 180</td>
<td>1175 ± 185</td>
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<tr>
<td>Electrolyte</td>
<td>1154 ± 181</td>
<td>758 ± 121³, ²</td>
<td>589 ± 121³, ²</td>
<td>773 ± 175³, ²</td>
<td>996 ± 177³, ²</td>
</tr>
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</table>

Values are mean ± SD.
LVEDP = left ventricular end-diastolic pressure; other abbreviations as in table 1.
³p < .05 vs preocclusion; ²p < .05 vs untreated.

five experimental groups, and the heart rate remained unchanged throughout the 2 min occlusion and 3 min reperfusion period.

Systolic aortic pressure decreased during untreated coronary occlusion from 106 ± 23 to 94 ± 20 mm Hg (p < .05), but treatment with arterial blood and oxygenated or unoxygenated Fluosol maintained aortic pressure at preocclusion levels during the 2 min occlusion. Use of the electrolyte solution resulted in a decrease in systolic pressure from 105 ± 17 to 75 ± 8 (p < .05) at 2 min occlusion.

Left ventricular end-diastolic pressure increased from 4.2 ± 1.2 to 7.7 ± 2.0 mm Hg without treatment and then returned to preocclusion levels within 1 min of reperfusion. Left ventricular end-diastolic pressure also increased with infusions of arterial blood and oxygenated Fluosol, reaching 6.5 ± 1.9 and 7.3 ± 2.1 mm Hg, respectively at the end of the 2 min occlusion. The electrolyte solution and unoxygenated Fluosol resulted in the highest left ventricular end-diastolic pressures, 9.0 ± 3.0 and 10.3 ± 1.5 mm Hg, respectively (p < .05 compared with no treatment).

Positive and negative dP/dt were significantly decreased after 2 min of untreated occlusion compared with preocclusion values and then returned to preocclusion levels within 1 min of reperfusion. In contrast, arterial blood and oxygenated Fluosol maintained dP/dt at preocclusion levels during the occlusion. The dP/dt decreased slightly with unoxygenated Fluosol. The electrolyte solution, on the other hand, resulted in a marked decrease in both positive and negative dP/dt (40% and 49%, respectively) at 2 min of occlusion, and both positive and negative dP/dt remained abnormal during the early reperfusion period (p < .05 compared with no treatment).

Two-dimensional echocardiographic data. There were
no significant differences in ischemic zone systolic fractional area change among the five experimental groups before occlusion. Figure 1 illustrates in one dog the computer-assisted two-dimensional echocardiographic results in the preocclusion state and subsequently after 2 min of coronary occlusion, with and without infusion of Fluosol and arterial blood. Without treatment, ischemic zone fractional area change decreased significantly from 46% to 8% after 2 min of occlusion. With intracoronary infusion of arterial blood, normal contraction was maintained throughout the coronary artery occlusion (46% vs 52%). Infusion of oxygenated Fluosol was associated with a decrease in fractional area change after 2 min of occlusion (45% vs 27%), but regional ischemic zone contraction was significantly improved compared with no treatment (27% vs 8%). Similar results were noted in all dogs (table 4, figure 2). Ischemic zone regional function was similar before occlusion for all treatment groups. Without treatment, ischemic zone systolic fractional area change decreased from 52 ± 8% to 5 ± 9% (p < .05) after 2 min of occlusion, with return to preocclusion values (51 ± 8%) after 1 min of reperfusion.

Infusion of arterial blood prevented the impairment in systolic fractional area change at 2 min of occlusion (50 ± 7% vs 49 ± 7%). Treatment with oxygenated Fluosol resulted in a decrease in ischemic fractional area change after 2 min of coronary occlusion in four of the six dogs and a decrease in the group values from 53 ± 7% to 31 ± 10% (p < .05). Nevertheless, the 2 min occlusion value with oxygenated Fluosol was significantly improved compared with no treatment (31 ± 10% vs 5 ± 9%; p < .05).

Treatment with unoxygenated Fluosol did not prevent the reduction in ischemic zone function with coronary occlusion as the fractional area change decreased from 52 ± 9% to 14 ± 14% (p < .05). The ischemic zone fractional area change remained within the normal range in only one of the unoxygenated Fluosol-treated occlusions (dog 5).

Treatment with Plasmalyte A resulted in ischemic zone hypokinesis (three of six) or dyskinesis (three of six) and a decrease in fractional area change from 52 ± 11% to 2 ± 13%.

Ischemic zone fractional area change, however, did return to the preocclusion levels after 3 min of reperfusion after each occlusion both without treatment and with each of the treatments (figure 2).

No significant differences were noted in nonischemic zone fractional area change, either among the five treatment groups or during the experimental occlusion.

Electrocardiographic data (figure 3). Untreated coronary occlusion resulted in significant ST segment elevation of 1.8 ± 1.1 mV (p < .05) at 2 min of untreated occlusion. Of all the interventions studied, only infusion of arterial blood resulted in no ST segment changes. Oxygenated Fluosol caused an even higher ST segment elevation (2.7 ± 1.8 mV) compared with no treatment, although the difference was not statistically significant. Infusion of unoxygenated Fluosol and electrolyte solution resulted in ST segment elevations of 4.3 ± 1.9 and 5.8 ± 1.2 mV, respectively, significantly higher (p < .05) than the ST segment elevations encountered with untreated occlusion.

Lactate extraction (figure 4). Before occlusion, mean lactate extraction was between 28% and 33% and there were no significant differences between the groups. For each of the five treatment groups, lactate extraction decreased significantly after occlusion. Untreated coronary occlusions as well as occlusions supplemented with oxygenated and unoxygenated Fluosol were associated with negative lactate extraction after occlusion (-28 ± 19%, -8 ± 11%, and -16 ± 22%,...
respectively). On the other hand, treatment with arterial blood and Plasmalyte A was associated with normal lactate extraction in the earliest reperfusion phase (20 ± 12% and 16 ± 5%, respectively).

Discussion

To examine the potential of supplemental treatment during extended or complex percutaneous transluminal coronary angioplasty procedures, we studied in closed-chest dogs the effects of various intracoronary infusions during 2 min occlusions of the left anterior descending coronary artery.

The principal observations were as follows: (1) Infusion of arterial blood distal to the coronary artery occlusion maintained normal myocardial function (measured by two-dimensional echocardiography) and metabolism (lactate extraction), along with unchanged preischemic ST segment levels. (2) Infusion of oxygenated Fluosol resulted in no deterioration of global myocardial function, but regional function in the ischemic zone was impaired during the coronary artery occlusion, although improved compared with untreated occlusion. ST segment elevations during intracoronary infusion of Fluosol were similar to those encountered during untreated coronary occlusions, and there was myocardial lactate production. (3) During infusion of unoxygenated Fluosol there was significant impairment in cardiac function compared with that during infusion of oxygenated Fluosol. (4) Infusion of an electrolyte solution resulted in a worsening of the effects of acute ischemia when compared with no treatment controls.

**Arterial blood.** Infusion of arterial blood into occluded coronary arteries as a means of reducing ischemia has been studied, but practical application for extended periods appeared problematic because of potential catheter-induced blood hemolysis and thrombo-

<table>
<thead>
<tr>
<th>%FAC-IZ</th>
<th>Preocclusion</th>
<th>1 min occl.</th>
<th>2 min occl.</th>
<th>30 sec reperfusion</th>
<th>3 min reperfusion</th>
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<tbody>
<tr>
<td>Untreated</td>
<td>52 ± 8</td>
<td>16 ± 7</td>
<td>5 ± 9</td>
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<tr>
<td>Arterial blood</td>
<td>50 ± 7</td>
<td>48 ± 10</td>
<td>49 ± 7</td>
<td>52 ± 7</td>
<td>51 ± 5</td>
</tr>
<tr>
<td>FL-O₂</td>
<td>53 ± 7</td>
<td>37 ± 8</td>
<td>31 ± 10</td>
<td>47 ± 9</td>
<td>49 ± 8</td>
</tr>
<tr>
<td>FL-UN</td>
<td>52 ± 9</td>
<td>22 ± 11</td>
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<tr>
<td>Electrolyte</td>
<td>52 ± 11</td>
<td>7 ± 8</td>
<td>2 ± 13</td>
<td>39 ± 12</td>
<td>50 ± 9</td>
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</table>

**%FAC-NIZ**

<table>
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<th>%FAC-NIZ</th>
<th>Preocclusion</th>
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<th>2 min occl.</th>
<th>30 sec reperfusion</th>
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<tr>
<td>Untreated</td>
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<td>62 ± 5</td>
<td>62 ± 9</td>
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<td>FL-O₂</td>
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<td>57 ± 12</td>
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<td>60 ± 8</td>
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</table>

Values are mean ± SD.

%FAC = systolic fractional area change; IZ = ischemic zone; NIZ = nonischemic zone; other abbreviations as in table 1.

* p < .05 vs preocclusion; †p < .05 vs untreated.

FIGURE 2. Effects of coronary occlusion and reperfusion on ischemic zone fractional area change (%FAC) without treatment (A) and with treatment with arterial blood (B), oxygenated Fluosol (C), unoxygenated Fluosol (D), and electrolyte solution (E). Each dog is represented by a different symbol: dog 1; dog 2; dog 3; dog 4; dog 5; dog 6. The dashed horizontal line represents the lower limit of normal regional systolic function in anesthetized dogs. Before occlusion and 3 min after reperfusion all values are within the normal range. At the end of 2 min occlusion %FAC was abnormal in all six untreated occlusions (A), normal in all occlusions treated with arterial blood (B), normal in two of six and hypokinetic in four of six occlusions treated with oxygenated Fluosol (C), normal in one of six, hypokinetic in four of six, and dyskinetic in one of six occlusions treated with unoxygenated Fluosol (D); and hypokinetic in three of six and dyskinetic in three of six occlusions treated with electrolyte solution (E).
Thrombosis. Timmis et al. demonstrated in 10 patients that distal intracoronary infusion of arterial blood (average rate 46 ml/min) through an angioplasty catheter during 1 min coronary occlusions reduced the manifestations of ischemia. Our study demonstrated that arterial blood infused over 2 min into the occluded coronary artery at a rate of 50 ml/min afforded complete protection to the myocardium, maintaining normal contractile function and metabolism during the ischemic period. The selected infusion rate corresponds to the upper limit of normal left anterior descending arterial flow previously measured by us in open-chest, enflurane-anesthetized dogs and is consistent with canine coronary flows previously reported by others.

We did not monitor perfusion pressure or assess hemolysis and recognize that the latter may be a factor, particularly when high perfusion pressures are used. However, since the total volume of the infused blood was small (100 ml), we did not think that hemolysis would be a significant problem in our protocol. Thrombosis was not encountered because the infused blood was well heparinized in our experiments.

We also found that infusion of arterial blood maintained lactate extraction (28 ± 10% and 20 ± 12% before and after occlusion, respectively). The absence of lactate production and ST segment elevation indicated that arterial blood could maintain aerobic metabolism during the coronary artery occlusion.

Fluosol. Fluosol, an emulsion of perfluorodecaline and perfluorotripropylamine, has been recommended as an oxygen-carrying artificial substitute for patients requiring blood transfusion. It dissolves approximately 6 vol% oxygen when the Po2 is 600 mm Hg, approximately one-third of the normal arterial blood oxygen content. Another characteristic of Fluosol is its low viscosity compared with that of blood, making it possible to infuse Fluosol at a high flow rate. Forman et al. demonstrated that Fluosol tended to promote and improve flow delivery to endocardium.

Anderson et al. demonstrated during percutaneous transluminal coronary angioplasty that, when compared with oxygenated lactated Ringer’s solution, perfusion of the distal coronary artery with Fluosol (60 ml/min) reduced but did not fully prevent ischemia during coronary occlusion. Myocardial function was not studied. Cleman et al. demonstrated that infusion of oxygenated Fluosol prevented the regional myocardial dysfunction encountered during a 1 min occlusion by percutaneous transluminal coronary angioplasty without treatment, but they did not report the effects of the infusion on hemodynamics, ST segment changes, or myocardial metabolism. Our data indicate that intracoronary oxygenated Fluosol significantly reduces the severity of myocardial dysfunction produced by coronary artery occlusion. Thus ischemic region fractional area change (an index of wall contraction) decreased by about 40% from the preocclusion value during the oxygenated Fluosol infusion, compared with a 90% decrease in regional function during coronary artery occlusion in the absence of any treatment. It has pre-

FIGURE 3. Electrocardiographic effects of intracoronary treatment. Only intracoronary infusion of arterial blood prevented ST segment elevation during the coronary occlusion. There was significant ST segment elevation at 2 min after occlusion with oxygenated and unoxygenated Fluosol and with electrolyte solution. Both unoxygenated Fluosol and the electrolyte solution resulted in significantly higher ST segment elevations compared with no treatment.

FIGURE 4. Regional myocardial lactate extraction measured before and 20 sec after untreated and treated 2 min coronary artery occlusions. Myocardial lactate extraction was equivalent before each of the coronary occlusions. Untreated occlusion led to significant lactate production. Lactate production was also noted after treatment with both oxygenated and unoxygenated Fluosol. Arterial blood treatment was the only intervention that resulted in normal lactate extraction in spite of the coronary occlusion. Infusion of electrolyte solution led to apparent positive lactate extraction early after perfusion; however, this may be attributed to acetate in the electrolyte solution, which reduces the rate of lactate metabolism (see Discussion). *p < .05 compared with preocclusion.
viously been suggested that an inflated intracoronary balloon might, on occasion, occlude a side branch of the coronary artery, leading to maldistribution of Fluosol and associated impairment of cardiac function in a portion of the myocardium distal to the balloon. We believe this was unlikely in our study because intracoronary arterial blood infusion did not result in impairment of myocardial function in the region beyond the occlusion.

We believe that the incompleteness of the reversal in ischemic dysfunction is related to inadequate oxygen delivery of the Fluosol. Thus, whereas a normal arterial-coronary sinus oxygen content difference is about 10 vol%, oxygenated Fluosol (Po₂ > 600 mm Hg) delivers only 6 vol%. To overcome this limitation would require increasing the rate of Fluosol delivery to approximately 85 ml/min, which is beyond the limits of the catheter and infusion pump used in this study.

Unoxygenated Fluosol did not ameliorate the effects of coronary occlusion on regional left ventricular function, suggesting that it is the oxygen-carrying capacity of Fluosol and not the other constituents that is responsible for its beneficial myocardial effects.

Pronounced ST segment elevations occurred with unoxygenated Fluosol and electrolyte solution compared with the untreated control occlusions. We were surprised to note that whereas the elevation was highest in the electrolyte-treated and least in the untreated occlusions, oxygenated Fluosol produced an intermediate level of ST elevation greater than that noted without treatment. Anderson et al. reported that Fluosol reduced the resultant ST segment elevation when compared with oxygenated lactated Ringer's solution, but they did not compare Fluosol with untreated controls. When we infused oxygenated Fluosol at 50 ml/min through the central lumen of the balloon catheter in the absence of coronary artery occlusion, we noted ST segment elevation of a degree similar to that noted with coronary artery occlusion. It thus appears likely that the ST segment elevation was due to the composition of Fluosol itself as well as to ischemia produced by the intracoronary balloon occlusion.

We also measured regional myocardial lactate extraction to assess metabolic changes during untreated ischemia and during treatment with the different intracoronary infusions. A transmyocardial lactate extraction ratio below 10% is usually interpreted to indicate ischemia; however, a large number of factors, including ketones, free fatty acid levels, and the arterial lactate concentrations, can also affect the myocardial extraction. In our study of intracoronary infusion of oxygenated Fluosol distal to the balloon inflation, preocclusion lactate extraction changed to production after the 2 min occlusion. This would indicate that the myocardial ischemia was not sufficiently reversed by the intracoronary Fluosol treatment. Our results contradict those of Rude et al., who assessed ischemic intramyocardial oxygen tension using mass spectrometry and reported that intravenous fluorochemical emulsion elevated intramyocardial oxygen tension in the central ischemic zone during ventilation with 100% oxygen. However, Engelman et al. during 1 hr of Fluosol perfusion in the isolated pig heart, noted an increase in contractility compared with hemic perfusion but negative lactate extraction. The presence of lactate production in the isolated heart preparation is consistent with our observations. Thus the results of our Fluosol experiment, indicating partial improvement of regional myocardial function in the presence of aerobic metabolism, may have been due to both inadequate oxygen content of Fluosol and an inadequate infusion flow rate.

**Infusion of electrolyte solution.** We chose Plasmalyte A as the electrolyte solution because it has a pH of approximately 7.4, whereas the pH of other electrolyte solutions such as lactated Ringer's solution or saline is between 5.0 and 6.0. An electrolyte solution was chosen to determine the effects of washout, in the absence of substrate delivery, on myocardial ischemia. However, contrary to our expectations, infusion of electrolyte into the ischemic zone resulted in even worse myocardial function than was the case with no treatment. The lack of protection is not surprising since Plasmalyte-A does not supply oxygen or glucose, which are essential for aerobic and anaerobic myocardial metabolism, respectively, and lacks calcium, which may also be a factor in the noted impairment in left ventricular function. However, the increase in ischemic zone systolic dysfunction documented by two-dimensional echocardiography compared with untreated coronary occlusion may be secondary to a negative inotropic action of sodium acetate in Plasmalyte A. Sodium acetate has been reported to cause a direct dose-related decrease in myocardial contraction, which might be due to a decrease in intracellular pH caused by either the acetate ion itself or by elevation of carbon dioxide as a result of its metabolism. Despite the echocardiographic and electrocardiographic evidence of ischemia, lactate production did not occur because acetate reduces the rate of lactate metabolism. Bricknell and Opie demonstrated that in glucose-perfused hearts the source of the glycolytic flux is mostly from glucose uptake and the rest from glycogenolysis during ischemia, whereas in acetate-perfused hearts.
the source is only glycogenolysis. Therefore glycolytic ATP is extremely low and lactate output is markedly depressed. Therefore one cannot use lactate extraction as an index of myocardial ischemia during the infusion of acetate. It is nevertheless interesting to note that infusion of Plasmalyte A appeared worse than no infusion at all, despite the fact that a washout of ischemia-mediated metabolites may have occurred.

The effects of oxygenated Plasmalyte A were not studied; however, oxygenated saline has been previously shown to be inferior to oxygenated Fluosol in a model of prolonged coronary occlusion and therefore it is extremely unlikely that oxygenated Plasmalyte A would provide significant myocardial protection during brief occlusions.

Limitations of the experiment. A limitation of this study was that the infusion rate was maintained at 50 ml/min regardless of the animal’s size. Another approach would have been to vary the infusion rate in an attempt to equal the preocclusion resting coronary flow to the ischemic bed. This, however, would have required direct measurement of coronary artery flow since there may be a twofold difference in total coronary flow per myocardial weight in normal dogs and humans. Moreover, the percentage of total coronary flow to the left anterior descending artery is variable, as is the size of the ischemic bed after coronary occlusion, particularly in the dog, which often has extensive collaterals. Therefore, since the purpose of this study was to attempt to mimic the clinical technique of coronary angioplasty in which coronary blood flow is not routinely measured, a fixed infusion rate equal to or greater than that necessary for preservation of aerobic metabolism in anesthetized dogs (of similar weight to the dogs used in this study) was employed. The flow rate used in this study when compared with body weight was actually two to four times that used by Timmis et al. during clinical angioplasty.

Another limitation of our method was that we could not appropriately quantify lactate metabolism during coronary artery occlusion. The great cardiac vein has been shown to predominantly drain the left anterior descending coronary artery and therefore lactate measurements obtained from the great cardiac vein provide information concerning metabolism in the territory of the left anterior descending coronary artery. However, with the exception of the untreated occlusion, all the other occlusions were treated by intracoronary infusions of fluids at a rate of 50 ml/min. Consequently, when lactate in the great cardiac vein was measured 20 sec after reperfusion, it was not only a reflection of the lactate produced during the occlusion but also depended on the amount that was washed out by each of the treatment agents. Moreover, the lactate level in the great cardiac vein at the beginning of reperfusion would be dependent on reactive hyperemia, which itself could vary with each treatment. Nevertheless, our limited data on lactate extraction suggested aerobic metabolism during infusion of arterial blood and anaerobic metabolism during infusion of Fluosol into the ischemic zone.

A third limitation of our method was that we did not evaluate the extent of ischemic injury by precordial electrocardiography. The mechanisms responsible for ST segment elevations are not fully understood since multiple factors, including potassium concentration, affect ST segment changes. ST segment elevation during infusion of Fluosol does not directly indicate ischemic change. More detailed studies with epicardial ST segment mapping are needed to provide sufficiently representative measurements of local ST alterations associated with acute and highly regional ischemic injury.

Implications of study. This study demonstrates that brief untreated coronary occlusion results in a significant impairment in systolic left ventricular function that can be prevented by infusion of arterial blood through the central lumen of the occluding catheter. Oxygenated Fluosol provides partial amelioration of the effects of coronary occlusion on myocardial function. This is of potential clinical importance, not because the impairment produced by a 2 min occlusion is permanent (in this study the dysfunction was reversed after 3 min of reperfusion in all cases), but rather because it potentially increases the safety of therapeutic procedures such as coronary angioplasty in which temporary coronary occlusion is used. This may be particularly important as more patients with multivessel disease and impairment in left ventricular function are being treated with coronary angioplasty. It may also permit increased durations of balloon inflation, which may improve the efficacy of the angioplasty technique.

Infusion of arterial blood can be performed easily compared with infusion of Fluosol and it is currently possible to infuse blood at a rate of 60 ml/min through the angioplasty catheter. Oxygenated Fluosol, which provides partial myocardial protection, may be of value during angioscopy or laser angioplasty of coronary arteries, procedures that require a bloodless field for lesion visualization but that nevertheless produce transient myocardial ischemia. Although currently available Fluosol is not transparent, further development might provide a clear perfluorocarbon emulsion that
can adequately protect the myocardium against ischemia.

In view of the fact that infusion of Plasmalyte A resulted in increased myocardial impairment when compared with no treatment, it would be inappropriate to use Plasmalyte A as a control for experiments studying the effects of agents such as Fluosol and arterial blood, since such a comparison may exaggerate the efficacy of these agents.

We emphasize that our results should be considered preliminary and that more studies are needed before the distal coronary perfusion technique can be accepted routinely for protection during short coronary occlusions.

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