Heparin in Experimental Myocardial Infarction

By Norman B. Roberg, M.D., and William H. Requarth, M.D.

Heparinization, started one hour following coronary ligation, was maintained for twenty-four hours. One week after recovery the hearts were perfused in vivo with india ink. After clearing, the proportion of ventricular mass infarcted was determined. No appreciable difference from the control series was found.

Solandt and Best found that coronary artery thrombosis, and consequent myocardial infarction, did not occur in 11 of 12 dogs when a sclerosing solution was introduced into a segment of coronary artery after beginning a twenty-four-hour period of heparinization. The influence of heparinization upon the extent of myocardial infarction following coronary artery occlusion was not determined. During the course of this study it was noted that the excellent reports by Beattie and associates, Blumgart and co-workers, and Le Roy and Nalefski indicated that dicumarol therapy, started postoperatively, had no appreciable effect upon the nature or extent of myocardial infarction following coronary artery ligation. Blumgart used heparin early postoperatively, in addition to dicumarol, in 3 dogs and noted no difference in the reaction of these dogs from that of dogs receiving dicumarol alone. There has been no published study of the effect of heparinization, maintained during the immediate postocclusion period, upon the extent of myocardial infarction; this constitutes the present study.

PROCEDURE

To approximate clinical conditions and to allow early thrombosis in the surgical wound, constant intravenous injection of heparin was started one hour after ligation of the anterior descending branch of the left coronary artery. Dogs weighing 5 to 10 Kg. were operated on, using morphone and Nembutal anesthesia and intratracheal air or 100 per cent oxygen. The artery was dissected free near its origin and ligated. The pericardium was not sutured before closure of the wound. Short lengths of Vinylite tubing were tied into the cephalic and caudal ends of a divided external jugular vein to facilitate both the removal of blood to determine clotting time and the infusion of heparin. The dosage of heparin recommended by Solandt and Best was followed: an initial dose of 0.45 mg. per Kg. of body weight and a maintenance dose of 0.35 mg. per Kg. per hour. The heparin was diluted to 0.02 per cent in physiologic saline solution. Clotting time was determined by allowing 1.0 cc. of blood to drop from the Vinylite cannula into a clean, saline-rinsed glass tube of 25- by 10-mm. capacity. Definite loss of fluidity, rather than clot formation, was taken as the end point. The clotting time was maintained usually at thirty to sixty minutes, the control readings varying from five to ten minutes. The clotting times were often erratic, frequently rising unexpectedly to from one hundred twenty to one hundred eighty minutes about eight hours after the infusion was started. Fatal intrathoracic hemorrhage usually occurred when such prolongation of clotting time was present, and also occurred when the prescribed dosage was exceeded because the clotting time apparently was below thirty minutes. The dogs were kept lightly narcotized with intravenous Nembutal, and the infusion of heparin was maintained for twenty-four hours. After one week without medication, the dogs were sacrificed under morphone-Nembutal anesthesia. The sternum was split, the superior and inferior veins cavae were clamped, and, as the heart began to collapse, the aorta was clamped. Following the
procedure of Wearn, 25 to 50 cc. of 50 per cent india ink in distilled water were injected into
the left ventricular cavity, followed by 5 mg. of histamine base. The heart was stopped with
fair promptness by the intraventricular injection of 10 cc. of 10 per cent formalin. Wearn’s
technic of perfusing the excised heart gave better filling in normal hearts, but this pro-
cedure was abandoned because of the difficulty in maintaining vigorous beating in hearts
which had undergone coronary ligation and myocardial infarction. With the perfusion by
india ink, the myocardium turned black except for the area of infarction, which was whitish-
gray. Inasmuch as the integrity of the capillary circulation is the final determinant of circula-
tory adequacy, the obliteration of the capillary bed as demonstrated by perfusion with india
ink was considered indicative of the extent of myocardial infarction. The hearts were fixed in
10 per cent formalin after the auricles and great vessels had been dissected away. The hearts
were then cleared by the method of Spalteholz. 6 After clearing, the area of infarction was highly
translucent, the remainder of the myocardium being opaque. A bright light was held within
the left ventricular cavity and the irregularly infarcted area was cut out. The weight of the
ventricles and of the infarcts was determined, and the percentage weight of ventricular muscle
which had been infarcted was computed.

Results

One hundred and two dogs were operated upon. Thirty-two (31.5 per cent) died during
or within minutes of coronary ligation. Twelve (11.8 per cent) died in the first two hours. Ten
(9.8 per cent) died with massive intrathoracic hemorrhage during the twenty-four-hour period
of heparinization. Five (4.9 per cent) died during heparinization without gross evidence of
hemorrhage. Only 4 dogs (2 with heparin, 2 controls) died between the second and seventh
days. Of the 39 surviving dogs, in 13 the hearts were discarded because of uncertainty as to the
ligation of the entire descending branch of the left coronary artery, because of injury to, or
ligation of, the accompanying veins, or be-

cause of poor perfusion. Fourteen hearts
remained as satisfactory controls, and 12 as satisfactory trials with heparinization. The weight
of the infarcted areas, expressed as percentage of the total weight of both ventricles before re-
moval of the infarcted area, was as follows:

<table>
<thead>
<tr>
<th>Controls (per cent)</th>
<th>Heparin series (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.8</td>
<td>5.2</td>
</tr>
<tr>
<td>11.5</td>
<td>9.1</td>
</tr>
<tr>
<td>13.0</td>
<td>9.8</td>
</tr>
<tr>
<td>13.2</td>
<td>10.1</td>
</tr>
<tr>
<td>13.4</td>
<td>12.7</td>
</tr>
<tr>
<td>15.4</td>
<td>13.8</td>
</tr>
<tr>
<td>15.8</td>
<td>15.4</td>
</tr>
<tr>
<td>18.0</td>
<td>16.6</td>
</tr>
<tr>
<td>18.0</td>
<td>18.6</td>
</tr>
<tr>
<td>19.7</td>
<td>20.8</td>
</tr>
<tr>
<td>21.5</td>
<td>22.2</td>
</tr>
<tr>
<td>26.7</td>
<td>23.5</td>
</tr>
<tr>
<td>28.4</td>
<td>Average 14.8</td>
</tr>
<tr>
<td>28.6</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>16.7</td>
</tr>
</tbody>
</table>

The small difference between the two series of
experiments is not considered to be significant.

Conclusion

Heparinization of dogs, starting one hour
after ligation of the anterior descending branch
of the left coronary artery, and maintained for
twenty-four hours, had no appreciable effect
upon the extent of the myocardial infarction.

References

1 Solandt, D. Y., and Best, C. H.: Heparin and
Coronary Thrombosis in experimental animals.
2 Beattie, E. J., Cutler, E. C., Fauteux, M.,
dicumarol in experimental coronary occlusion.
3 Blumgart, H. L., Freedberg, A. S., Zoll, P. M.,
Lewis, H. D., and Wessler, S.: The effect of
dicumarol on the heart in experimental acute
4 LeRoy, G. V., and Nalefski, L. A.: Dicumarol in
experimental myocardial infarction. J. Lab. &
5 Wearn, Joseph T.: The extent of the capillary
6 Spalteholz, W.: Die Arterien der Herzwand.
Leipzig, Hirzel, 1924.
Heparin in Experimental Myocardial Infarction
NORMAN B. ROBERG and WILLIAM H. REQUARTH

Circulation. 1950;1:1193-1194
doi: 10.1161/01.CIR.1.5.1193

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/1/5/1193

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/