Thrombo-embolism in Acute and in Healed Myocardial Infarction

II. Systemic and Pulmonary Arterial Occlusion

By R. Drew Miller, M.D., Robert A. Jordan, M.D., Robert L. Parker, M.D., and Jesse E. Edwards, M.D.

The purpose of this investigation was to study the incidence and location of systemic arterial occlusion and pulmonary embolism in a consecutive series of cases of fatal acute myocardial infarction. Another consecutive series of cases in which healed myocardial infarction was demonstrated at necropsy was similarly studied. In none of the cases included in this study had anticoagulant therapy been employed.

Massive pulmonary embolism was the most frequent fatal thrombo-embolic complication found among the cases of acute myocardial infarction. Cerebral infarction was the most frequent fatal thrombo-embolic complication found among the cases of healed myocardial infarction. Cerebral infarction was the most frequent fatal systemic arterial thrombo-embolic lesion in both groups. Acute splenic and renal infarcts were frequently demonstrated but with one exception appeared to play an incidental role in the clinical course of the patients. Although systemic arterial occlusion was frequently found in association with intracardiac mural thrombi, there were many other cases in which evidence of systemic arterial occlusion was found in the absence of intracardiac mural thrombi. A positive correlation existed between the presence of pulmonary and systemic arterial occlusion and the occurrence of congestive cardiac failure.

The present study was undertaken to determine the incidence of pulmonary embolism and of systemic arterial insufficiency in myocardial infarction as observed at necropsy in cases in which anticoagulants had not been used. Furthermore, since some clinicians feel that anticoagulants should not or cannot, because of limited facilities, be used routinely in all cases of acute myocardial infarction, a definite effort was made to observe the conditions under which thrombo-embolic complications are more likely to occur. It was also desired to ascertain the relationship of systemic arterial insufficiency to the presence or absence of thrombi in the left side of the heart. The cases employed, totaling 327, are identical with those reported by us\(^2\) regarding the incidence and location of intracardiac thrombi in myocardial infarction.

**Material and Methods**

The material consisted of 327 cases of acute or of healed myocardial infarction in which necropsy was performed. Two hundred and ten of these cases were classified as acute myocardial infarction. In each of these cases there was an acute myocardial
infarct and in 110 of these there were healed myocardial infarcts as well. In 117 cases, only healed myocardial infarcts existed.

In each case with an acute myocardial infarct death was considered to be related to the existence of the infarct. The cases with healed myocardial infarction alone were obtained from a consecutive series of routine necropsy examinations. While some of these patients died of causes related to coronary arterial disease many died of unrelated causes. None of the patients had received anticoagulants.

In each case included in this study the heart was available for re-examination as to the age and location of the infarct and the occurrence of intramural thrombosis. Clinical and necropsy records, histologic sections and in some instances gross specimens of additional organs were also available for the study of the incidence and nature of extracardiac thrombo-embolic complications. The age of the infarct in each case was based on the clinical history and on the histologic criteria of Mallory and associates. Those cases in which the infarct appeared to be less than six weeks old were classified as acute myocardial infarction. The remainder of the cases were classified as healed myocardial infarction. In almost all the cases in the latter group the infarcts appeared to be several months to years old. The diagnosis of arterial occlusion was based entirely on pathologic observations. This diagnosis was made on the demonstration of a thrombus or embolus in an artery or typical changes of recent infarction of a particular organ. In many cases it was impossible to determine whether a mass of thrombotic material occluding an artery was a thrombus formed in situ or an embolus. In still other circumstances no thrombotic material could be found in arteries leading to a zone of obvious recent infarction. Whenever either thrombotic material was found in an artery or an area of recent infarction was demonstrated in an organ even without demonstration of an occluded artery, the case was classified as one of acute arterial occlusion. In each case ventricular mural thrombosis and congestive failure were noted in order to determine their significance in the occurrence of these "thrombo-embolic" complications.

**INCIDENCE OF SYSTEMIC AND PULMONARY ARTERIAL OCCLUSION IN MYOCARDIAL INFARCTION (TABLE 1)**

Of the 327 cases studied in this series 58 patients (18 per cent) at necropsy were found to have one or more pulmonary arterial occlusions with or without pulmonary infarction.

There were 210 cases in which the myocardial infarction was classified as acute. Of these, there were 33 (16 per cent) who were found to have pulmonary embolism. A slightly higher incidence of pulmonary arterial occlusion was found among cases of healed infarction. Of the 117 cases of healed myocardial infarction 25 patients (21 per cent) were found to have pulmonary embolism of varying degrees of severity.

Evidence of systemic arterial occlusion in one or more locations was found in 84 patients (26 per cent) of the total (327) cases studied.

The incidence of systemic arterial occlusion in acute myocardial infarction was 25 per cent.

**TABLE 1.—Incidence of Pulmonary and Systemic Arterial Occlusion among 327 Cases of Acute or Healed Myocardial Infarction**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Pulmonary Arterial Occlusion</th>
<th>Systemic Arterial Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Acute</td>
<td>210</td>
<td>33</td>
</tr>
<tr>
<td>Healed</td>
<td>117</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>327</td>
<td>58</td>
</tr>
</tbody>
</table>

**TABLE 2.—Relation of Systemic and Pulmonary Arterial Occlusion to the Presence of Left-sided Intracardiac Mural Thrombi in 327 Patients with Acute or Healed Myocardial Infarction**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Cases with Systemic Arterial Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>With mural thrombi</td>
<td>114</td>
</tr>
<tr>
<td>No mural thrombi</td>
<td>213</td>
</tr>
<tr>
<td>Total</td>
<td>327</td>
</tr>
</tbody>
</table>

(52 cases among a total of 210 patients). Among the patients with healed infarction, there was an incidence of systemic arterial occlusion of 27 per cent (32 cases among a total of 117 patients).

**INCIDENCE OF SYSTEMIC ARTERIAL OCCLUSION IN PATIENTS WITH AND WITHOUT INTRACARDIAC MURAL THROMBI (TABLE 2)**

Of the 327 cases, there were 114 having intracardiac mural thrombi. Of the 114 cases, 39 were found to have evidence of systemic arterial occlusion, an incidence of 34 per cent. Of the 213 cases in which the heart contained
no mural thrombi, there was an incidence of systemic arterial occlusion of 21 per cent (45 among 213 cases).

**Incidence of Systemic and Pulmonary Arterial Occlusion in Acute Myocardial Infarction**

Eighty-three of the 210 hearts from patients with acute myocardial infarction contained left-sided cardiac mural thrombi, 80 of which were twice as frequent in the patients with systemic arterial occlusion (57 per cent) as compared with the patients without systemic arterial occlusion (30 per cent) (table 4). This greater incidence of congestive failure in patients with systemic arterial occlusion as compared with those without systemic arterial occlusion was similar both in the group with and the group without left-sided cardiac mural thrombi. Sev-

---

**Table 3.—Incidence of Systemic Arterial Occlusion in Patients with Fatal Acute Myocardial Infarction: Relation of Mural Thrombosis to Systemic Arterial Occlusion**

<table>
<thead>
<tr>
<th></th>
<th>With Systemic Arterial Occlusion</th>
<th>Without Systemic Arterial Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left-sided cardiac mural thrombi present</td>
<td>83</td>
<td>29 35</td>
</tr>
<tr>
<td>Left-sided cardiac mural thrombi absent</td>
<td>127</td>
<td>20 16</td>
</tr>
<tr>
<td>Total</td>
<td>210</td>
<td>49 23</td>
</tr>
</tbody>
</table>

**Table 4.—Relation of Congestive Failure to Incidence of Systemic Arterial Occlusion in 210 Cases of Fatal Acute Myocardial Infarction**

<table>
<thead>
<tr>
<th></th>
<th>With Congestive Failure</th>
<th>Without Congestive Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic arterial occlusion present</td>
<td>49</td>
<td>28 57</td>
</tr>
<tr>
<td>Systemic arterial occlusion absent</td>
<td>161</td>
<td>48 30</td>
</tr>
<tr>
<td>Total</td>
<td>210</td>
<td>76 36</td>
</tr>
</tbody>
</table>

---

left ventricular alone or associated with a thrombus in the left atrium, and three in which only left auricular mural thrombi were found. In 29 (35 per cent) of the 83 cases of left-sided cardiac mural thrombi a pathologic diagnosis of systemic arterial occlusion was made. However, of the remaining 127 patients with acute myocardial infarction but without left-sided mural thrombi 20 (16 per cent) fulfilled the criteria for a diagnosis of systemic arterial occlusion (table 3). Congestive failure was nearly twenty-six patients with acute myocardial infarction showed evidence of congestive failure. In this group systemic arterial occlusions were found in 37 per cent of the cases. By comparison 134 patients with acute myocardial infarction showed no evidence of congestive failure. In these patients the incidence of systemic arterial occlusion was only 16 per cent. There were 87 organs or extremities with systemic arterial occlusion found in 52 patients (fig. 1). Thus, multiple lesions of this nature occurring in one patient were common. In 23 of the 87 organs involved in systemic arterial occlusion there
was clinical evidence of this complication. In nine patients systemic arterial occlusion was considered to be a major factor causing death (4 per cent of 210 cases). Of these nine cases there were two in which major arteries to the lower extremities were occluded, two in which superior mesenteric arterial occlusion had occurred and five in which a major cerebral artery was occluded. In one of the latter five cases an embolus was demonstrated at the site of arterial occlusion. The other four occlusions were thrombotic in nature and related to rather severe cerebral atherosclerosis.

Pulmonary embolism or infarction was present in 33 cases (16 per cent of 210 cases of acute myocardial infarction) (fig. 1). In six of these 33 cases sudden death was caused by massive pulmonary embolism. In seven other cases pulmonary embolism (with or without infarction) was relatively large, causing occlusion of an artery supplying the major portion of one lobe, and was considered a major factor contributory to death. The remainder of the pulmonary thrombo-embolic lesions consisted of small pulmonary infaracts which apparently played only a minor role, if any, as a cause of death. Pulmonary embolism and infarction were found in five of the eight cases of acute myocardial infarction with mural thrombi in the right ventricle. In none of these cases did pulmonary embolism appear to have caused sudden death. In one of the five cases there were numerous small pulmonary emboli and infarcts which were considered to have been contributory to death. In three additional cases with right ventricular mural thrombi pulmonary embolism was not present.

Of the 33 patients with pulmonary embolism or infarction 22 (67 per cent) had had congestive failure (table 5). Of the 177 patients without pulmonary thrombo-embolism only 54 (31 per cent) had had congestive failure. Seventy-six of the 210 cases of acute myocardial infarction showed evidence of congestive failure. Of these 76 cases with congestive failure complicating acute myocardial infarction 22 (29 per cent) were complicated by pulmonary embolism or infarction.

**Incidence of Systemic and Pulmonary Arterial Occlusion in Healed Myocardial Infarction**

This portion of the study dealt with 117 consecutive cases in which necropsy demon-

---

**Table 5.—Incidence of Pulmonary Embolism in 210 Fatal Cases of Acute Myocardial Infarction**

<table>
<thead>
<tr>
<th></th>
<th>With Congestive Failure</th>
<th>Without Congestive Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolism</td>
<td>33</td>
<td>22</td>
</tr>
<tr>
<td>Pulmonary embolism absent</td>
<td>177</td>
<td>54</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>210</td>
<td>76</td>
</tr>
</tbody>
</table>

---

**Table 6.—Incidence of Systemic Arterial Occlusion in 117 Fatal Cases in which Healed Myocardial Infarcts Were Found**

<table>
<thead>
<tr>
<th></th>
<th>With Systemic Arterial Occlusion</th>
<th>Without Systemic Arterial Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left-sided cardiac mural thrombi present</td>
<td>31</td>
<td>8</td>
</tr>
<tr>
<td>Left-sided cardiac mural thrombi absent</td>
<td>86</td>
<td>24</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>117</td>
<td>32</td>
</tr>
</tbody>
</table>

---

strated healed myocardial infarction. There was no significant difference between the incidence of systemic arterial occlusion among those cases with and those without left-sided cardiac mural thrombosis (table 6). Among 31 cases with left-sided cardiac mural thrombi eight cases showed systemic arterial occlusion (26 per cent). Of 86 cases without left-sided cardiac mural thrombi systemic arterial occlusion was observed in 24 cases (28 per cent). There were 45 organs involved by systemic arterial occlusion in 32 patients with healed myocardial infarction. In 11 of the patients these complications were considered to be of major significance in causing death (fig. 2). In 29 patients the complication was clinically evident, being cerebral in 20 instances, extremital in seven and mesenteric in two (fig. 2). It is of interest that
among the 20 patients with cerebral infarcts, occlusion of a cerebral artery by thrombotic material was found in only four. In the remaining 16 cases only severe localized atherosclerosis was found. There was no significant difference in the incidence of congestive failure between those cases with and those cases without systemic arterial occlusion (table 7). Of 32 patients with systemic arterial occlusion 14 (44 per cent) had congestive failure while among 85 patients without systemic arterial occlusion 30 (35 per cent) had congestive failure. However, 22 patients without congestive failure had had a recent major operation or severe trauma while only two patients with congestive failure had had a recent operation. These complicating circumstances appeared to nullify the effect of congestive failure on the presence of systemic arterial occlusion in the group of cases with healed myocardial infarcts as compared with the positive correlation in patients with acute myocardial infarction.

Pulmonary embolism or infarction was found in 25 of the 117 cases with healed myocardial infarction (21 per cent). In 11 of these cases the emboli were clinically evident, eight being massive and causing sudden death. In eight of these 11 cases there was a history of recent major operation for cancer or fracture of an extremity. The remaining three cases manifested congestive failure alone, which was probably related in part to the healed myocardial infarct. Right ventricular mural thrombi were not found in any of the cases with healed myo-

**Table 7.—Relation of Congestive Failure to Incidence of Systemic Arterial Occlusion in 117 Fatal Cases in which Healed Myocardial Infarcts Were Found**

<table>
<thead>
<tr>
<th></th>
<th>WithCongestive Failure</th>
<th>Without Congestive Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic arterial occlusion present</td>
<td>32 14 44 18 56</td>
<td></td>
</tr>
<tr>
<td>Systemic arterial occlusion absent</td>
<td>85 30 35 55 65</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>117 44 38 73 62</td>
<td></td>
</tr>
</tbody>
</table>

- **Fig. 2.** Incidence and location of systemic and pulmonary arterial "occlusions" in the 32 patients having vascular occlusions among 117 cases of healed myocardial infarction.

* Total fatal cases of systemic arterial occlusion numbered 11. In one case occlusion of a femoral artery with gangrene of the leg and a cerebral infarct coexisted.

**COMMENT**

The ultimate purpose of this study was to demonstrate anatomically the incidence and location of pulmonary and systemic arterial occlusion in a consecutive series of cases of fatal acute myocardial infarction. Another consecutive series of cases in which healed myocardial infarction was demonstrated at necropsy was similarly studied to determine the nature of these vascular complications. It should be re-emphasized that in none of these cases were anticoagulants used as part of the therapy. It is hoped that this will serve in part as a control study for a review of a group of cases of fatal
myocardial infarction in which anticoagulants were used.

This study did not include venous thromboses of the extremities without pulmonary embolism, for many of these extremital venous lesions were out of reach of routine necropsy dissection. When pulmonary embolism or infarction occurred in the absence of mural thrombosis in the right side of the heart, systemic venous thrombosis was considered the most likely source of this complication, and it was demonstrated. However, since venous thrombosis could not always be demonstrated anatomically, a statistical study of this complication, per se, was not undertaken.

Bean has reported pulmonary arterial occlusion in 75 per cent of cases of myocardial infarction in which there was right ventricular mural thrombosis, and he compared this with an incidence of systemic arterial occlusion occurring in only 34 per cent of cases with left ventricular mural thrombosis. Similarly, we found pulmonary infarcts in five of eight cases of acute myocardial infarction with right ventricular mural thrombi. Yet, in none of these five cases was there massive pulmonary embolism. We feel that the chief danger of major embolization of the pulmonary arteries in acute myocardial infarction lies in venous thrombosis, particularly of the lower extremities. In all our cases of massive pulmonary embolism the thrombotic material was of such configuration that it appeared to have been formed in a large systemic vein and was coiled on itself in the major pulmonary arteries. In none of the cases with right ventricular mural thrombi was the pulmonary embolism of this nature. Usually a portion of one lobe was infarcted and the lesion did not appear to have played a dominant role in the clinical course.

In the interest of proper perspective concerning the nature of the systemic arterial occlusion it should be emphasized that interruption of adequate blood flow may be produced by embolism, thrombosis in situ or atherosclerotic narrowing alone or associated with shock or local alterations in blood flow. The latter possibility is particularly likely in cases of infarction of the brain affecting elderly patients with cerebral atherosclerosis. This type of peripheral arterial insufficiency may occur with acute myocardial infarction or with healed myocardial infarction complicating postoperative recovery or an acute infectious process.

In support of the postulate that many arterial occlusions are due to thrombus in situ or atherosclerotic narrowing is the fact that while acute infarction in areas supplied by systemic arteries occurred in 26 per cent of patients with healed myocardial infarction and intracardiac mural thrombi, this complication occurred in 28 per cent of patients with healed myocardial infarction but without intracardiac mural thrombi. While it may be assumed that some of these systemic arterial occlusions, in the absence of mural thrombi in the left side of the heart, represent embolization by the dislodgement of an entire intracardiac mural thrombus, it is unlikely that all of these lesions are examples of this phenomenon.

Evidence that many systemic arterial occlusions are embolic in origin may be had by using these same figures and comparing them with the incidence of systemic arterial occlusion in acute myocardial infarction. Among patients with acute myocardial infarction, arterial occlusion was more than twice as common when intracardiac mural thrombi were present (35 per cent) as when mural thrombi were absent (16 per cent). Among patients with healed myocardial infarcts, there was no significant difference between the incidence of systemic arterial occlusion in those cases with and those without intracardiac mural thrombi. Blumer has stressed the difficulty encountered in determining anatomically at necropsy whether a given lesion is thrombotic or embolic in origin.

In reporting the incidence of thromboembolic complications of acute or healed myocardial infarction it is of equal importance to ascertain the significance of the various lesions as possible causes of death. Forty-four of the 87 systemic arterial occlusions associated with acute myocardial infarction involved the spleen or kidneys. Only one of these 44 lesions was clinically evident. In this case embolization to a branch of the left renal artery produced infarction of the inferior half of the left kidney, causing severe, steady pain in the flank. This
complication seemed a contributory cause of death. Recent splenic and renal infarcts are frequently found incidentally at necropsy, particularly in association with congestive failure without acute myocardial infarction. Many of the splenic and renal infarcts found in this series were probably of coincidental etiologic relationship to the myocardial infarction and, more than likely, had little effect on the clinical course in the cases in which they occurred.

In many reports of clinical studies a frequent thrombo-embolic complication listed is that of a "second coronary thrombosis," "extension of the myocardial infarct" or like designations.2-5 12 It will be noticed that in this report this designation is not made, for the reasons indicated in the following paragraphs.

It is not uncommon during convalescence from acute myocardial infarction for patients to manifest attacks of precordial pain, sweating and tachycardia. Such attacks may even be associated with additional electrocardiographic changes. That such attacks indicate a poor prognosis is accepted.13 14

Nevertheless, a diagnosis of a second coronary thrombosis on such findings is not justifiable in every case. The initial myocardial infarct itself might have occurred in the absence of intravascular thrombosis but as a result of ischemia secondary merely to coronary atherosclerosis. This phenomenon, the occurrence of acute myocardial infarction in the absence of coronary thrombosis, has been demonstrated in one sixth15 to one third16 17 of the cases among several series of patients with acute myocardial infarction. Furthermore, recurrent thoracic pain may be due to repeated episodes of coronary insufficiency with or without infarction and not to so-called thrombo-embolic complications. In examining a large number of hearts of patients who had died of acute myocardial infarction we have found relatively few cases in which two acute infarcts of distinctly different ages could be demonstrated histologically even in those cases with histories of recent recurrent precordial pain.

In regard to propagation of a coronary thrombus as a cause of further acute myocardial infarction we have found very few thrombi more than 1 cm. in length and then only occasionally in the right coronary artery. The short course of a thrombus along a coronary artery has been pointed out by others and technics of dissection of these arteries have been proposed in order to avoid overlooking thrombi at necropsy. It seems unlikely that coronary arterial thrombi tend to propagate. Thus it would seem that the main danger of intravascular thrombosis during convalescence following acute myocardial infarction lies in the walls of the cardiac chambers and in the systemic arteries and veins, but not in the coronary arteries.

In our cases of fatal acute myocardial infarction systemic and pulmonary arterial occlusion occurred as a major or lethal complication in 10 per cent of the 210 cases. Systemic arterial occlusion was considered to have been a major cause of death in nine cases of the group of 210 patients with acute myocardial infarcts (4 per cent). Pulmonary embolism caused sudden death in 3 per cent of 210 cases with acute myocardial infarcts and played a major role in the death of an additional 3 per cent of the patients. Thus, pulmonary embolism comprised the largest portion of these major vascular complications. Similarly, this relatively high incidence of pulmonary embolism among the occlusive vascular complications of acute myocardial infarction has been noted by Conner and Holt,18 Rosenbaum and Levine,19 Woods and Barnes,19 Nay and Barnes,20 Mintz and Katz14, Harrington and Wright,20 Doscher and Pindexter11 and Hellerstein and Martin.21

The distribution of systemic arterial occlusion was somewhat different in the group of cases with healed, as compared with the group with acute, myocardial infarcts. Cerebrovascular occlusion comprised a relatively larger portion of systemic arterial occlusions in the group with healed, as compared with the group having acute, myocardial infarcts. Furthermore, in all but three of the deaths in the group with healed myocardial infarcts which were due to systemic arterial occlusion a cerebral lesion was found exclusively. In two of the remainder, occlusion of an artery to a lower extremity was considered to be the fatal complication. In the eleventh case occlusion of a femoral artery with gangrene of the leg and a cerebral infarct coexisted.
Pulmonary embolism or infarction in the patients with healed myocardial infarction was usually related to some noncardiac factor such as a recent major operation, or severe trauma necessitating immobilization of the patient. However, in some of the cases with healed myocardial infarction congestive failure alone appeared to play a role in pulmonary thromboembolism.

**SUMMARY AND CONCLUSIONS**

1. A study was made of the incidence of systemic and pulmonary arterial occlusion in 210 cases of acute myocardial infarction and 117 cases of healed myocardial infarction.
2. Occlusion of a systemic artery or infarction of an organ may occur either in the presence or in the absence of left-sided intracardiac mural thrombi.
3. In acute myocardial infarction systemic arterial occlusion is more common when left-sided cardiac mural thrombi are present than when they are absent.
4. In acute myocardial infarction congestive cardiac failure favors the occurrence of systemic arterial occlusion.
5. In acute myocardial infarction congestive failure favors the occurrence of pulmonary embolism.
6. In healed myocardial infarction the incidence of systemic arterial occlusion was similar in the group with and the group without left-sided intracardiac mural thrombi, and there was found to be no greater incidence of systemic arterial occlusion in those cases having congestive failure than in those cases without congestive failure. The frequent occurrence of recent trauma or major operations in the group with healed myocardial infarction made the evaluation of congestive failure and its relation to the incidence of systemic arterial occlusion difficult.
7. Pulmonary embolism in some cases of healed myocardial infarction appeared to have been related to congestive cardiac failure. In many cases of healed myocardial infarction with and without congestive failure extracardiac factors such as recent trauma or major operations were related to the development of pulmonary embolism.

**REFERENCES**

Thrombo-embolism in Acute and in Healed Myocardial Infarction: II. Systemic and Pulmonary Arterial Occlusion

R. DREW MILLER, ROBERT A. JORDAN, ROBERT L. PARKER and JESSE E. EDWARDS

Circulation. 1952;6:7-15
doi: 10.1161/01.CIR.6.1.7

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1952 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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/6/1/7

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/