Pathology of Heart Valve Replacement Surgery:
Autopsies of 62 Patients with Starr-Edwards Prostheses*

Nelson R. Niles, M.D.** and John R. Sandilands, M.A., M.D.†

Hemorrhage in the atroventricular conduction system and myocardial necrosis commonly occur in the first week after valve replacement. Later, thrombosis on the prosthesis and infarcts in other organs become important but developing or persistent myocardial damage continuously menaces. Occlusion of small vessels, especially by embolism of foreign material, may contribute to the development of these lesions. Although the extracorporeal circulation, anticoagulation, cardiac pacing and steroid therapy generally applied to patients undergoing Starr-Edwards valve replacement either are necessary to the surgery or effectively overcome some potent dangers, these practices may disguise progression to more serious levels of some maladies induced by operation. Data accumulating from these autopsies and from clinical records include many and varied complications of surgery.

INTRODUCTION

As radical innovations advance the treatment of heart disease, new clinical syndromes appear and pathologic anatomy becomes more complex. Patients with Starr-Edwards prostheses form the content of this résumé of anatomic findings. Some abnormalities, though previously noted, are known but slightly and understood less. After presenting these details we propose to draw appropriate implications about pathogenesis, pathologic physiology, clinical expression and therapy.

MATERIAL

Files of this department include 62 autopsy reports of subjects who died after placement of Starr-Edwards prostheses. We examined the heart in all cases, and usually were able to see it and other organs in the fresh state. In ten cases, the autopsy was performed elsewhere; of these, we received the heart, together with paraffin blocks and slides of major organs and complete autopsy description including clinical history, in seven cases; in three we were given only the heart. All operations had been performed by the same group of surgeons.

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At surgery, cross-clamping of the aorta arrests the heart and unclamping, with defibrillation whenever necessary, restarts it at the end of operation. Coronary arterial perfusion is applied at intervals of 15-30 minutes during bypass. The pump prime consists of whole blood, mannitol, lactated Ringer’s solution, glucose and water and a flow of 2.4 liters/ meter²/minute is maintained. Hypothermia, either systemic or selective coronary, was formerly common, but is now rarely used. During surgery, anticoagulation is accomplished with intravenous heparin and controlled with protamine. A coumarin derivative is given regularly after the sixth or seventh postoperative day, unless the patient is then placed on a double-blind study of anticoagulant effects, or unless there are medical contraindications. Corticosteroids in pharmacologic doses are administered to many of the patients, particularly those in whom complications are expected.

Lesions of patients surviving surgery by less than seven days differed from those of the rest and we chose to group

<table>
<thead>
<tr>
<th>Lesion</th>
<th>36 early deaths</th>
<th>36 late deaths</th>
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<tbody>
<tr>
<td>Operative or postoperative myocardial necrosis</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Small-particle embolism*</td>
<td>6 (14)</td>
<td>8 (15)</td>
</tr>
<tr>
<td>Hemorrhage of A-V conduction system</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>Thrombosis on prosthesis</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td>Peripheral infarct</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Thrombotic embolism to coronary artery</td>
<td>—</td>
<td>7</td>
</tr>
<tr>
<td>Pneumonia or acute bronchitis</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Renal hemosiderosis</td>
<td>4</td>
<td>17</td>
</tr>
</tbody>
</table>

*Additional cases of probable small-particle embolism (no foreign material identified) indicated by parentheses.
the cases accordingly. Deaths occurred variously from the

time of operation to 76 months later. The particular valve(s)

replaced did not seem to affect the findings except by post-

operative contraction of the aorta about the prosthesis

and by degeneration of the Silastic ball in aortic prosthesis.

Twenty-eight patients accepted prosthetic aortic valves; 17

had mitral, 11 aortic and mitral, one mitral and tricuspid,

five aortic, mitral and tricuspid. Eighteen subjects had re-

peated cardiac surgery. In six, the prosthesis was replaced,

in one only the ball.

In 57 cases, as a product of autopsy and clinical study,

heart disease with or without surgical or other complications

was deemed responsible for death. Other unrelated events or

conditions were to blame in two patients. One subject died

unexpectedly at home, but with other important diseases

and cause of death was not established. In the remaining

two cases, with incomplete material and information, the

fatal process was unclear also.

**Findings**

Table 1 lists lesions encountered, each of which is later discussed.

**Myocardial Necrosis**

Table 2 outlines the incidence of myocardial destruction and its relation in time (as estimated by standard criteria) to most recent open-heart surgery. In 19 cases, lesions from more than one episode of injury appeared. Preoperative (26 cases) lesions were always small, quiescent and apparently inconsequential except when they seemed to follow previous operations, as may have happened in ten cases. We felt that they usually resulted from the rheumatic or bacterial carditis which had distorted the valve initially; they may have been due to naturally occurring occlusions of small intramyocardial vessels, as demonstrated by James. These scars resembled those commonly found in routine autopsies. Larger or more prominent ones occurred in patients who had had more than one operation (Fig 1).

In 13 cases, ischemic necrosis or scars appeared of which the estimated age indicated onset at or close to the time of surgery. These infarcts had the following characteristics:

1. They tended to be widespread, often patchy

or miliary, and to involve most heavily the inner layers of the left ventricular walls. In several areas they included only the two or three fibers closest to the endocardium (Fig 1).

2. Although all of the customary histologic elements attended the infarct, the number of polymorphonuclear leukocytes in them was usually absent or much reduced (Fig 4). Many scars contained much calcification.

3. Contraction bands commonly appeared on the periphery. These were evident, particularly by histo-chemical methods, in some biopsies taken during surgery. A single fiber might contain normal structure and contraction bands juxtaposed (Fig 5).

4. Thromboses in small intramyocardial vessels were found in six cases with operative or possibly operative infarcts, sometimes outside of the infarcted area. Occasionally these

<table>
<thead>
<tr>
<th>Case</th>
<th>24 early DEATHS</th>
<th>57 Total</th>
<th>Multiple Cardiac Surgeries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>21</td>
<td>5</td>
<td>26</td>
</tr>
<tr>
<td>Operative</td>
<td>11</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Postoperative</td>
<td>3</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>2</td>
<td>25</td>
<td>27</td>
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</table>

*Includes only cases with myocardial necrosis or scar.
several theoretic possibilities come to mind as plausible explanations of this fault. With chest pain, fever and prostration normally occurring in the postoperative state and treated routinely with narcotics, the value of these signs in diagnosis may shrink. The scattered distribution of the lesions might prevent the necessary electrocardiographic imbalance. Steroid therapy, by promoting stabilization of lysosomes during bypass,15,16 may reduce both the anatomic and physiologic expression of inflammation,17,18 which is cardinal to infarction.

The pathogenesis of these infarcts is both unsettled and important. Some hints deserve consideration. Seeing in cases of this series the frequency of some unidentified foreign material in the tissues (see Small-Particle Embolism), the wide distribution of the infarct, the frequency of infarcts in the other organs (Table 1), particularly the military

FIGURE 3. Multiple myocardial infarcts. Left ventricular wall contains many scattered but strikingly discrete scars involving endocardium as well as myocardium. Death occurred ten months after aortic and mitral valve replacement.

thrombi adjoined foreign-body granulomas which involved vessels (Fig 6).

5. Acute infarcts in patients dying during or shortly after surgery were always hemorrhagic (Fig 1). Having noted several similar features, Reichenbach and Benditt believe that these changes are peculiar, but not restricted, to patients following open-heart surgery. We have seen contraction bands in canine myocardium after coronary artery ligation, as well as in non-surgical human infarcts.

6. The diagnosis of operative or early postoperative myocardial infarct was never correctly made antemortem. In view of the usual size of the infarct this was perplexing at first; but cerebral infarcts, and the association of granulomas with some vascular occlusions and with many infarcts, we regard embolism of some material introduced to the vascular system during surgery as the most likely proximate cause.19,20 Other factors have for years aroused argument, such as the lack or inadequacy of coronary blood flow during surgery.21-25 Probably a combination of some or all of these factors, and possibly of others26,27 as well, is causal; and if so, the relative significances of each vary among the cases. Identified, if not specifically incriminated, causes of myocardial infarction in these cases are listed in Table 3. On first examination, thrombosis on the prosthesis, paraprosthetic leak, ball variance, aortic periprosthetic contraction and endocarditis seem improbable causes of myocardial ischemia. Yet each may possibly provoke at coro-

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FIGURE 4. Characteristic acute necrosis. Myocardial nuclei have disappeared, but fibrocytes and endothelial cells abound. Cytoplasm of myofibers is opaque, clumped and lacking striations; no leukocytes are present. The border of the lesion extends across the upper right corner of the photo. Death occurred on the sixth day after aortic valve replacement (hematoxylin-eosin, 425X).

FIGURE 5. Contraction bands. Transverse clumps of myosin interrupt the normal striations. They occur on the edge of acute infarcts and, maturing, acquire the characteristics of coagulation necrosis (Mallory-Heidenhain stain, 600X).
nary ostia abnormal dynamics which can further impair a limited blood supply to an hypertrophied myocardium. More than one of these lesions, perhaps several, act in most cases; rather clearly at least the coronary emboli are associated with the thrombi on prostheses.

A common claim has held that postoperative myocardial degeneration and dysfunction are most closely related to the duration of extracorporeal circulation.\textsuperscript{25,28} In support of this, cases requiring prolonged bypass were most apt to give histochemical evidence of degeneration during surgery\textsuperscript{29} and patients dying after very long surgery generally showed the most infarction (Fig 1). If one applies standard histopathologic methods, necrosis is recognizable postmortem only if cell death has occurred at least five-six hours earlier.\textsuperscript{10,11} Either special tech-

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure6.jpg}
\caption{Intravascular foreign body reaction partially occluding. No exogenous material being identified, only the diagnosis of probable small-particle embolism is made. Patient had mitral commissurotomy eight years before death and aortic and mitral valve replacement 16 months before death. Such lesions may be found in many sites. Same patient as in Figures 11, 14, 15 (hematoxylin-eosin, 150X).}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure7.jpg}
\caption{Foreign particle embolism. The refractile anisotropic material (arrows), now intracellular, has aroused a bland chronic inflammation with several multinucleate cells. Patient died following aortic valve replacement five, three and one month previously complicated by bacterial infection of the valve site (hematoxylin-eosin, X425).}
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\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure8.jpg}
\caption{Hemorrhage distending interatrial septum, viewed from posterior. Left atrial endocardium is abraded. The atrioventricular node lies in the middle of the hemorrhage. Death occurred at the end of prolonged cardiac bypass for triple valve replacement.}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure9.jpg}
\caption{Slight hemorrhage in bundle of His. Patient died three days after operation with acute myocardial necrosis (Mallory-Heidenhain stain, 56X).}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure10.jpg}
\caption{Hemorrhage distending interatrial septum, viewed from posterior. Left atrial endocardium is abraded. The atrioventricular node lies in the middle of the hemorrhage. Death occurred at the end of prolonged cardiac bypass for triple valve replacement.}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure11.jpg}
\caption{Slight hemorrhage in bundle of His. Patient died three days after operation with acute myocardial necrosis (Mallory-Heidenhain stain, 56X).}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure12.jpg}
\caption{Hemorrhage distending interatrial septum, viewed from posterior. Left atrial endocardium is abraded. The atrioventricular node lies in the middle of the hemorrhage. Death occurred at the end of prolonged cardiac bypass for triple valve replacement.}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure13.jpg}
\caption{Slight hemorrhage in bundle of His. Patient died three days after operation with acute myocardial necrosis (Mallory-Heidenhain stain, 56X).}
\end{figure}

\textbf{Small-Particle Embolism} (Table 1)

This complication, suggested by numerous petechiae involving serosal surfaces distant from the operative site, was diagnosed according to the criteria of Helmsworth et al\textsuperscript{19} and first regarded as silicone embolism. Microsections usually showed clear spaces, 8–15 \textmu m in diameter, with foreign-body reaction about them, most easily visible in lymphoid tissue and renal glomeruli. In a minority of cases...
some exogenous material was evident in these positions (Fig 7) and here the diagnosis of embolism was made. If no foreign material presented but other criteria were fulfilled, only the diagnosis of probable embolism was made (Fig 6). Staining with Oil Red O demonstrated fat in a crescentic or circular shape only at the edge of the defect, as mentioned by Helmsworth et al.\textsuperscript{19} The importance of this condition to the patient is not clear, but the frequency in this series of microscopic lesions suggests that crucial hemodynamic change may also occur. The many infarcts (especially the mililiary infarcts, Fig 18) could easily result from multiple microemboli. Air,\textsuperscript{20} fat,\textsuperscript{2} calcium\textsuperscript{9} and platelet aggregates,\textsuperscript{9} as well as silicone\textsuperscript{20} are substances which merit consideration. At any rate this is a common event of the operation, not simply a histologic oddity, and its ubiquity emphasizes its importance.

To sum up the matter, small-particle embolism is commonly apparent, but not clearly serious; in some cases it may be critical to the production of acute heart failure and to infarcts of many organs including the heart.

Hemorrhage Involving the Atrioventricular Conduction System.

The interatrial or the membranous interventricular septum contained acute hemorrhage in 24 cases; in all, this involved the conduction system. It generally was easily visible grossly though sometimes overlooked until the septa were cut (Fig 8). It was small enough in six hearts so as to be better appreciated microscopically (Fig 9). Timing of the deaths varied from the operative period until 17 days later, except for one case of bacterial endocarditis. (This patient died on the 33rd day; the inflammation included some hemorrhage and had progressed to the atrioventricular conduction bundle.) Usually there had been clinical suggestion of inadequate cardiac output, and therefore we regard this lesion as another possible cause of fatal postoperative heart failure.

Frequencies of arrhythmias and conduction defects in the early postoperative period\textsuperscript{1,2,31} and of scarring and myocytolysis in the conduction tissues seen later (Fig 10) indicate that some hemorrhage may commonly occur here after valve replacement.

<table>
<thead>
<tr>
<th>Table 3—Possible Causes of Myocardial Necrosis—57 Cases</th>
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<tr>
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<tr>
<td>Coronary arteriosclerosis</td>
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<tr>
<td>Coronary embolism</td>
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<tr>
<td>Thrombosis on prosthesis affecting function</td>
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<tr>
<td>Other valve site anomalies</td>
</tr>
<tr>
<td>Small vessel occlusion</td>
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<tr>
<td>Small-particle embolism</td>
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<tr>
<td>Possible small-particle embolism</td>
</tr>
<tr>
<td>None of the above</td>
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Interest in the postmortem examination of the conduction system now runs high and yields increasingly better correlation of clinical and electrocardiographic with anatomic findings.\textsuperscript{32,33}

Etiology. Most frequently the cause of this unusual feature, decidedly rare in any other setting, was occult. Of 14 patients dying within the first postoperative day, six had hemorrhage involving the atrioventricular node without other significant abnormality except acute visceral congestion.

Anatomic indications of possible etiologic factors are listed in Table 4. One more possible etiologic

<table>
<thead>
<tr>
<th>Table 4—Findings Related to Hemorrhage in the A-V Conduction System—24 Cases</th>
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<tbody>
<tr>
<td>Operative or postoperative myocardial infaract</td>
</tr>
<tr>
<td>Extension of hemorrhage from adjacent bleeding site</td>
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<tr>
<td>Endocardial abrasion</td>
</tr>
<tr>
<td>Bacterial endocarditis with extension</td>
</tr>
<tr>
<td>Multiple hemorrhages</td>
</tr>
<tr>
<td>None of the above</td>
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</tbody>
</table>

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FIGURE 10. Late degeneration (myocytolysis and scar) in the atrioventricular node. Patient died nine months following aortic valve replacement (hematoxylin-eosin, 425X).
Thrombosis on prosthesis cage. The thrombi extend along the struts; since organization occurs only when they are connected to living tissue or woven fabric, they may dislodge and embolize at any time. Death occurred seven and one-half months following mitral replacement. Patient had splenic, renal and two cerebral infarcts. Figure 12. Occlusive prosthetic thrombosis. The luxuriant thrombus is attached only on one side of the ring, but has fallen across the lumen and obstructs flow; the ball lies hidden beneath. Same patient as in Figure 6, 15, 17. Figure 13. Organization with Teflon. Fibroblasts may be found in the smooth, adherent, translucent tissue on the cloth covering the struts and base of the prosthesis. This patient had regained full health and activity following mitral valve replacement nine months before dying in automobile accident. Figure 14. Recent acute thrombosis. Patient died on the sixth postoperative day. The multiple small thrombi are mostly unorganized. The mass projecting from the coronary ostium is contused edematous intima. Figure 15. Ball variance. The aortic ball has been removed from the prosthesis for comparison with the mitral one which was implanted simultaneously; the ball is dull, opaque, yellow and asymmetric. Subacute myocardial infarction involves the left ventricular wall. Same patient as in Figure 6, 12, 17. Figure 16. Partial fracture. This aortic prosthesis was placed six years before the patient's sudden and unexpected death. Note roughening and discoloration. Figure 17. Periprosthetic aortic contraction. This has restricted movement of the ball. Contact with the aortic wall has produced intimal grooves opposite each strut; the one on the right is nearly buried in the thickened intima. Same patient as in Figures 6, 12 and 15.
factor might be cardiac pacing, used routinely at this hospital\^{34} and which undoubtedly prevents dangerous dysrhythmias and conduction blocks; probably it carries many patients effectively through a vulnerable period when they have some transient hemorrhage here. But two potential dangers loom; the stimulating electrode inserted through the atrial wall, or the indifferent electrode placed on the interatrial groove, may incite or sustain this bleeding by direct abrasion. Also, the pacer gives assurance which may occasionally be false by masking a hemorrhage until it causes intractable heart failure; therefore, although the lesion is not now correctible, it may be preventable.

In the case of one death 30 hours postoperatively, the extent and number of hemorrhages attested to a lack of coagulant, and similar lack in others may have elicited hemorrhage in the interatrial septum. Since a small volume of blood may be critical in this region, alertness to this possibility is recommended.

The frequent coexistence of myocardial degeneration or necrosis indicates that the specialized muscular cells of the conduction system may deteriorate acutely. As noted before, acute operative myocardial infarcts are always hemorrhagic. Perhaps the hemorrhage follows that disruption in the specialized fibers.

**Thrombosis Involving the Prosthesis** (Tables 1 and 5)

As others have described,\^{8,35,36} these thrombi started at the border of the ring and bases of the struts; they extended upward along the struts, particularly on the inner surface, and this extension occurred even on nine of the 15 prostheses with Teflon-covered struts, but has not there caused dysfunction. Thrombi on the mitral and tricuspid prostheses commonly grew from the ring over the lumen and tended either to narrow this lumen progressively or to extend across it as a flap, thus being potentially acutely obstructive. They did not appear to limit movement of the ball in these positions, but often did so in the aortic because of growth within the cage and on the aortic side of the ring internally (Fig 11, 12). Organization was in progress in the majority of thrombotic material on the Teflon-covered struts (Fig 13), but in one case, a thrombus from such a prosthesis embolized to a major coronary artery. Unorganized thrombi, growing on bare struts, constituted a trenchant danger (Fig 14). In nearly half the cases with thrombosis, dysfunction of the prosthesis on this basis was apparent by postmortem examination (Table 5).

**Other Valve Site Abnormalities** (Table 5)

Technical problems with the prosthesis have resulted in some changes or refinements of surgical and other techniques which have greatly reduced the recent incidence of these complications. Paravalvular leak is apparently a result of loosening or tearing of the sutures with separation of tissues.\^{35} Ball variance\^{37} has been seen only in the aortic prostheses (Fig 15, 16) and since early 1967, Stellite balls have been used here, although Silastic is still preferred for other positions. Contraction of the lower aorta about the prosthesis results from scarring, due presumably to the irritative effect of the cage moving on the intima (Fig 17). The contraction only becomes important when it restricts the movement of the ball. Now the operative procedure includes dilatation of this segment or use of smaller prostheses to prevent this result. In one case, localized edema with degeneration of the intima involved a coronary ostium, possibly as a result of cannulation (Fig 14).

Bacterial endocarditis had caused the initial valvular deformity in three cases; in all, the infection was apparently overcome. In five others the prosthetic site was involved by infection. This necrotic focus, including prosthesis, was resected in one patient terminally; another sustained re-operation twice only to die of mycotic (Candida albicans) infection of the ring.

**Peripheral Infarcts**

Twenty-six cases harbored a total of 47 organs with infarcts; most of these organs held multiple lesions. The brain was visibly affected 15 times, kidney ten, spleen eight, pituitary five, pancreas five and less frequently the adrenal, bowel, and gallbladder. In none of these foci was thrombotic

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**Figure 18.** Miliary cerebral necrosis. Two of the minute infarcts in a patient dying nine days following mitral and aortic valve replacement (Luxol fast blue, X195).
embolism surely identified, but circumstantial evidence originally led us, perhaps mistakenly, to that cause. The indications were: 1) appropriate history; 2) lack of occlusive disease in major nutrient vessels of the organ; 3) a source of emboli (i.e., thrombosis either on the prosthesis or in the left atrium); 4) infarcts in organs such as the spleen which are not particularly susceptible to the effects of arteriosclerosis; 5) multiple infarcts, especially in different organs. Also seven coronary arterial emboli were identified grossly, five occurred in these 26 cases. After evaluation of small-particle embolism we concluded that many infarcts might have resulted by this means, with arterial thrombosis following the particulate embolism (Fig 6, 7).

Vascular spasm, whether due to medication or other cause, could not be ruled out as a cause of infarction. The frequent use of various vasopressor agents suggests that these may have had such effect in some.27

**Respiratory Tract Inflammation** (Table 1).

Respiratory infection, such a common event in the moribund whether a cause of death or incidental to it, was apparently effectively suppressed in these patients. We presume that the rigid antibiotic precautions and therapy were responsible.25 Bacterial pneumonia or bronchitis was evident in two subjects dying less than one week after operation and in ten dying later. In two cases of late death it had existed before operation.

**Renal Hemosiderosis** (Table 1)

Renal tubular epithelial cells, though normal by hematoxylin-eosin stain, contained stainable iron in 21 cases. This sort of hemosiderosis has no significance regarding renal function, but does reflect intravascular hemolysis.38 Additional iron present in infarcts or other focal lesions is not included here.

**Pathology of Some Clinical Features**

There were four cases in which jaundice appeared postoperatively. In three of these, advanced acute and chronic passive congestion of the liver was found; in one there was also marked canalicular bile stasis, serum bilirubin level having risen to 100 mg percent.39 In the fourth, hemolysis incidental to surgery and mild hepatic congestion were present. There was no evidence of a chemical or infectious cause of liver failure. Renal failure was apparent from clinical and laboratory observations in three cases; the cause was acute renal tubular degeneration and necrosis and appeared to have resulted from impairment of renal blood flow in all three.

The low-output syndrome was mentioned in only two patients’ records. Details of examination supporting this diagnosis are inconsistent. A discussion of the medical aspects of the problem has been presented.1 The postoperative delirium noted by Blachly and Starr2 appears to have a likely cause in the miliary cerebral infarcts (Fig 18) which have been found in eight cases; pathogenesis of these is presumably microembolic but again the substance of the emboli has escaped indentification.

The postperfusion pulmonary congestion syndrome has such nonspecific and variable features40 that after initial attempts to classify cases according to presence or absence of this condition, we abandoned the project.

We have found no anatomic evidence of the postpericardiectomy splenomegaly1 nor of the infectious agent found by Braimbridge et al.41 However, the frequency of unexplained myocardial disease in this series suggests that the application of all of Braimbridge’s methods might have revealed some factor similar to theirs. As was pointed out, evidence of transmissible agents causing cardiomyopathy perhaps cannot be found in paraffin sections of formalin-fixed tissue.

Many other physiologic and biochemical aberrations mentioned in connection with open-heart surgery1,2,38 have found no specific etiology except as mentioned or presumed. Two of the likeliest reasons for metabolic acidosis, for instance, are anoxia and necrosis of myocardium and other parenchyma.

**Comment**

Clinical diagnosis of patients in the postoperative period is notoriously pocked with traps. This is especially true when the surgery is cardiac and requires extracorporeal circulation.26,42 But expertise in these fields has developed to the point where collapse resulting from devastating bombardments is temporarily or permanently prevented. Routine use of artificial pacemakers probably carries many patients through periods when transient hemorrhages involving some part of the conduction system could be dangerous or fatal; yet this very safeguard prevents accurate and early clinical diagnosis in some patients by masking, at least initially, certain major lesions. Resort to high doses of corticosteroids may add to this risk.16-18

Although the term “low-output syndrome” lacks specificity and seems to be passing out of use, decreased output in varying degrees remains common. Myocardial necrosis, having escaped detection in life, probably represents the nearest anatomic equivalent of this syndrome and here reveals itself.
as the most frequent and serious threat to patients accepting valve surgery. Development of myocardial cell death in the dog requires 40-60 minutes of ligation of a coronary artery, although the anatomic evidence may need longer to evolve. Yet immediately upon ligation the area undergoes marked modification of its gross appearance because of altered vascularity, changes in response to injected dye and changes in contractility and in electrical activity. These disturbances, untended, may lead to fatality either immediately or later. Momentous intracellular distortions must attend these functional disturbances even if standard methods fail to show them. Only lack of an adequate technology appears to have prevented recognition of the structural alterations. Not only do means exist for examining the cells and their chemistry under conditions most similar to those in vivo, but by detecting intracellular abnormalities the physician can expect to modify the dysfunction and clarify the later pathology. perhaps he will also discover how to avoid these untoward effects.

Cardiac muscle reacts easily and often dramatically to various stimu and we can expect that the variations and disturbances of intracellular organization which authorize those reactions should also be detectable. Naturally enough then, cytochemical evidence at hand reflects both alterations in the strength of protein-lipid bonds in cell membranes and disruptions of the integrity of the cellular hydrogen-transport system, while histologic study of the same specimens reveals no change. Early degenerations so demonstrated within myocardium may or may not proceed to necrosis, but these are delicate stimuli. Cell biology in this framework offers aid to the surgeon and his colleagues, for by such means they may be able to determine rather simply, as well as more reliably than otherwise, those elements of operation, extracorporeal circulation, anesthesia or pharmacotherapy which affect the heart favorably or adversely.

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NUTRITION AND AGING

There is perhaps no field in which biologic and social factors are so intertwined as in eating. Numerous studies have shown the relation between psychologic and nutritional problems. Since eating is frequently a form of compensatory behavior and related to deep emotional drives, food habits of the neurotic are not easily changed. There are, however, today millions of aging persons who are becoming interested in the preservation of health and vigor and who believe that they are willing to follow any prescribed plan in order to remain healthy. No doubt the majority hope for a pill which will solve all their problems, but many would be willing to revise eating habits if they were sure that advice available to them is authentic.