Aneurysms of the Previously Ligated Patent Ductus Arteriosus

By Richard S. Ross, M.D., Frederick P. Feder, M.D., and Frank C. Spencer, M.D.

Patency of the ductus arteriosus is, under most circumstances, a relatively benign condition. Surgical therapy has been available since 1938,1 results are excellent, and the operative risk is small.2-6 Recanalization of a ligated ductus arteriosus occasionally occurs and may be associated with the formation of an aneurysm. Recanalization and aneurysm formation are serious complications associated with sizable risks whether they are attacked surgically or allowed to remain untreated. These complications are presented in case 1 of this report. Four similar cases found in the records of The Johns Hopkins Hospital are also briefly abstracted here.5,7,8 These five cases have been combined with 12 collected from the literature and are summarized in table 1.

Case Reports

Case 1

(J.H.H. 85 01 86): P. H., a white woman was known to have a heart murmur in childhood but was asymptomatic until age 21. At this time, during her first pregnancy, she noted swelling of her legs, feet, hands, and face, and developed mild dyspnea on exertion. She was treated for pre-eclampsia. After delivery her symptoms subsided, but she remained weak and tired easily.

At age 30, at another hospital, a patent ductus arteriosus was ligated with silk sutures. The patient developed a wound infection with Staphylococcus aureus that was "resistant" to penicillin but responded to treatment with Furadantin and chloramphenicol. Three weeks after operation, a faint continuous murmur was heard in the pulmonary area. Several examinations by her local physician after her return home revealed only a systolic murmur.

Six months after operation the patient developed chills and fever, and blood cultures were positive for Staph. aureus, again "resistant" to penicillin. She was treated for 5 weeks with streptomycin, dihydrostreptomycin, and chloramphenicol. During this illness, the attending physician heard a continuous murmur, whereas he had heard only a systolic murmur previously.

During the 4 years between the endarteritis and admission to this hospital, the patient was seen regularly by a cardiologist, who noted an increase in the size of the heart and persistence of a continuous murmur. The patient took prophylactic oral penicillin daily during these 4 years. Her only symptoms were mild dyspnea on exertion and occasional palpitations.

On admission to this hospital, 4½ years after the first operation, the pertinent findings were a blood pressure of 132/64 mm. Hg, an accentuation of the second heart sound in the pulmonary area, and a loud continuous murmur in the second left interspace. Calcium was present in the region of the pulmonary artery on chest roentgenogram, suggesting the possibility of aneurysm formation (fig. 1). Cardiac catheterization demonstrated a large left-to-right shunt in the pulmonary artery, but the pulmonary arterial pressure was normal.

At thoracotomy with hypothermia of 31 C a 5-cm. aneurysm in the region of the ductus arteriosus was found and scar tissue on its anterior surface enveloped the vagus and phrenic nerves. A strong thrill was palpable over the aneurysm. The aneurysm was freed from the left bronchus and adjacent nerves by sharp dissection. Clamps were placed across the aorta above and below the aneurysm and obliquely across the left pulmonary artery. The aneurysm was then removed, and the openings in the aorta and pulmonary artery were sutured. The aorta was occluded for 10 minutes.

The aneurysm was 3 cm. in internal diameter. The sac had a 1-cm. communication with the aorta (fig. 2) and an 8-mm. communication with the pulmonary artery. One silk suture lay free in the lumen of the aneurysm. Microscopically the specimen revealed a scarred, thickened, hyalinized vessel wall with much chronic inflammation in the adventitia and a foreign-body reaction within the wall about the sutures.

The postoperative course was complicated by the development of loculated pleural effusions and...
fever. Approximately 1 month after operation the patient became afebrile and was discharged. One year after operation she was asymptomatic and living a normal life.

Case 2

(J.H.H. 54 53 73) A. E., a 5-year-old girl, had a 1.6-em. ductus ligated with three silk pursestring sutures, one mattress suture, and a ligature of braided silk. Convalescence was uneventful, and at discharge 17 days after operation no diastolic murmur was heard. At 2 months and again at 5 months after operation respiratory infections were treated with penicillin by the family physician. The second of these febrile episodes persisted for 1 month, and during this illness a typical continuous murmur was heard. A single blood culture was sterile, but penicillin, aureomycin, and streptomycin were given for 3 weeks.

Seven months after operation, at the time of return to The Johns Hopkins Hospital, the patient was found to be chronically ill, and the typical physical findings of a patent ductus arteriosus were demonstrated. Blood cultures were positive for *Staphylococcus albus*. The patient was treated for 10 weeks with aureomycin, streptomycin, and chloramphenicol. Nine and one-half months after the initial operation, at re-exploration a large saccular aneurysm was found arising from the pulmonary end of the ductus. The aneurysm was mobilized and excised, but a tear in the aorta led to a fatal hemorrhage. The surgical specimen contained a thick vessel wall consisting of fibrinous clot, polymorphonuclear leukocytes, a few macrophages, and old suture material. In addition, postmortem examination revealed giant-cell granulomata in the lung, suggestive of fiber emboli, presumably from suture material.

Case 3

(J.H.H. 54 57 94) J. M., a white man, was first seen at age 18 for evaluation of congenital heart disease. Significant physical findings were a blood pressure of 115/65/0 mm. Hg, collapsing radial pulses, and a loud, continuous, machinery murmur, maximal in the pulmonary area.

At operation a short patent ductus arteriosus, 1.3 cm. in diameter, was occluded with silk purse-string sutures at the aortic and pulmonary ends and a single transfixed suture in between. The pulmonary arterial thrill was obliterated by this procedure. The postoperative course was benign. On examination 18 days after operation significant physical findings were a blood pressure of 112/88 mm. Hg and a faint but definite continuous murmur in the pulmonary area.

Examination 1 year after operation revealed an increase in the systolic component of the continuous murmur and a blood pressure of 120/65 mm. Hg. A diagnosis of recanalized ductus arteriosus was made but surgery was deferred. Three years after operation a grade-II continuous murmur was again heard in the pulmonary area and cardiac catheterization was carried out. The pulmonary blood flow was 4.5 times the systemic flow, and the pulmonary arterial pressure was 100/40 mm. Hg. Surgery was not advised because of the pulmonary hypertension. A second catheterization 5 years later showed no change in the pulmonary artery pressures, but the pulmonary flow had decreased to that of the systemic flow, indicating that there had been an increase in pulmonary vascular resistance during the 5 years between studies.

At age 26, 8 years after the initial operation, re-exploration revealed an aneurysm measuring 1.5 cm. in diameter. The ductus was divided, and the aortic and pulmonary stumps were sutured; but when the aortic clamp was removed, moderate bleeding from the suture line was followed by myocardial failure and death.

Pathologic examination of the ductus revealed a calcified sac with hyaline walls and old hyaline mural thrombi on the anterior lateral surface of

Figure 1

*Chest* x-ray, case 1. A faint ring of calcium can be seen in the region of the enlarged pulmonary artery.
Aneurysm of the Ligated Ductus Arteriosus

<table>
<thead>
<tr>
<th>Case report</th>
<th>Sex/age</th>
<th>First operation</th>
<th>Technic</th>
<th>When recanalized</th>
<th>Onset symptoms of bacterial endocarditis</th>
<th>Organism</th>
<th>X-ray diagnosis and cause</th>
<th>Subsequent operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1. P. H.</td>
<td>F 35</td>
<td>ligation; 3 ligatures</td>
<td>1 mo.</td>
<td>1 mo.</td>
<td>Staph. aureus</td>
<td>yes 4 yr.</td>
<td>excised</td>
<td></td>
</tr>
<tr>
<td>Case 2. A. E.</td>
<td>F 5 1.6 cm.</td>
<td>suture-ligation; 4 ligatures</td>
<td>5 mo.</td>
<td>6 mo.</td>
<td>Staph. albus</td>
<td>yes 6 mo.</td>
<td>excised; operative hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Case 3. J. M.</td>
<td>M 18 1.3 cm.</td>
<td>suture-ligation; 3 ligatures</td>
<td>18 da.</td>
<td>2 mo.</td>
<td>Staph. aureus</td>
<td>yes 3 mo.</td>
<td>excised</td>
<td></td>
</tr>
<tr>
<td>Case 4. H. R.</td>
<td>F 23 1.2 cm.</td>
<td>suture-ligation; 5 ligatures</td>
<td>46 da.</td>
<td>6 mo.</td>
<td>Staph. albus</td>
<td>no</td>
<td>excised</td>
<td></td>
</tr>
<tr>
<td>Case 5. T. M.</td>
<td>F 4</td>
<td>&quot;large&quot; suture-ligation; 4 ligatures</td>
<td>15 da.</td>
<td>10 da.</td>
<td>Staph. aureus</td>
<td>yes 15 da.</td>
<td>excised</td>
<td></td>
</tr>
<tr>
<td>Jones et al., case 3</td>
<td>F 13</td>
<td>ligation; 2 ligatures</td>
<td>33 da.</td>
<td>30 da.</td>
<td>Staph. aureus</td>
<td>yes 33 da.</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Gerbauer</td>
<td>--- 18</td>
<td>ligation</td>
<td>---</td>
<td>---</td>
<td>kept murmur</td>
<td>---</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>Tubb case 4</td>
<td>F 10</td>
<td>ligation</td>
<td>28 da.</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Holman et al., case 4</td>
<td>F 11</td>
<td>ligation, #1—1 lig.</td>
<td>30 da.</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Das et al., case 1</td>
<td>F 25</td>
<td>ligation, 2 ligatures</td>
<td>105 da.</td>
<td>1 yr.</td>
<td>coag. neg.</td>
<td>1 yr.</td>
<td>excised; loss of vagus and recurrent laryngeal nerves</td>
<td></td>
</tr>
<tr>
<td>Das et al., case 2</td>
<td>F 5</td>
<td>.4 cm. ligation, 2 ligatures</td>
<td>no diastolic murmur</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>excised; pneumonectomy to control hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Servelle et al.</td>
<td>--- 7</td>
<td>.7 cm. ligation, 4 ligatures</td>
<td>35 da.</td>
<td>29 da.</td>
<td>Staph. aureus</td>
<td>yes 38 da.</td>
<td>#2-endaneurysmorrhapy</td>
<td></td>
</tr>
<tr>
<td>Kerwin et al.</td>
<td>F 34</td>
<td>2.5 cm. ligation, 4 ligatures</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>yes 7 mo.</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>Lindskog et al.</td>
<td>F 16</td>
<td>ligation, 3 ligatures</td>
<td>between 2 and</td>
<td>---</td>
<td>---</td>
<td>yes 8 mo.</td>
<td>excised</td>
<td></td>
</tr>
<tr>
<td>Crafoord</td>
<td>F 22</td>
<td>4.6 x 3 cm. division and 60-90 da. suture</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>gamma</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>Humphreys, case 6</td>
<td>M 11</td>
<td>1.5 cm. ligation, 2 ligatures</td>
<td>7 da.</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>Milstein et al.</td>
<td>F 19</td>
<td>1 x 2.4 cm. ligation</td>
<td>&quot;some weeks&quot;</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>excised</td>
<td></td>
</tr>
</tbody>
</table>

Table 1

the ductus. A lung biopsy revealed multiple thrombi and recanalized thrombi in dilated vessels with dense hyaline walls.

Case 4

(J.H.H. 56 36 12) : H. R., a white woman, was told she had a "bad heart" at age 2. The diagnosis of patent ductus arteriosus was made at age 23 on the basis of a typical continuous murmur and slight left ventricular enlargement. At thoracotomy a large ductus measuring 1.2 cm. in diameter was ligated with two silk pursestring sutures and three transfixion sutures.

Seven weeks later the patient had a dental extraction without prophylactic penicillin. Five days afterward she developed anorexia, fatigue, chills, and intermittent "dark urine."

On readmission, 10 weeks after operation, she appeared chronically ill with a temperature of 101.3 F. (rectal), a blood pressure of 120/55 mm. Hg, and a grade-II continuous murmur in the pulmonary area, accompanied by an accentuated second pulmonic sound and diastolic tap. Seven blood cultures were positive for hemolytic staphylococcus albus. Treatment was begun with
PATENT DUCTUS ANEURYSMS AFTER LIGATION

<table>
<thead>
<tr>
<th>Result</th>
<th>Related pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>living</td>
<td></td>
</tr>
<tr>
<td>died at operation</td>
<td>fiber emboli in lungs</td>
</tr>
<tr>
<td>died at operation</td>
<td>pulmonary vascular sclerosis, pulmonary hypertension</td>
</tr>
<tr>
<td>living</td>
<td></td>
</tr>
<tr>
<td>living</td>
<td>Staph. cultured from sutures</td>
</tr>
<tr>
<td>died (bacterial endocarditis)</td>
<td>sutures loose in wall of aneurysm</td>
</tr>
<tr>
<td>died</td>
<td>evidence of arteritis in aneurysm; recanalized</td>
</tr>
<tr>
<td>died (bacterial endocarditis)</td>
<td>loose sutures in aneurysm; pulmonary infarcts</td>
</tr>
<tr>
<td>living</td>
<td>loose sutures in aneurysm; calcified aneurysm</td>
</tr>
<tr>
<td>living</td>
<td>recanalization demonstrated</td>
</tr>
<tr>
<td>living</td>
<td>loose sutures in lumen, culture Staph.; persistent bacterial endocarditis likely</td>
</tr>
<tr>
<td>died—hemoptysis</td>
<td>ruptured mycotic aneurysm of left pulm. artery; loose old ligatures with pulm. emboli; recanalized ductus arteriosus</td>
</tr>
<tr>
<td>living</td>
<td>appeared to be infected hematoma between aorta and P. A.</td>
</tr>
<tr>
<td>died 1 yr. postoperative</td>
<td>large false aneurysm, pulmonary hypertension</td>
</tr>
<tr>
<td>died 2 hr. postoperative</td>
<td>lung hypertension</td>
</tr>
</tbody>
</table>

Table 2

6.4 million units of penicillin with 2 Gm. of Benemid per day. The temperature was normal after the third day.

After 3 weeks of chemotherapy, a second thoracotomy was performed. The previous sutures were found in a small aneurysm immediately adjacent to the ductus. The surgeons noted that "it looked as if the sutures had cut through and been extruded and the ductus had reformed." Vegetations were found only at the pulmonic end and were sterile on a bacteriologic culture. The ductus was divided, the ends were sutured, and a flap of pericardium was interposed between the two suture lines. The patient was discharged on the twenty-third postoperative day and is asymptomatic and well at the present time, 8 years after the second operation.

Case 5

(J.H.H. 70 67 68): T. M., a 10-year-old white girl, was referred to The Johns Hopkins Hospital for surgical treatment of a patent ductus arteriosus. At operation a large, thick-walled, patent ductus arteriosus was exposed and closed by the suture-ligation technic. Pursuesting sutures were placed at the aortic and pulmonic ends and a through-and-through mattress suture was placed between them. The thrill in the pulmonary artery was obliterated by the closure. Ten days later the temperature per rectum rose to 105 F.; blood cultures were positive for hemolytic staphylococcus aureus. Therapy was begun with six million units of penicillin intravenously and 1 Gm. of Benemid per day. An area of consolidation was observed in the left upper lung field near the mediastinum on a chest roentgenogram (fig. 3); it was thought to be either an aneurysm or an abscess. On the same day a faint continuous murmur was heard in the second left intercostal space. The continuous murmur increased in intensity and serial chest roentgenograms during the next 5 weeks showed a gradual increase in the opacity in the left upper lung field (figs. 4 and 5). An aneurysm of the ligated, recanalized, and presumably infected ductus was considered likely. After 7 weeks of intensive antibiotic therapy the patient still maintained a low-grade, intermittent fever.

At the second operation, exactly 2 months after

Figure 2

Relationships at operation in case 1. The aneurysm has been opened and its aortic opening is visualized.
the first, a soft, pulsating aneurysm 8 cm. in diameter was found in the region of the ductus. The aorta and pulmonary artery were mobilized, the lung was dissected from the aneurysm, the aorta and pulmonary artery were cross-clamped, and the sac was incised. The three silk ligatures used in ligation were found within the wall of the sac. The aneurysm communicated with the aorta and pulmonary artery through 6-mm. openings. These openings were sutured and a flap of pericardium was interposed between them. *Staphylococcus aureus* was cultured from the ligatures found in the wall. Grossly, the cyst-like aneurysmal cavity was lined by a smooth, opaque membrane, free of vegetations. Microscopically the aneurysm wall showed smooth muscle and dense collagenous tissue. The intimal portion was composed of dense granulation tissue. Many plasma cells infiltrated all layers.

The postoperative course was uneventful and the chest roentgenogram 16 days after operation is shown in figure 6. When the patient returned 2 months after discharge, she was entirely asymptomatic. There was a soft, short systolic murmur over the pulmonary area and the heart size had decreased. Three years after operation she was living a normal life.

**Discussion**

The clinical features of postoperative aneurysms of the ductus arteriosus can be determined from inspection of table 1. The female preponderance in the 17 cases presented is consistent with the greater frequency of patent ductus arteriosus in women. Eleven of the aneurysms appeared in patients treated by simple ligation, five occurred after suture-ligation, and one after division. In the four cases treated at this hospital by the suture-ligation technic, the patent ductus was large, being 1.6, 1.3, and 1.2 cm. in diameter in three cases and probably larger than 1 cm. in the fourth. In the one case of aneurysm formation from a divided ductus, Crafoord's case, preoperative infection existed, and it was believed that the aneurysm originated from an infected hematoma between the aorta and pulmonary artery. Recanalization seems to be essential to the formation of postoperative aneurysm and was present in all 17 cases. Recanalization apparently occurred at some time during the first 6 months after operation. This observation fits well with autopsy evidence that a ligated ductus arteriosus is converted into a fibrous cord with intima sealing the vessel at its ends within 1 year after operation.

A ligated ductus arteriosus may become reanualized if the ligatures cut through the vessel wall, allowing re-establishment of its lumen. Such an area of suture transection could easily result in a hematoma and false aneurysm formation or serve as a site for bacterial growth. It has been suggested that post-stenotic dilatation of the ductus distal to a stenosing aortic end ligature may at times be responsible for true aneurysmal formation.

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ject to aneurysmal dilatation. A similar sequence of events would be possible with surgical closure if the pulmonary ligature was more effective than the aortic one in occluding the ductus. Recanalization could easily precede or accompany this process and the addition of infection could accelerate dilatation. It is known that the ductus becomes friable in the presence of pulmonary hypertension, which was present in case 3 and in the cases reported by Kerwin and Jaffe and by Milstein and Brock, and this condition may have contributed to the aneurysm formation.

Infection was present in 11 of the 17 cases. Bacterial endarteritis existed preoperatively in two cases and appeared after operation in nine cases. In six case reports no clinical or pathologic evidence of bacterial infection was described. In four of the nine patients with postoperative infection, evidence of infection antedated the appearance of signs, indicating that the ductus had recanalized. In three patients, recanalization and infection appear to have occurred simultaneously, and in one individual recanalization apparently preceded infection. Neither the onset of infection nor that of recanalization of the ductus can be dated precisely enough to permit conclusions regarding the causal relationship of these events. The absence of clinical and pathologic evidence for arteritis in six cases indicates that infection is not a sine qua non for aneurysmal formation. The two cases dying of bacterial endarteritis occurred in the pre-penicillin era. In the eight postoperative infections in which an organism was cultured, Staphylococcus was invariably present. The arteritis in case 1 was probably cured by chemotherapy 4 years prior to the removal of the aneurysm, and no evidence of infection was found in the wall of the aneurysm. It is

Figures 4 and 5

Chest x-rays, case 5, 5 weeks (left) and 8 weeks (right) after operations show progressive enlargement of the mediastinal mass.
remarkable that a cure was possible in this case in view of the persistence of suture material in the wall of the aneurysm. The infecting organism was cultured from the old ligatures in case 5 even though blood cultures were sterile before surgery.

The high incidence of staphylococcal infections in these postoperative patients is in sharp contrast to the high incidence of streptococcus viridans infections on a simple patent ductus arteriosus. Eight of the nine cases of postoperative infection were known to be due to staphylococcus, and seven of these eight patients developed symptoms of bacteremia within 2 months of operation (mean time: 35 days). These facts suggest that the infection originated at operation and persisted because of contaminated ligatures, as postulated by Bahnson, Spencer, and Bennett.1 The presence of a lag period between operation and evidence of bacteremia might be cited as an objection to this hypothesis; it is easy, however, to visualize a small, well-encapsulated suture abscess around a ductus remaining silent until a communication with the recanalized vessel lumen is established. The antibiotics prescribed in the postoperative period can be cited as a second explanation for the time elapsing between operation and clinical signs of sepsis. The persistence of infection, despite antibiotic therapy, can be attributed to the antibiotic "resistance" of the staphylococci and the potentiating effect of the foreign-body reaction about silk suture material. It is thought that the most likely source of infection in the cases of postoperative arteritis reviewed here is the inoculation of organisms on ligatures or the surgical field during operation.

The clinical picture in these cases was dictated by the presence or absence of infection. When the ductus aneurysm was infected, the typical syndrome of bacterial arteritis on a patent ductus arteriosus was present. Clinical evidence of pulmonary embolization and infarction appeared in six of the 11 infected cases and in three of the six noninfected cases. In five infected cases and in one noninfected patient, suture material was found loosely attached to the interior of the aneurysm. Foreign-body granulomata, which may have originated from suture fiber emboli, were found in the lungs of three patients. If infection was not present, the clinical findings included murmurs suggesting recanalization and rarely massive hemoptysis and hoarseness. The presence of interscapular pain in case 1 may have been a direct symptom of the forming aneurysm. The clinical evidence for formation of an aneurysm is provided chiefly by x-ray. Pulmonary hypertension was present in case 3, in the case reported by Kerwin and Jaffe,15 and in the case of Milstein and Brock.19 The presence of an aneurysm was detected prior to death or operation in eight of the 17 cases. This was accomplished roentgenographically by the demonstration of a mass in the region of the ductus (fig. 3) or by finding calcific densities suggestive of an aneurysm (fig. 1).

Figure 6

*Chest* x-ray, case 5, 16 days after excision of the aneurysm shows disappearance of mediastinal mass.
PATENT DUCTUS ANEURYSMS AFTER LIGATION

The ductus aneurysm was successfully excised in seven patients and closed by the endaneurysmmorrhaphy technic in another. The morbidity of the eight surviving patients included one emergency left pneumonectomy, the loss of the left vagus and left recurrent nerves in two cases, a possible persistent arteritis in one case, and loculated pleural effusions in one case. The mortality in these cases was 53 per cent. Three of the deaths occurred during or shortly after operation, two were due to persistent arteritis, one resulted from the rupture of a mycotic aneurysm of a pulmonary artery, and the cause is unspecified in three cases.

Summary

Five cases of postoperative aneurysm of the ductus arteriosus are presented and discussed, together with 12 from the literature. The ductus had become recanalized in all 17 patients. Infection was present in 11, having existed preoperatively in only two of these cases. The evidence suggests that contamination at the time of surgery was responsible for the infection in at least seven cases.

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References

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