Patent ductus arteriosus

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Patent Ductus Arteriosus

by

Frank L. Eagle

SENIOR THESIS

Presented To The College of Medicine

University of Nebraska, Omaha, 1941
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Introduction

During fetal life the incomplete expansion of the lungs produces a high resistance to blood flow in the pulmonary vascular bed. It is necessary, therefore, to have a compensatory mechanism whereby blood can be short-circuited around the lungs. Nature provides this shunt in the form of the ductus arteriosus, which diverts blood from the pulmonary artery directly into the aorta; this vessel originates at the beginning of the pulmonary artery and terminates in the aorta, distal to the origin of the left subclavian artery. When the fetus is born and the lungs expand, the ductus normally closes and all of the blood passes through the lung bed to be aerated, and in time the vessel becomes obliterated and known as the ligamentum arteriosum. When the duct remains patent in post-fetal life there exists then a direct communication between the systemic and pulmonary systems.

Since considerable material in the literature is in the form of case reports, a statistical analysis was undertaken, as this was considered the most efficient manner of study. Only those cases of patients over four years of age without associated cardiac lesions and confirmed by autopsy were used in this analysis; in the various divisions of this discussion, my finding from these 50 case reports have been included. Apologies must be made for the frequent repetition of Maude Abbott's monumental studies on congenital heart disease; however, her work is so outstanding on this subject that it is worthy of considerable discussion.
My interest in the subject of patent ductus arteriosus was lighted by being permitted to examine a patient diagnosed as such. Being present at the operation for ligation of the duct and examining the heart post-operatively further increased this interest. This case is discussed in the final section.

The outstanding features of this so-called anomaly appear to be: (1) incidence, (2) complications and (3) prognosis. If such a condition is so rare that one may never encounter a case, it may only be of academic interest. On the other hand if the lesion is not too uncommon, and its complications warrant such, we have a cardiac case which appears amenable to surgical ligation. In regards to a hypothetical case of a child three years of age diagnosed with a patent ductus arteriosus, one might ask:

1. What is the possibility of this child living to the age of 50?
2. What criteria are necessary to indicate surgical intervention?
3. At what age should surgery be done?
4. Will ligation prevent the complications that so frequently develop?

In other words does the diagnosis of patent ductus arteriosus mean an innocent, rare lesion only of academic interest, or does it markedly alter the prognosis of the individual unless surgical ligation is undertaken?
HISTORICAL RESUME

According to Poynter (67) and Strassmann (78), the first to describe the duct was not Leonardo Botallo (born 1530), after whom it has received its name, but Galenos who long before had described, more clearly, the duct and the changes it incurs, after birth. Galen, as quoted by Wells (85), states,

"Since there is a space between the two large vessels (aorta and pulmonary) nature has provided a third smaller one, a communicating vessel between the two."

"Whereas, as the time of birth approaches, all parts of the living being increase in size, the vessel which unites the larger artery with the lung vein does not, but instead becomes smaller than before and finally is eaten away and dries up."

Galenos had no knowledge of the true function of the duct and believed its purpose was to provide the fetal lungs with pneuma obtained from the aorta, (78, 85).

The description of Botallo, according to Strassmann (78), is unclear, and the drawing illustrating the position and insertion of the duct is inaccurate. About the same time (as Botallo's recording) the ductus was rediscovered and described by Aranzi (58).

In the sixteenth century Galenos' description was well nigh forgotten. Strassmann (78) writes that Vesalius (1542) did not mention it; however, Holman (44) quoted Vesalius, "Miratus fui quamobrem Galenus hic tam dilucide privatim meninit quo vena arterialis in magnam arteriam pertinet", as the latter's admiration for the clear manner in which Galen
had originally described the ductus. The duct was also known to Fallopia and his school, and Carcanus (1574) describes a valve at the insertion of the duct in the pulmonary artery which prevents a back flow of blood into the aorta. He also knew as did Folius, that the duct could remain open after birth (67, 78, 85).

The function of the ductus arteriosus seems to have been first correctly described by William Harvey (90) in his de Motu Cordis et Sanguinis in 1648. To quote,

"Another union is that by the vena arteriosa, or pulmonary artery, and is effected when that vessel divides into two branches after its escape from the right ventricle of the heart. It is as if to the two trunks already mentioned a third was superadded, a kind of arterial canal, carried obliquely from the vena arteriosa, or pulmonary artery, to perforate and terminate in the arteria magna or aorta. In the embryo, consequently, there are, as it were two aortas, or two roots of the arteria magna, springing from the heart. This canalis arteriosus shrinks gradually after birth, and is at length and finally almost entirely withered, and removed, like the umbilical vessels.

The canalis arteriosus contains no membrane or valve to direct or impede the flow of the blood in this or in that direction; for at the root of the vena arteriosa, or pulmonary artery, of which the canalis arteriosus is the continuation in the foetus, there are three sigmoid or semi-lunar valves, which open from within outwards, and oppose no obstacle to the blood flowing in this direction or from the right ventricle into the pulmonary artery and aorta; but they prevent all regurgitation from the aorta or pulmonic vessels back upon the right ventricle; closing with perfect accuracy, they oppose and form an obstacle to everything of the kind in the embryo. So that there is also reason to believe that when the heart contracts, the blood is regularly propelled by the canal or passage indicated from the right ventricle into the aorta."
Harvey (90) was also aware of the patency of the duct and relates how in dissecting an old mouse he thought he had discovered something new, as had Botallo years before. He writes,

"But we further observe that the passages in question are not only pervious up to the period of birth in man, as well as in other animals, as anatomists in general have described them, but for several months subsequently, in some indeed for several years, not to say for the whole course of life; as, for example, in the goose, snipe, and various birds, and many of the smaller animals. And this circumstance is what, perhaps, that imposed upon Botallus, who thought he had discovered a new passage for the blood from the vena cava into the left ventricle of the heart; and I own that when I met with the same arrangement in one of the larger members of the mouse family, in the adult state, I was myself at first led to something of a like conclusion."

Hunter in 1783 (67) was the first to publish a case with postmortem findings, although it remained for Almagro (70) in 1862 to elaborate the pathological findings into a clinical entity. In 1898 Vierordt (85) could find but 26 cases reported in the literature in which the existence of patency was established by postmortem examination. Gibson (31) of Edinburgh called particular attention to the pathognomonic murmur associated with this defect and increased the infrequency of diagnoses. All previously reported cases were fully analyzed by both Wells (85) and Goodman (31) in the early part of the twentieth century. In 1936 Maude Abbott (2) published her classical study of 1,000 congenital heart cases with a complete analysis on 92 cases of patent ductus arteriosus.
The treatment of this anomaly was seldom mentioned in the literature. However, in 1907 Munro (61) boldly suggested the possibility of surgical ligation of an uncomplicated ductus. His suggestion went unheeded by the pediatricians and surgeons until 1938, when Graybiel, Strieder and Boyer (34) reported the first unsuccessful attempt to ligate the vessel in a patient with subacute bacterial endarteritis. The first successful ligation was performed by Gross and Hubbard in August, 1938 (37). Since that time the main interest in the subject has been centered upon the surgical aspects of the problem. No less than 27 patients have been reported (16, 37, 38, 39, 80, 81) to date in the literature who have had surgical ligations attempted on a patent ductus.
It is to be emphasized that in this discussion we are here mainly considering only simple patency of the ductus arteriosus, for in nearly every form of congenital heart lesion and anomaly of the great vessels the ductus frequently remains open for compensatory purposes; but in such cases the persistence of the duct is usually over-shadowed by the other abnormalities, and the entire picture is quite different from the one under consideration.

In 1898 Vierordt (85) states that he could find but 26 authentic instances recorded in the literature, in which the existence of uncomplicated persistence of the ductus arteriosus was established by postmortem examination. These constituted but about four percent of all the recorded cases of congenital diseases of the heart and great vessels.

In 1910 Wells (85) reported 15 more cases which had not been reported nor included in Vierordt's series. Wells writes there were also about a half a dozen other probable cases in which he had not been able to obtain complete records. In his series of 41 patients only 20 reached maturity and 11 were less than one year of age. Wells states his figures gave an erroneous impression as to the frequency of persistent patency of the ductus, as many reports in the literature were not included in which a clinical diagnosis had been made without postmortem corroboration. He also was
of the opinion that quite frequently the condition was overlooked by the examiner at autopsy, for unless one's attention has been called to the possible occurrence of such an anomaly, it is easily missed in a careless or hasty examination; the usual manner of removing the heart is of itself disadvantageous, for the knife frequently severs the great vessels at or near the point at which the duct connects them.

In Poynter's monograph (1911) on congenital anomalies of the heart (67) 183 cases were listed with their author. In his study open ductus arteriosus was present in slightly more than 25% of the hearts studied, making it the third lesion in order of frequency; however, he writes that as an isolated lesion it was present in only 3.7% of these congenital heart cases.

In 1905 Ellis (26) found that there were 51 cases of cardiac defects in 3,875 autopsies at the Pennsylvania Hospital, or 1.16%; of this number 42 were patent foramen ovale or persistent patency of the ductus arteriosus.

Of 5,000 consecutive autopsies at the Massachusetts General Hospital, according to White (87), patent ductus was found 96 times, but only in 7 patients over one year of age; however, Hubbard, Emerson, and Green (47) have different figures for the autopsies performed at this same hospital.
They write in 1939 that only 5 cases of uncomplicated patent ductus had been found in 7,580 consecutive autopsies conducted over a period of 40 years.

Next to a patent foramen ovale, a persistent ductus arteriosus was considered the most frequent congenital cardiac defect by Dry (23) in 1931. Patten (63) states that patency is exceeding rare except as a compensatory mechanism, but quotes no figures. Dunn (24) is of the opinion that 21 of his 304 patients with a congenital heart lesion meet the qualifications for clinical diagnosis of patent ductus; none of his cases were supported by post-mortem examination. In a review of congenital heart lesions in Bristol school children, Perry (60) finds eight instances of clinical uncomplicated patency among 121 patients (6%). In the series reported by Muir and Brown (60) of 88 cases of congenital heart disease occurring in school children, they find no less that 23% of the total to have signs which suggest a patent duct of Botalli as the sole abnormality.

In the course of 13,115 autopsies which were performed during the period from 1889 to 1933, in the pathological department of the Johns Hopkins Hospital, there were 170 true congenital anomalies, an incidence of 1.29%. Of these 170 Leech (54) finds 75 with records sufficiently complete to be included in his study; seven additional instances of
delayed closure of the ductus arteriosus and foramen ovale were also tabulated with his findings. Of this total of 83 patients Leech finds 27 with a patent ductus; however, in only four patients over 2 months of age did the lesion occur alone.

To Maude Abbott (2) goes the most credit for her analysis of 1,000 cases of congenital cardiac defects obtained from the literature. Her classification, compiled in 1936, shows primary or uncomplicated patency of the ductus is not a rare anomaly in subjects attaining adult life. In her series of 1,000 cases, a patent duct was a complicating defect in 150 cases and in no less than 92 instances was it the primary or sole abnormality. Of these 92 primary lesions only 20 were in infants or children under 5 years of age, while the remaining 72 were in later childhood or adults.

An analysis by Bullock, Jones, and Dolley (16) of the 21,000 autopsies performed at the Los Angeles County Hospital shows an occurrence of a patent duct in 36 of the 133 congenital heart cases. Of these 36 cases the 21 with other defects were all dead before 9 months of age with the exception of one that lived to 2\(\frac{1}{2}\) years. Of the 15 uncomplicated cases 4 lived to be more than 3 years of age, while the other 11 died before 4 months of age. This study, though small and incomplete, leads one to the general supposition that uncomplicated cases are the only ones that live beyond childhood.
The relative frequency of uncomplicated patent ductus is further evidenced when one considers the number of cases that have been ligated in the past 3 years. Since Graybiel, Strieder and Boyer (34) reported the first unsuccessful attempt to ligate a patent duct in a patient with subacute bacterial endarteritis in May of 1938, no less than 27 attempts at surgical ligation have been reported in the literature. Evidently, the literature portrays an erroneous picture in regards the incidence of ductus arteriosus as a primary lesion for more patients have been operated upon in the past three years for this condition than are recorded in the literature from Hunter's first case in 1783 (67) to Wells' review in 1910 (85). Possibly earlier cases of this lesion were not reported or overlooked at the autopsy table, or the condition is now being more frequently recognized in view of recent interest and new methods of diagnosis.
Statements regarding the closing time of the duct of Botalli vary markedly in the literature and the standard text-books. In Gray's "Anatomy" (33) it states the ductus begins to contract immediately after respirations are established, and its lumen slowly becomes obliterated. Griffith and Mitchell (21) give the closing time of the ductus as one or two weeks after birth. Arey (6) says in four out of five cases the ductus becomes impervious within three months; Abbott (3) writes the duct is closed in the third week of life, and Muro (61) considers the vessel is closed by the twentieth day.

The origin of the concepts expressed in texts until a few years ago, can be traced to the first statistical study of this subject, which was published over 100 years ago by the French clinician Billard (71). This investigator collected data on the obliteration of the ductus arteriosus in a series of 128 children who died in the first eight days of life. He finds instances of the obliteration on the first day after birth. The duct was closed in over 50% of his cases on the eighth day. He therefore concludes that the obliteration of the fetal blood passages proceeded very rapidly in the first few days of life--an opinion held by a number of writers in the 18th century. The results of Billard's study were published in his "Traite des maladies de enfants nouvænes" in 1828 (71).
This work was extremely popular in its time and passed through a number of editions. In several publications of the middle of the last century Billard's figures are cited and his name is quoted in connection with them. In 1865 Bernutz confirms Billard's observation and finds the ductus arteriosus closed in 1/4 cases in a series of 21 children who died between 10 and 20 days after birth. Since this time no observer has substantiated these findings, although a number of series much larger than those of Billard and Bernutz have been collected. Thus Elsasser (1852) in a series of nearly 300 cases of first month deaths finds obliteration of the ductus in about 2% and Alvarenga (1869) finds practically no instances of obliteration before 60 days. The findings of later observers Alexeieff, Theremin, and Kucheff agree essentially with those of Elsasser and Alvarenga although they note some instances of earlier obliteration of the passages (71).

Scammon and Norris (71) compiled the following chart from an analysis of 1,095 autopsies performed upon infants from birth until one year of age.

<table>
<thead>
<tr>
<th>AGE</th>
<th>TOTAL CASES</th>
<th>OBLITERATED CASES</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 8 days</td>
<td>311</td>
<td>1</td>
<td>0.3%</td>
</tr>
<tr>
<td>8 days to 15 days</td>
<td>148</td>
<td>3</td>
<td>2.0%</td>
</tr>
<tr>
<td>15 days to 22 days</td>
<td>143</td>
<td>16</td>
<td>11.2%</td>
</tr>
<tr>
<td>22 days to 32 days</td>
<td>117</td>
<td>13</td>
<td>11.1%</td>
</tr>
<tr>
<td>32 days to 46 days</td>
<td>75</td>
<td>28</td>
<td>37.3%</td>
</tr>
</tbody>
</table>
AGE | TOTAL CASES | OBLITERATED CASES | PERCENTAGE
---|-------------|-------------------|------------------
46 days to 61 days | 57 | 27 | 47.4%
61 days to 91 days | 92 | 70 | 76.0%
91 days to 120 days | 63 | 52 | 82.5%
120 days to 365 days | 89 | 84 | 94.5%

Scammon and Norris's article also includes 187 observations by Parrot (71) on the obliteration of the vessel. Parrot finds the duct patent in 4 of 33 cases of 1 year; in 1 of 54 of 2 years; and in 17 cases of 3 years and over the duct was always obliterated.

A statistical study of autopsy material obtained from the dissection of 558 normal hearts of infants from one day to one year was reported by Christie (21). From his data he concludes that in the duct there was a rapid and uniform time of closure up to about eight weeks of age, at which point there was a marked slowing and deviation from the curve. At eight weeks 88% of his cases showed a closed duct and only 1.2% remained open at the end of one year.

Until several years ago all articles concerning the normal closing time of the ductus arteriosus have been based upon postmortem findings and their analyses. However in 1938 Barclay et al (7, 8) injected a radiopaque substance into the vascular systems of lambs delivered by cesarean section and observed the ductus underwent a "functional closure" within a few minutes after birth. However, subsequent autopsy
upon such an animal showed the ductus to be still morphologically open. The only way to correlate these findings was to assume that the ductus was functionally closed during early life by a neuromuscular mechanism which, of course, would not be operative after death (7,8,39).

After considering this review of the literature, at what age, then, can the persistence of the vessel be considered as pathologic? Leech (54) suggests that delayed closure is likely to occur by the age of 4 months or not at all. A more conservative vein was taken by Gross (38) by his stating a duct of Botalli still open after the first year of life should be regarded as abnormal.

In order to understand the reasons for the failure of the ductus arteriosus to undergo normal occlusion and involution, it is necessary to become familiar with the mechanism by which this process is theoretically accomplished. There have been many hypotheses advanced to explain how this occlusion takes place and it may be of interest to review the most conspicuous opinions. King (52) believes the compression of the duct followed the expansion of the left bronchus. Chevens (20) discredits King's view by observing the canal does not close by general flattening and apposition of its sides, as would probably be the case if it were compressed by a wide surface like that of the bronchus; he supports the
opinion that each inspiration of the infant further tightens the recurrent laryngeal nerve until the duct is permanently constricted. W. S. Forbes (30) of Philadelphia, offers an ingenious explanation to the effect the duct lies in a network of fibrous tissue attached to the diaphragm. On inspirations or descent of the diaphragm the duct is mechanically constricted allowing clot formation which eventually closes the vessel.

Cruveilhier (31) thinks the closure of the duct and its involution is brought about by pseudo-membranous adhesions, rarely by thrombus formation, and sometimes by action of both factors. The duct was supposed by Magendie to exert some change on the aorta whereby the latter became bent, and Walkhoff believes that three factors play a role, namely, (1) Change after birth, in relation of structures in thorax causing a kinking of the duct with subsequent slowing of the blood stream and final obliteration of the duct. (2) Proliferation of fibrous tissue in the intima. (3) Thrombosis (31).

Landau (85) is of the opinion the vessel collapses owing to the fact that with the first inspiration the blood is aspirated from the duct, leaving it empty, while Virchow (85) holds that there is active contraction of the muscular layers of the wall of the duct, an opinion shared by Billard and by Langer; this latter view has received recent corroboration
roentgenologically by the work of Barclay et al (7, 8).

Schultze thinks obliteration of the duct is caused by fall of blood pressure causing in turn a stagnation of blood in the vessel, a condition aided by the preponderance of contractile substance over the elastic (23). Shantz criticizes this view and adds another hypothesis to the list, believing that with the inception of respiration the thoracic viscera suffers a change in position, causing tension and closure of the duct (85).

Strassmann (78) rejects as improbable the contraction of the vessel and other changes in the vessel walls as being causes of occlusion. He writes that thrombosis of the duct is scarcely possible, and was supported in this view by Rauchfuss (75) who found in 1400 autopsies on infants, thrombosis but twelve times, and of these two were purulent. Strassmann (78) in many autopsies on human and animal fetuses does not find a single thrombus, and Goodman (85) agrees with him. Strassmann (78) calls particular attention to a valve-like arrangement of the aortic opening of the duct and ascribes to this the main role of closure of the duct.

In 1910 Goodman (85) reviews the various theories set forth and writes,

"However plausible some of these explanations may be, it is quite certain that not all of them apply to the normal process of closure of the duct. This is a physiological
process taking place spontaneously and instantaneously in every newborn child, and therefore there must be some mechanism which can be relied upon always to perform this occlusion. Any explanation which involves connective tissue proliferation must be inadequate, for the duct is patent and carrying on its full function up to the moment of delivery, and then is at once occluded when the child begins to breathe; it is necessary to distinguish between the instantaneous occlusion of the duct and its subsequent obliteration. All the hypotheses that are based upon the intermittent pressure from the respiratory act are obliged to assume the formation of thrombi to account for the permanence of the occlusion, since intermittent respiratory motions would only produce an intermittent form of occlusion, and hence these views must all be incorrect. What seems to be the proper explanation is the outcome of the investigations begun by Zuntz and carried on by Strassmann. Zuntz observed that at the aortic opening of the duct in full term animals there is present a thin, crescentic fold along the upper margin, which is formed through the manner of insertion of the duct into the aorta; this insertion is at an extremely acute angle, about 33 degrees, so that the margin is thinned out to form the fold. This observation was extended by Strassmann to foetuses of various species, including human, and investigated experimentally and microscopically. Zweifel corroborated the correctness of these findings in the human fetus, and the work has received further support from Roeder.

Kirstein (85) believes that Strassmann's "valve-like" structure is more or less mythical, as does Munro (61). He devises several interesting experiments which prove to his mind that such a structure could not possibly exist, and that the ascribing of the closure of the duct to the action of this was based on wrong foundation. A compensatory endarteritis as a possible factor was first mentioned by Kirstein. The theory of pressure changes and an obliterating endarteritis is the explanation given at the present time by text books such as Holt and McIntosh (45). Schaeffer's experimental
dissections of postfetal pigs further corroborated Kirstein's view (72). He finds a hypertrophy of the internal elastic membrane and these elastic fibers play an important part in the occlusion of the lumen of the postfetal pig ducti. The changes found to take place histologically were similar to endarteritis obliterans. Patten (63) considers the normal occlusion of the ductus to be a gradual and progressive affair; he sees the occlusion of the vessel as an active process as indicated by prodromal histological changes evident in its intima in fetuses which died without breathing, and consequently were never subjected to postnatal living conditions. The duct sometimes closes in individuals with congenital defects of the heart of a type in which the persistence of the ductus would obviously increase the changes of survival, which also suggests an active process to Patten (63).

The roentgenological experiments of Barclay et al (7, 8,) on lambs injected with thorotrast show a functional closure of the vessel within several minutes after birth. This vessel does not appear to close by a simple contraction of its walls, but by the action of individual localized bundles of muscle fibers. This produces twisting and kinking of the lumen which leads in most instances, to loculation and beading of the contents. For as long as their records were taken (one hour),
though the ductus was functionally closed, contractions of its walls continued, as shown by the variation in the size and distribution of the beads and other traces of thorotrast occluding the lumen of the vessel.

After this review of the theories regarding the normal occlusion of the duct, one must then consider the cause for persistent patency. From postmortem records it appears that this embryonic shunt between the pulmonary artery and the aortic arch persists into postnatal life in over two-thirds of the cases as a compensatory mechanism. Thus, if there is obstruction at the aortic valve from bicuspid or stenotic leaflets, or if there is coarctation of the aortic arch, the ductus may remain open and allow blood to escape from the pulmonary artery to the aorta. Such a combination is rare, and when it does occur, it is necessarily accompanied by some degree of cyanosis. A second compensatory mechanism is concerned with stenosis or atresia of the pulmonary valve or hypoplasia of the pulmonary artery, wherein the direction of blood flow through the ductus must be from aorta to pulmonary artery. In this latter type of case there are usually other associated anomalies, the most frequently encountered combination being the tetralogy of Fallot in which there are stenosis of the pulmonary valve, a defect of the interventricular septum, hypertrophy of the right ventricle, and a right
sided aorta (1, 2, 3). Persistent patency upon a compensatory basis is of interest in this discussion, only in so far as it concerns the differential diagnosis.

Gerard (31) says the following causes may be of influence on the patency of the duct.

1. Anomalies in the circulatory physiology.
2. Anomalies in the respiratory physiology.
3. Absence of the processes of obliteration.

Wells (85) carefully analyzed early literature and imagined the duct may fail to become occluded for one of the following three reasons:

1. When the insertion of the duct into the aorta forms a less acute angle than normal, the condition necessary for the formation and functionation of the membranous fold of Zuntz and Strassmann (78) at the aortic orifice of the duct are not present.

2. Premature birth, as the fold is not completely developed until the end of the eighth month.

3. Respiratory difficulties in the newborn or stenosis of the pulmonary arteries, or atelectasis, by increasing the pulmonary pressure, may be a cause.

It is believed by Virchow that patency may be divided into two classes; those cases in which the duct had never closed and those in which after having become occluded, has again become patent (78, 85). This secondary patency was said to be produced by these two ways:
1. If after birth the duct has become occluded, the pulmonic pressure is raised as by bronchitic, atelectasis, pleural effusion, etc., the blood may be forced through the duct and the walls having become weakened by the degenerative changes going on during obliteration the duct remains permanently patent. In long labor or difficult instrumental deliveries the intima is commonly damaged but may remain so with no evil effect on the child so long as there is no intercurrent affection to raise the pulmonary blood pressure.

2. The fibrous obliterations may be faulty, though of long standing, and as the child develops and the blood pressure increases, the valve-like arrangement at the aortic orifice may give way, and the entering blood gradually forces open the old canal.

The majority of recent writers (2, 3, 16, 38, 75) deny or fail to mention this membranous fold of Zuntz and Strassman (78) in discussions on etiology. However, Leech (54) found a higher incidence of patency in premature infants which is in agreement with Goodman (31); the latter having considered this being produced by the absence of formation of the fold, which was supposedly not developed until the end of the eighth month.

Gross (38) agreed with Wells (85) that the anatomic position and direction of the vessel is an important etiological factor. Gross says,

"If one examines postmortem material of infants who have died in the first few months of life, the ductus, or its obliterative remnant, sweeps backward and to the left with a gradual curve to run alongside the aorta and then to enter it at a rather acute angle. The nature of this angle of entrance into the aortic arch in the fetus obviously has the
function of directing the oxygen-deficient blood from the right ventricle downward in the aorta so that it might be distributed to the hypogastric arteries and thence to the placental circulation. The sharpness of this angle must serve another purpose, namely, to help obliterate the ductus in postnatal life. At birth, when the lungs expand and the blood flow through them increases, a diminishing amount of blood is forced from the pulmonary artery into the ductus. When this state of affairs obtains, the arterial blood rushing around and down the aortic arch must now have somewhat of a sucking action on the ductus which enters it so acutely. This sucking action would tend to collapse the vessel. If, however, the ductus joins the arch at a more obtuse angle or at a right angle, the lumen of the ductus will be subjected directly to the high pressure existing in the aortic arch, and the ductus will thereby be kept distended. Thus, it is probably correct to believe that the principal reason for persistence of a ductus is due to its anomalous position and direction."

The smooth muscle fibers in the ductal wall of some animals have been shown to be under vagus nerve control (38). Barclay, Barcroft, Barron, and Franklin (7, 8) from their roentgenological experiments on lambs believe the ductus undergoes a "functional closure" within a few minutes after birth; however, subsequent autopsy upon these animals shows the ductus still to be morphologically open. Gross (38) interprets these findings by assuming the ductus is functionally closed at birth by a neuromuscular mechanism; he does not believe the ductus to be held in a state of obliteration throughout the newborn period by smooth muscle contraction alone. He is of the opinion the smooth muscle contractions assist in the closure of the ductus and tends a deficiency in the neuro-muscular apparatus tends to make morphological obliteration more difficult.
Another possible factor which might contribute to the persistency of a ductus is some defect in its wall. This deficiency may concern the internal elastic membrane, the elastic tissue of the media, or even the smooth musculature. Such deficiencies of the ductal wall would allow the vessel to distend under low internal luminal pressures which would not distend a vessel possessing normal elasticity. Such a consideration is hypothetical, for there is no published account of histologic examination of the wall of persistent ducti as compared with those which are normally closing in the first or second month of infancy. That a thin or deficient wall might be a factor in persistency in some instances is also supported by those cases in which the ductus have actually dilated to aneurysmal proportions (2, 25, 73); mention is made by Gross (38, 39) that the ductus in one operated patient was as thin as an ordinary vein.

Heredity seems to play an important part in all forms of congenital heart disease, and it may be concerned in this particular form of circulatory malformation, as shown by the family studied by de la Camp (85). In this family of six children all showed clinical evidence of having persistence of the ductus arteriosus. In a few cases (13, 43, 85) there have been observed other developmental defects, suggesting that the arterial abnormality might be due to defective developmental forces; Poynter in 1919 considers the tendency is to
explain the majority of cardiac irregularities as due to arrest of development caused by a variety of factors, although he makes no specific mention concerning patent ductus arteriosus. Leech (54) is of the opinion that repeated pregnancies had no relation to the instances of delayed closure.

Wells (85) is one of the first to mention the preponderance of females with a patent ductus; his analysis showed a ratio of females to males of approximately 2:1. Maude Abbott's series of 92 cases showed a similar ratio. The total surgical cases show a ratio of 4:1 (16, 34, 37, 38, 39, 80, 81), and my analysis of 50 give a ratio of 3:1. Several authors consider the preponderance of females with this anomaly to be merely a matter of change (43, 77). However the statistical studies are rather convincing and no explanations have been offered in the literature for this apparent female preponderance.
In fetal life nature provides a shunt in the form of the ductus arteriosus which diverts blood from the pulmonary artery directly into the aorta; this has been known since the time of Harvey (90) and was recently corroborated by roentgenological studies on mammalism fetuses (8). When the fetus is born and the lungs expand, the ductus normally closes and all of the blood passes through the lung bed to be aerated.

However, when this communicating vessel remains patent after birth, is there a change in the direction of flow? Owing to the position of the abnormal communication between the two great trunks above the valves (which close simultaneously) the pressures in the columns of fluid on either side of the opening should theoretically become equalized and no shunt take place (3). At birth the pressure in the pulmonary artery is suddenly reduced from a value of about 80 mm. of mercury in the fetus to a lower one, of from 6 to 60 mm. of mercury in the adult as compared with 80-150 mm. of mercury in the aorta (4), Durno and Brown (25) assume that the aortic pressure is transmitted via the ductus to the pulmonary circuit so the pressures are the same in the aorta and the pulmonary artery. The majority of writers do not agree with this view (2, 3, 14, 16, 17, 36, 37, 85, 86): instead, they assume that in persistent patency a continuous
leakage takes place from the aorta (in which the pressure is normally much higher than in the pulmonary artery) into the latter, an arterial-venous shunt existing. They also consider these relative pressures are maintained, in spite of the open communications between the two circulations, until some cause for respiratory obstruction sets in, such as long-continued crying, spasmodic coughing, etc., which raises the pressure in the pulmonary circulation and causes a temporary reversal of flow through the canal with the sudden appearance of a transient cyanosis, which passes off with the exciting cause (4, 16, 36, 37). That the course of the blood is from left to right through the canal under otherwise normal conditions is evident from the pathology of these cases, for the pulmonary artery is most often dilated and the left ventricle is hypertrophied more frequently than the right (3, 85). Moreover, in the infective processes that frequently supervene the pulmonary end of the ductus with the immediately adjacent tissues is most always the initial seat of the vegetative inflammatory lesion, a very suggestive feature as indicating that this point has been the seat of strain in the continuous passage of a left to right shunt through the defect (2, 4). The arteriovenous shunt hypothesis is corroborated by an experiment chanced upon by Brooks (14). In one dog he determined the carotid blood pressure and found that during expiration it rose and
during inspiration it fell, results exactly contrary to the respiratory variations in the normal animal. It must be supposed that inspiration lowered the resistance in the pulmonary circuit, caused an inflow of blood into the pulmonary artery, from the aorta (an arterio-venous shunt), and so lowered the carotid blood pressure while expiration produced an opposite effect; this latter effect, however, was not of sufficient degree to reverse the shunt, at least in no important degree, for no cyanosis of the mucous membrane was observed. At autopsy of the dog a widely patent ductus was observed.

What is there for further evidence of the existence of an arterio-venous shunt in patent ductus patients, and what suggestions may be made to explain the transient cyanosis that sometimes occurs? If Durno and Brown are correct (25), there is evidently no reason why the blood should flow from either the aorta into the pulmonary artery or from the pulmonary artery into the aorta. Let us consider the effect of exertion. The systemic blood pressure rises rapidly, but the pulmonary pressure probably does not rise, providing the respiratory movements are not hampered. Blood, therefore, passes from the aorta into the pulmonary artery where these vessels communicate and in greater degree from the left ventricle into the right. Ill results follow. The tissues
do not get the increased supply of blood which they demand from the left heart, because it leaks away faster than usual into the pulmonary circuit. The right ventricle has to work against an unusual distension of its chamber or an increased pressure due to congestion of the pulmonary circuit; the mechanical result is the same, additional overwork for the musculature of the right ventricle. If the exertion be great the pulmonary circuit is congested with blood, which may stimulate the vagal endings in the lungs and interfere with the normal sequence of respiratory movements. The pulmonary blood pressure is raised; lung edema is a possibility; and cyanosis may result from insufficient oxygenation of the blood in the lungs by a lengthening of the diffusion path of the oxygen traversing the alveolar and capillary walls toward the carrier red blood cells (4).

The epic experimental work of Eppinger, Burwell, and Gross (17, 28) in substantiating the arterio-venous shunt produced by a patent ductus is outstanding. They state, conclusions from 5 dog experiments:

1. After the establishment of the aortic-pulmonary artery connection the oxygen content of the blood in the pulmonary artery is always greater than that in the right ventricle. Therefore, the blood flow through the shunt is toward the pulmonary artery.

2. In two dogs, a comparison of the oxygen content of the blood from the right and
left branches of the pulmonary artery at the hilus showed an approximate identity, indicating adequate mixture.

3. In each case, the shunt from the aorta to the pulmonary circulation was more than 50% of the output of the left ventricle; the output of the left ventricle, therefore, was more than twice that of the right. In one animal the shunt was 75% and the left ventricle was putting out four times the output of the right. The situation in this dog was essentially the same 8 weeks later.

4. In some animals, the left ventricle output was not greatly increased but the flow of blood to the periphery was diminished. In others the output of the left ventricle increased to such an extent that the volume expelled by the right was less severely reduced.

Their observations made on six patients subjected to ligation of patent ducts arteriosus by Gross (38) were comparable to those studies in dogs and were summarized as follows:

1. When the ductus arteriosus is open the blood flow is from the aorta to the pulmonary artery.

2. There is no flow of blood from pulmonary artery to aorta. Therefore, these patients do not have arterial unsaturation and are not cyanotic.

3. The volume of blood flowing from aorta to pulmonary artery varied from 4 to 9 liters per minute, which is 45% to 75% of all the blood pumped into the aorta by the left ventricle. These flows occurred in patients with large ducts and under temporary conditions which are known to elevate the output of the heart.
4. The left ventricle expelled from 2 to 4 times the volume of blood expelled by the right ventricle in a given period of time.

5. Adjustment of the circulation to the patent ductus may be made by an increase in the output of the left ventricle. If this is not sufficient to compensate completely for the leak through the ductus, there may be, in addition a diminution in the blood flow to the periphery.

The amount of blood passing through the ductus per unit of time has been calculated by Plesch (21); however, he uses a method which in light of present knowledge is not valid (17, 21). In persons with no abnormal connection between the peripheral and pulmonary circuits the volume of blood passing through the lungs is essentially the volume of blood put out by the right ventricle, which is necessarily the same as the volume put out by the left ventricle; however, when a patent ductus permits the passage of blood from the aorta to pulmonary artery, the output of the right ventricle is made up of blood which comes to this ventricle from the peripheral circulations and from no other source.

The output of the left ventricle in patients with patent ductus arteriosus is made up of two components---the blood from the right ventricle and the blood entering the pulmonary artery by way of the patent duct. These confluent streams pass through the lungs and enter the left side of the heart. Since the blood entering the lung capillaries is thus only partly blood from the right ventricle, the oxygen content of the
right ventricle cannot be used in calculating the pulmonary flow. If there are at hand figures expressing the oxygen consumption per minute, the oxygen content of arterial blood, the oxygen content of mixed venous (right ventricle) blood, and the oxygen content of the mixed arterial and venous blood in the pulmonary artery, the output of each ventricle may be calculated. Obviously, the difference between the outputs of the two ventricles is the volume of the blood which passes through the ductus. It is this method and line of reasoning that is used by Eppinger, Burwell, and Gross (17, 27). However, they maintain the cardiac outputs of the patients examined are not basal. They were determined during cyclopropane anesthesia, and when the chest was open, so this is evidence they were much above the basal level. They conclude the work of the right ventricle is probably not greatly altered since it is not pumping more than the usual amount of blood and may be pumping less. The pulmonary pressure against which this blood is pumped may be elevated to some degree in the presence of a patent ductus, but probably when the lungs are normal this increase is not great (28). It is not possible to make precise calculations of the work of the left ventricle; however, it is probably justifiable to conclude that the work of the left ventricle is considerably increased (17, 27, 28).

Holman (38, 43, 44) is the only author considering that
the flow in a patent ductus arteriosus may be either arteriovenous or venoarterial on a permanent basis. He postulates that with the venoarterial type a larger volume of blood flows through the right heart than through the left. From a physiological point of view, this half of the heart would develop more fully than the left, this development being a response to the increased flow of blood through this part of the heart. This increased flow requires increased effort, and hypertrophy will inevitably result if the increased flow is large and if it is permanently maintained. Sixteen cases are cited from the literature in which the right heart shows an abnormal development, in most instances equal to, and in several cases in excess of, the left heart; in these cases the ductus was on the average of smaller caliber than his arteriovenous fistula cases with left ventricular hypertrophy. Holman maintains it is self-evident that the propulsive forces exerted by the hypertrophied preponderant right ventricle would produce a greater blood pressure in the pulmonary artery than the pressure produced in the aorta by the less well developed left ventricle; under such circumstances the direction of blood flow could only be from pulmonary artery to the aorta (43, 44). The experiments of Levy, Blalock, Eppinger, Burwell, and Gross (17, 27, 28) contradict Holman's statement, and their experimental work shows that even when a powerful left ventricle is pumping
large volumes of blood into the pulmonary artery, the pressure in the pulmonary artery does not rise to anything like that in the aorta; their explanation is that the resistance in the lung is much less than in the periphery (28). The frequency of aortic sclerotic changes and aneurysms of the aorta is used by Holman as indications for his so-called venoarterial fistula with a patent ductus (43).

The length and diameter of the ductus, as well as the thickness of its wall, have considerable bearing on the prognosis, complications, and its possibilities of surgical ligation. Unfortunately, the literature gives but scanty accounts of desired anatomic facts. In most instances the internal diameter of the lumen is about all that is listed. The following verbatim descriptions are gleaned from my analysis of 50 cases.

1. **Kidd**—Size of goose quill.
2. **Murray**—Size of ordinary quill.
3. **Thomson**—One-quarter of an inch long and admitted a No. 4 catheter.
4. **Walsham**—One-half inch long and one-quarter of an inch in diameter. Size of No. 4 catheter at pulmonic orifice.
5. **Wasastajerne**—Round lumen with 1.2 cm. diameter.
6. **Duroziez**—Ductus opened by orifice size of large pea.
7. **Luys**—Ductus orifice admitted index of little finger.
8. **Schnitzler**—Aortic opening 6 mm.; pulmonic opening 5 mm.
9. **Josefson**—Pulmonic orifice round and 4 mm.; aortic orifice oval and 10x6 mm.
10. **Mead**—One cm. in length; aortic orifice 10 mm.; pulmonic orifice 4 mm.
11. **Gibson**—Opening admitted a 12-1½ bougie.
12. **Schrotter**—Circumference of 3½ cm. Large as branches of pulmonary artery.
13. Foulis------------Narrowest diameter $\frac{3}{8}$"; size of goose quill at pulmonic orifice.
15. Gaylor------------Aortic end 6 mm. in diameter.
16. Crouzet----------Internal circumference 19 mm. or equal to innominate. Admitted a penhandle 6 mm. in diameter.
17. Thompson and Drummond---------Diameter of $\frac{3}{8}$".
18. Wasastjerna-------Lumen as large as thick as pencil.
19. Murray-------------3$\frac{3}{8}$" long, Truncated cone. Admitted ordinary goose quill.
20. Gerhardt----------Circumference and length were 2 cm. Width of canal equal and admitted a thin scalpel.
21. White-------------Size of anterior tibial vessel.
22. Drasche----------Admitted 3 mm. thick probe.
23. Brady and Asher----------14 mm. long; 4 mm. diameter at pulmonic and 9 mm. in diameter at aortic opening.
24. Griffith---------Passed no. 9 catheter.
25. Stoddard--------5 mm. diameter at aorta.
26. Trimble----------1.5 cm. in length; 5 mm. in diameter.
27. White-------------2.25 cm. long; 1 cm. diameter at aorta and 4 mm. at pulmonic orifice.

From these descriptions one gathers only about 50% of the reports give the meagerest of information concerning the anatomical dimensions of the vessel.

In his classical article upon this subject Gerhardt (85) divides the forms assumed by the duct itself into four groups, as follows:

1. Extreme shortening of the canal, so that it forms little more than the margin of the opening in both vessels.

2. Funnel shaped, with the wide end toward the aorta.

3. Cylindrical form, the duct being variable in length and width.
4. Aneurysmal dilatation of the canal.

Of these forms, by far the most common are the second and third types (2, 75, 85), in which there is a definite duct, as may be seen by the previously mentioned descriptions. Even in the cylindrical type the aortic orifice is generally larger than the pulmonary opening, so there is more or less approximation to the funnel shape in the great majority of cases.

The length of the ductus is of great importance, for if the vessel is very short, dissection between the aortic arch and the pulmonary artery may be impossible. In some adults as in the case cited by Mallory (55) the ductus is so short that a direct communication exists between pulmonary artery and aorta—an anatomic arrangement which would make it practically impossible to close the shunt by surgery. In newly born infants the ductus is usually 1 to 1.5 cm. long (38). In those cases subjected to surgery (16, 39, 81) the ductus varies from 5 to 12 mm. in length. The thickness of the vessel's wall also varies; it is gathered from autopsy descriptions that the vessel is usually about as thick as an artery of similar size. (87). In one case, Gross (38) cites, considerable hemorrhage resulted from the manipulation of the ductus and the vessel was seen to have the consistency of a vein; in rare cases during an apparent normal life a thinned-
out ductal wall may dilate (23) and rupture (59). Earlier authors agree the ductal wall is deficient in elastic tissue as compared with the aorta and pulmonary artery, but D'Aunoy (22) finds the vessel contains a well-developed system of elastic fibers. Abbott (2) finds 13 cases of ductal aneurysms reported in the literature prior to 1936. That thrombosis of the ductus may occur in adult life is proved by Jäger's recent necropsy report (48); in this patient embolism had occurred into the superior mesenteric artery. A double ductus is reported by Salzer (3).

Even in the simplest cases the heart is usually more or less affected, as this arterio-venous shunt naturally throws an increased burden upon the heart (2, 17, 28, 73). Abbott's analysis of 92 cases shows right auricular hypertrophy in 21; right ventricular hypertrophy in 52; left ventricular hypertrophy in 49; and left auricular hypertrophy in 20. My analysis of 50 reports shows: right ventricular hypertrophy in 13; and left ventricular in 10.

Three cases of left ventricular atrophy are reported and two right ventricular atrophy cases are written in the literature (18,43). Postmortem findings of cases by Thomson, Walsham, and White (79, 83, 88) indicate a normal heart.

In view of these statistics on case reports certain
explanations are necessary. The left ventricular hyper-
trophy is ably explained by Burwell et al (17, 28). He
states,

"Obviously the patient with a patent ductus
arteriosus is between the devil and the deep blue sea;
either he must suffer a decrease in the blood supply to the
periphery or there must be an increase in the output of the
left ventricle sufficient to compensate for the shunt.
This necessitates left ventricular hypertrophy."

This explanation is held valid by the majority of writers
(2, 16, 17, 27, 28). However, what is the explanation for
the frequency of right ventricular hypertrophy, especially
in those cases where this side predominates over the left?
Durno and Brown (25) write that the right sided hypertrophy
is the attempt of nature to raise the pressure in the pul-
monary artery until it is equal to that of the aorta.
Schlaepfer (73) is of the same opinion, as is D'Aunoy and
Von Haam (22). Holman (43) explains these cases of right
sides hypertrophy upon a venoarterial shunt. In regards
cardiac hypertrophy, Patten (63) writes that following the
increase in pulmonary circulation and the closure of the
fetal blood passages there is a gradual increase in the left
ventricular muscle to equal the right at about the third
to fifth months; the left heart acquires a definite prepon-
derance by the second year and its full degree of prepon-
derance by the seventh year. In criticism of Holman's
venoarterial fistula theory, Eppinger, Burwell, and Gross
(27, 28) agree that most observations of right ventricular preponderance were seldom found after the age of infancy with an uncomplicated patent ductus, which would be a normal state of affairs as judged by Patten's experiments (63) and Leech's autopsy findings (54). It is true that all but one of the cases cited in Holman's 1937 article (44) are infants from one day to 10 months of age; however, in his original paper (43) he includes many reports of adults with right ventricular hypertrophy. Wells (85) writes,

"There is almost always some degree of hypertrophy of the right ventricle, and frequently dilatation, because of the obstruction to the emptying of the right ventricle caused by the inrushing arterial current."

This is the explanation held by several recent authors (1, 17, 38). Dawson and Abbott (24) add that the increased pressure in the pulmonary artery may force blood backwards into the right ventricle, even though the pulmonary valves be competent for a normal pulmonary pressure. This increase in work because of this direct communication must limit the cardiac reserve and in the long run may be a factor in the onset of failure of the left ventricle (3, 27, 73). Needless to say it would appear likely that the development of heart failure depends on the magnitude of the shunt and the extent to which it increases the normal load of the heart. That cardiac failure does occur in these patients is corroborated by case reports (39, 73, 83). Abbott (3) lists 13 deaths as produced by cardiac insufficiency.
As would be expected from the constant forcing of arterial blood into the pulmonary artery, the following line of pathological events may occur: dilatation with sclerosis of the pulmonary artery, aneurysms or endarteritis and endocarditis. Abbott's (2) 92 cases show the pulmonary artery to be dilated in 43 instances and hypoplasia is present in one. In my series dilatation is to be seen in 9 and sclerotic tendencies recognized in three.

Most authorities agree the aneurysms are produced by the constant pounding of the blood from the aorta into the pulmonary artery via the patent ductus (22, 54, 73), although Durno and Brown (25) consider the increased pressure is produced by the hypertrophied right ventricle. Costa (22) finds that in 46.5 of all pulmonary aneurysm cases some evidence of congenital defect could be found, the most frequent being persistent Botallo’s duct (20%). Very precise is the explanation of Krzyskowski (73) who considers the open Botallo’s duct as the most important factor in the formation of an aneurysm of the pulmonary artery. The degree of injury is dependent upon the force of the blood stream which, in turn depends upon the width of Botallo’s duct. In Krzyskowski’s case the aneurysm formed opposite the opening of the duct into the pulmonary artery. The inevitable result of this continuous localized injury and finally destruction of the wall
of the artery. Foulis (43) also emphasizes the width of the duct as an important factor in the formation of an aneurysm. One should not over emphasize the possibilities of aneurysm formation, as they are indeed rare. Costa (25) saw the condition only once in 20,000 autopsies at the Institute of Florence, and only 8 cases have been reported in the American literature (22, 25, 59, 73). Moench (59) states pulmonary aneurysms are more frequent in females. Von Schrotter (22) even makes the statement in 1901 that no aneurysms of the have been reported in the literature, but that all cases reported were merely of dilatation, "though some of them to a marked degree."

Because of the constant trauma to the pulmonary vessel opposite the patent ductus endarteritis or endocarditis may occur. Nineteen of Abbott's cases (2) were infants less than 2 years of age. For our immediate purpose these may be excluded from the series on the grounds that subacute bacterial endarteritis does not occur in infants (47), and that in early infancy it is difficult to determine whether we are dealing with a pathologically patent ductus or a delayed physiological closure. There remains, then, 73 cases, of which subacute endarteritis and endocarditis was shown to be present in 22. This gives an incidence for her series of 30%, but it is important to realize that this is a series of cases taken
from the literature. They present a striking clinical and pathological picture, and as such are obviously more apt to be reported than cases of patent ductus arteriosus where death was due to other causes (47).

There is a definite localization of the vegetative endarteritis in the pulmonary opposite the ductus opening and to the ductus wall (2, 65, 76, 82). There being recorded no less than 5 cases in which the vegetations are localized to the walls of the pulmonary artery in this situation without any involvement of the heart valves or aortic wall. These are the ones of Krzyskowski (73), Hamilton and Abbott (40), Schlaepfer (73), Philpott (65), and Gordon and Perla (32). Microscopic examination of Hamilton and Abbott's case (40) shows the pulmonary orifice of the ductus to be the oldest, and therefore the initial seat of the lesion. The location of the vegetations may be reasonably explained on the basis that the intima of the vessel walls at or near the ductus orifice is subject to sclerotic changes.

Grant, Wood, and Jones (73) have shown that such sclerotic areas favor the formation of platelet thrombi, which in turn become infected with bacteria in the blood stream, giving rise to bacterial endocarditis. Horder (46) suggests the predisposition to endocarditis in congenital lesion is best explained by the existence of chronic thickening of the
endocardium. Boldero (9) also maintains the thickened endocardium is a suitable culture media for bacteria present in the blood stream. However, Boldero (9) mainly emphasizes that frequency of endocarditis with patent ductus is due to the mixture of arterial blood in the right side of the heart. He regards the frequency of left-sided endocarditis and the imminity of the right side to infection to the fact that the arterial blood is the more favorable medium for bacterial growth; it being, undoubtedly true, that dextral endocarditis is more common in those congenital lesions that allow arterial blood to reach the right side of the heart (76). Hamilton and Abbott (40) mention the possibility of infected emboli in the vasa vasorum of the affected portion of the pulmonary artery; in minute tears of the intima resulting from mechanical strain, an infection with subsequent thrombosis may start through circulating micro-organisms.

Boldero (9) says the pulmonary valves most frequently escape; on the other hand Schlaepfer's analysis (23) shows an involvement of the pulmonary valves in 9 out 19 case studies. In the cases with a pulmonary or other valvular lesion the arteritis in the pulmonary artery is most always accompanied with thrombosis. The thrombus generally involved the anterior wall of the artery. In Foulis' (42) case the thrombus is more adherent to the left side of the stem of the
pulmonary artery. Kidd (40) finds a crop of warty vegetations attached to the posterior side of the pulmonary artery; he is the only author who does not stress the fact that the anterior and the upper walls of the stem of the pulmonary artery are the seats of the inflammation. In all instances the vegetations are described as soft and polypoid. Boldero (9) notes that in his case, the thrombus completely occupies the lumen of the vessel.

The aortic valve is damaged in the majority of cases. Many observations in which the mitral orifice is inflamed also show a lesion of the aortic valve. The aortic vegetations were the only lesion in the left heart in the cases of Kidd, Schlagenhaufer, Hart, Terplan, and Boldero (9, 68, 73). In all instances the lesions were acute except in Babington’s patient (73) in whom the ring was stenosed by calcified vegetations. The tricuspid valve was bordered by fresh vegetations in Murray’s case (62) with similar lesions on the mitral and the aortic valve.

What of the complications that may involve the aorta because of the patent ductus. Rokitansky (73), as does Hamilton (4) in one case, repeatedly notices a narrowing of the descending portion of the aorta; no explanation is given. Some findings of note deal with changes in the aorta in the vicinity of the opening of the duct. In Foulis’ case
(43), a saccular aneurysm with atheromatous changes is found opposite the mouth of the duct. An analogous observation is noted by Hochhaus (73). The inside of the sac is filled with small thrombi which are adherent to the wall. Rickards (43) notices similar adherent thrombi in the same location without any aneurysm formation. In answer to a question concerning the cause of such aneurysms of the aorta, Burwell (28) replies:

"In answer to this question, I am sure I do not know why patients with a patent ductus arteriosus develop an aneurysm of the aorta opposite the orifice of the patent ductus."

The first writer to emphasize the rather common marked sclerosis of the aorta just about the orifice of the duct is Wells (85). However, a fold arising from the aortic wall central to the opening of the duct, protruding into the lumen of the aorta, is previously noted by Babington, Buchwald and Hochhaus (73). Sclerosis and calcification of the aorta opposite the ductus is reported in several recent articles (3, 48, 62, 84, 87). Jager (48) examined the aorta in this area in 50 postmortem studies on adults, and calcified plaques are present in the aorta at this site in 29 instances. Non-calcified plaques are found in 9 cases in this same region at the site of the ligamentum arteriosum; however, other and at times larger atheromatous lesions are frequently found present in the aortic arch. In White's case (87) there is also marked calcification in the remainder of the aorta.
There is another complication of patency of the ductus arteriosus which may be briefly mentioned. Three cases by Mead, von Schrotter, and Chester (57, 79) are on record in which aphonia was attributed to pressure on the left recurrent laryngeal nerve. The first two are confirmed by postmortem examinations, although in Mead's case (57) the nerve shows no degeneration with Marchi's stain.

Associated congenital anomalies are relatively rare. The absence of a kidney is Kingsley's patient (53) and a polycystic kidney of Brody and Randall's report (13) are the two associated congenital defects encountered in my review of the literature. Abbott's analysis (3) shows associated anomalies in 13 of 92 cases.
Cardiologists, with any breadth of experience, have examined and cared for adults who have patent ducti and yet lead rather normal lives (4, 16, 38, 39, 87). In fact, the case reports by Brody and Randell, White, and Jofeson (13, 87) are on patients over sixty-five years of age. There is a general feeling that more of these cases are seen in childhood or adolescence than are encountered in the latter half of life (3, 16, 38, 54). One of two things must happen. Either these people grow up and die of their lesion after having been lost sight of, or else they have spontaneous closure of the ductus during middle life. Hamilton and Abbott (40) tell of a patient they followed from birth until he was 12 years of age; they examined him every six months and his murmur was always less pronounced until it disappeared when he was 9 years old. Nine cases of 21 under observation by Dunn (24) had their murmur and thrill disappear between the ages of 10 and 16. The disappearance of the murmur is taken by Dunn to indicate delayed closure of the ductus has taken place, and he places a favorable prognosis on these patients. A primary open ductus is viewed by Stoddard (77) to carry a favorable prognosis with an indefinite term of life. He suggests that only those open ducti patients with associated cardiac lesion die before one year of age, but adds,

"In spite of all that has been written on the subject, conclusions may be tentative until the extraordinarily small number of cases carefully and thoroughly observed is much increased."
Abbott (2) says the "expectation of life" in these patients is good under proper precautions and considers them only as "potential cardiacs."

Opposed to this preceding, rather optimistic view, one also finds a darker side when reviewing the literature on the subject. Numerous case reports are encountered describing patients who were known to have a patent ductus without apparent disability throughout adolescence, but who then dies of decompensation or subacute bacterial endocarditis (5, 15, 42, 46, 48, 56, 64, 84). Mallory's case (55) is on a boy 12 years of age who dies in cardiac failure within one hour after entering the hospital; he had been ill less than two weeks and symptomless prior to this time. Abbott (3, 4) lists 92 patients with autopsy proof of patent ductus. Twenty-eight of these died of subacute bacterial endocarditis, 24 died of slow cardiac decompensation, and 16 died of rather sudden cardiac failure. In this series, then the incidence of death from endarteritis or endocarditis is 30% and the incidence of cardiac decompensation is 43%. The average age of death was 24 years. In my series the average age at death is 29 years, and the incidence of endocarditis is 35%. Bacterial endarteritis rarely if ever occurs in infancy; if infants are included in a series, the hazard of this complication in later life is made to appear less important than it actually is.
Hubbard, Emerson and Green (47) in a series of 39 autopsied cases collected from the literature, found the youngest patient with infection to be 6 and the oldest 51. In other words, it is only by eliminating these younger cases from the series that the hazard of bacterial infection (at an age when surgical intervention would normally be considered) can be properly estimated. Therefore, in order to determine the expectation of life without operation, Bullock et al, have reviewed the original reports of 76 cases from the literature. They limit themselves to the cases in patients over the age of 3 years proved by autopsy to have no other significant cardiac anomaly. They find,

"By the age of 14, eleven (14%) of the patients had died from their heart lesion. By the age of 30 years, one-half were dead; by the age of 40 years, 71% were dead. Eighteen patients (23%) died of congestive failure, five (6%) of rupture of the ductus or left ventricular failure, forty-two (53%) of bacterial endarteritis, and in four (5%) there was an associated cause of death, but the heart lesion was obviously an important factor. Thus 69 persons (86%) died as the result of the congenital lesion."

Most recent authors (16, 38, 39, 79) consider any series to be influenced by factors which affect the reporting of cases. The cases in the older patient are more likely to be recorded because of an apparent competitive interest in reporting deaths at an advanced age from a congenital lesion. Cases with bacterial endarteritis are reported because of great interest in this disease and its dramatic course, whereas individuals
not dying from complications of a patent ductus are more likely unreported. These writers, therefore, imagine any summary of the literature gives a more serious outlook than the lesion probably warrants. Nevertheless bacterial endarteritis is relatively common in patients with a patent ductus arteriosus, and this complication carries with it a high mortality. The duration of the terminal illness of endarteritis with a fatal outcome varies from 2 months (40) to two years (9). The course is most always progressive; however, Chester (19) reports the one unoperated case of patent ductus recovering from bacterial endarteritis. In the large series of patients with bacterial endarteritis (not associated with a patent duct) Libman and Billings (19) find only a 2-3% recovery.

If the preponderance of this lesion in females, as evident from a survey of the case reports in the literature, is accurate, a point of great practical importance should be mentioned. This is the effect pregnancy has on the prognosis of an expectant Mother with a patent ductus. Andrews and Bronson (5) give a case history of a woman aged 33, who had borne four children with no ill effects. The most interesting patient is the one reviewed by Manges (56). This 50 year old woman had borne 8 children and had also had 3 miscarriages in spite of a patent duct without manifestations from her heart; this
diagnosis was also confirmed by Wessler's (86) necropsy findings. A striking illustration of views held by some obstetricians 35 years ago in regards the dangers attending labors in congenital cardiac lesions is provided by Rosenthal (70), who reports a woman with a patency upon whom a caesarian section was performed, so great were the fears that she might not go through her labor. No cases are reported where cardiac failure is produced by pregnancy or delivery.

What of the prognosis of those patients subjected to a surgical ligation? There is no definite proof that ligation of the vessel can prevent the deaths from bacterial endarteritis, although Touroff (80, 81) records one recovery of four patients operated upon with a diagnosis of endocarditis made by a positive blood culture of Streptococci viridans. Bullock et al (16) say their eldest patient, who had been bedridden for some years, is now leading a normal life; they further add the children, who had been forced to lead a sedentary life, are now skating and playing ball with other children without any signs of distress. Before the prognosis of operated cases can be anything but a matter of conjecture, all patients must be followed closely to note if bacterial endarteritis and cardiac failure continue to be the primary causes of death in these patients (38).
There has been a widespread tendency to classify individual s with a patent ductus arteriosus, merely, as having "Congenital heart disease", but now that surgical therapeutic procedures are available for alleviation of this lesion, it is important to find the ways in which the abnormality can be recognized. Since the turn of the century most authors (16, 17, 27, 28, 37, 80) agree that the diagnosis can be made with a high degree of accuracy. Considerable variety of opinions is to be found in the earlier literature in regards the ability to diagnose this condition. Recent articles by Gross, Hubbard, and Bullock et al (37, 38, 39) perhaps explain this difference of opinion by writing that the typical findings are not present until the third or fourth year of life. Gibson (85) in 1900 considers the diagnosis as exacting as a mathematical problem and writes,

"There is one particular variety of malformation so easy of detection as to be instructive even for the junior student of clinical medicine, this is the persistence of the arterial duct."

The histories of early case reports confirmed by autopsy study reveal little as an aid in diagnosis. Absence of cyanosis except as a transient or terminal phenomenon is the characteristic clinical picture of these subjects (40); however, Leech (54) believes that cyanosis may be occasionally observed in the retinal vessels when it is not otherwise discernible. About two-thirds of the patients are females (38, 39).
A physical retardation is rather common in the surgical cases (37); mental retardation is emphasized by Holman (43, 44), and denounced by later authors (37, 38, 80). Epistaxis may be profuse especially in children four to eight years. Some of the surgical cases mention a "buzz" or "hum" in the chest; in several instances the Mother of the patient would volunteer the information that he had felt a buzz when dressing or bathing her child. The symptoms of cardiac embarrassment prior to the onset of their terminal illness are seldom recorded in earlier reports; many of the surgical histories reveal varying degrees of cardiac embarrassment (7, 37, 38, 80).

The physical manifestations of this lesion may be entirely lacking in infancy and are apt to be extremely confusing in the first two or three years of life, but are almost typical after the fourth year (37, 40, 80). Evidently, it is in the absence of signs in infancy that is responsible for Stoddard (77) writing,

"No signs are necessarily present when the duct is open, then, which are sufficiently specific to afford us means of diagnosis."

Leech's (54) analysis of patent ductus in infants less than one year of age led him to conclude, that it is impossible to diagnose correctly more than a very small percentage of cases by the heart signs alone. Hochsinger (77) also emphasized the
difficulty of diagnosis in infants, but hardly in adults. His rules for diagnosis are still emphasized by present day authors; they are:

1. Murmur in 2nd left intercostal space, which in infancy is always systolic in uncomplicated cases, but as dilatation from the pulmonary artery develops may extend into the distole.

2. Thrill felt in the jugulum.

3. Palpable and much accentuated second pulmonic sound.


5. Enlarged pulmonary artery in x-ray.

One might imagine that considerable knowledge of this murmur might be learned from auscultation of new born infants; however, most clinicians with the exception of Leech (54) are of the opinion that no murmur is audible during the new-born period, even though the ductus is patent in most instances at this age. No explanation is offered in the literature for the absence of the characteristic murmur until the patient is three or four years of age. The murmur owes its origin, according to Hochsinger (85) to the mixing of the arterial and venous blood currents. In explanation of the absence of murmurs in case reports Stoddard (77) affords a new theory on the etiology of the murmur; it seems to him more reasonable to consider the murmur not the result of patency alone, but also dependent upon the presence in addition of some endocardial projection. He quotes the cases of Mead (57) and Wells (85)
because of their postmortem finding of a mound-like elevation about the pulmonary orifice. After reviewing the literature on the various and sundry descriptions of the murmurs in previous hospital records of their patients, Bullock et al (16) are convinced that the lack of description of this murmur does not mean that it is not present at the time of examination. Instead, they believe the pulmonic area is often overlooked and examiners may not be alert to the characteristics of this murmur. In one patient operated upon by Touroff (80) it was noticed that even though the ductus was cut across between two ligatures, the continuous murmur did not disappear. It was only when pressure was applied to the pulmonary artery that the murmur vanished. Libmon (17) considers this evidence that a dilated pulmonary vessel has a part in the production of the murmur. Perhaps dilatation of the pulmonary artery requires 3 to 4 years to develop and this explains absent murmurs in infants. Abbott (2) finds the murmur recorded as being present in only 3 of her case studies; However, recent surgeons (16, 39, 8) write they would never consider ligation regardless of other signs, unless the typical murmur was present. It was in 1833 that Fagge writes only few cases are on record in which a persistent ductus arteriosus has been believed to give rise to a murmur; he heard two loud murmurs but considered these due to co-existing disease of the aortic valves.
The characteristics of this murmur.

Gibson of Edinburgh (85) is the first to consider the murmur of patent ductus arteriosus as being pathognomonic. He says,

"Auscultation gives the second and most invariable evidence of the lesion in the presence of a murmur which is pathognomonic. Beginning distinctly after the first sound, it accompanies the latter part of that sound, occupies the first pause, accompanies the second sound, which may be accentuated in the pulmonic area or may be doubled, and finally dies away during the long pause."

From most descriptions one might gather the only characteristic feature of the murmur is its loudness (74). The characteristic murmur is described as, "humming top", "train 'n the tunnel", "machine-like", and "mill wheel". Abbott says this characteristic murmur occurs in only a third of the cases; she finds a number of other cases with a double murmur in which the systolic element is generated at the ductus, and the diastolic in explained by a pulmonic insufficiency. This again fits in with some views that the diastolic factor depends upon pulmonic artery dilatation (38). Accentuation of the murmur during minor illnesses is emphasized by Mead (57). Baldero (9) stresses the continuation of the murmur into the back. The most suggestive auscultatory finding by Munro (61) is a loud systolic "whir" conducted into the cervical vessels; Bullock et al (16) emphasize that a continuous hum is frequently heard over the veins of the neck in normal children, which may be heard below the clavicle, and should be excluded by jugular
Several cases reported in the journals are diagnosed antemortem as mitral stenosis (39,43). P. Burwell et al (17) cite a case with a mid-diastolic rumble at the apex, suggesting also a diagnosis of mitral stenosis; this murmur disappeared with ligation, suggesting to them that even a normal mitral valve may be too narrow for the silent passage of so great a volume of blood. All successful ligations have either resulted in disappearance of the murmur or a marked diminution in the pitch and loudness (16, 39, 81). Mention has already been made of the spontaneous disappearance of this typical murmur in certain adolescents by Dunn and Abbott (2, 4, 24). All authors observe the murmur to be accentuated in the second or third interspace just to the left of the sternum; most frequently the murmur is transmitted with diminished intensity over the entire heart. The extension of the murmur is emphasized by Boldero (9) and confirmed by Gross, Hubbard, Emerson and others (37, 38, 39). Segall (74, 75) stress the "harshness, loudness, and roughness" of the typical murmur.

Considering the physiology of this arteriovenous shunt, one might well expect an accentuated second pulmonic sound as well as a palpable thrill in the pulmonic area. Hoschsinger and Gibson (31, 85) both lay particular emphasis on these two signs. Stoddard (77) considers the accentuation of the
second pulmonic to be the most constant sign for diagnosis, but still of only limited value. Wessler (86) is of the opinion that a second pulmonic sound of normal intensity which is impure, should suggest diseased pulmonic valves—"most probably pulmonic stenosis." Gross, Hubbard, Touroff, et al (47, 80, 81) find a very coarse, precordial thrill, systolic in time, or continuous with systolic accentuation as a routine observation; they consider a rather large duct to be necessary for the production of a thrill.

The German clinicians lay much stress upon a band-like area of dullness along the left margin of the sternum in the second or third intercostal space, produced by the dilatation of the pulmonary artery. This feature was first recorded by Gerhardt (31). Articles by Schlaepfer, Hamilton-Aubott, Stoddard et al (72, 73, 40, 77) stress the sign. Either the art of percussion is being lost or older clinicians had a better imagination, as the most recent observers (17, 37, 39, 80) find the sign unreliable and difficult of interpretation.

A variation in the pulse also seems to have lost most of the diagnostic importance attached to it by earlier clinicians. Franck (85) writes of a fall in the pulse with inspiration and a rise with expiration and is corroborated by Fagge (29). Recent articles find only an increase in pulse rate after mild exercise in diversion from the normal (38).
An occasional early report mentions a Corrigan's pulse or Duroziez's sign (34, 46). Prior to the introduction of surgical reports of the subject in the literature, only six men (13, 32, 46, 55, 77, 87) record the blood pressure of their cases. The blood pressure shows no significant change in its systolic level, but there is a low diastolic frequently if the duct is large. Thus the leak from the aorta may be sufficient to produce a significant fall of peripheral pressure when the aortic valve is closed (during diastole). If the loss is great enough, a Water-Hammer pulse or a visible capillary pulsation can be detected on examination of the peripheral vascular system. One of the most interesting features about the low diastolic pressure is that it becomes still lower during exercise (in contrast to the normal rise), as first pointed out by Bohn (16), and produces an increase in the pulse pressure. In some instances the diastolic pressure goes practically to zero following mild exercise.

At the turn of the twentieth century the prominent bulging of the pulmonary artery (in the area corresponding to Gerhardt's dulness) was first recognized roentgenologically by Zinn (31). This "cap or zone of Zinn" was soon confirmed by de La Camp, Hochsinger, Bittorf (85) and others. From his studies of the orthodiagraph Wessler and Bass (86) consider an alteration in size or shape of the heart to indicate a complicating lesion.
Groedel (36) asserts that of all the congenital heart lesions the persistence of the duct of Botalli produces the most typical roentgen picture; he considers the round heart produced by the enlarged right ventricle, as significant a finding as the enlarged pulmonary vessel. Wessler and Bass (86) see a pulsation in the pulmonary artery with each systole under fluoroscopic examination. The roentgenological detection of calcified areas in the arch of the aorta in young individuals seems a confirmatory sign to Weiss (84). Still with his pessimistic view of the accuracy of diagnosis, Stoddard (77) writes the x-ray is also of little value. The possible deviations sought for by the present roentgenologists by film, fluoroscopy and kymograph is ably presented by Burwell and Eppinger (17); they include the following:

1. The greatly increased output of the left ventricle indicated the possibility of this chamber.

2. Since both the left ventricle and the pulmonary artery are transmitting with each beat and increased volume of blood, they may be expected to show an increased pulsation.

3. Since the pulmonary artery receives blood from two sources, and since it has been seen at operation to have overflowed, the silhouette of this artery may exhibit unusual prominence.

4. Because of the increased flow of blood into them the pulmonary vessels may show the signs of engorgement.

5. The combination of increased inflow and engorgement may lead to increased pulsation of the pulmonary artery branches. This is known as the "hilar dance".
6. If a normal mitral valve is not wide enough to transmit this large amount of blood without an elevated left auricular pressure, there may be a visible dilatation of the left auricle.

Maier (49) suggests the injection of diodrast according to the method introduced by Robb and Steinberg for the x-ray diagnosis. Bullock (49) considers the reaction from this drug to be too severe and frequent to warrant such a procedure, in light that diagnosis is generally clear-cut from physical signs alone. Gross (40) writes of having used this method in one case, but the results were not satisfactory however, he considers the method of merit for some cases in ruling out the possibility of other intra-cardiac defects.

No consistent electro-cardiographic findings are present. Bullock et al (16) mention a prominent Q-wave in three cases, but in none is it one-fourth the height of the largest QRS complex; he also mentions a slight depression of the ST segment in 3 instances and an inverted T-wave in one case. Burwell, Eppinger, Bullock, et al (17, 47) explain the absence of an axis deviation, as being due to the reversibility of the dilatation enlargement (rather than a hypertrophy enlargement) of the left ventricle. Gross (39) says an additional load falls on both sides of the heart, and is not surprised to find no axis deviation; he considers the electrocardiogram mainly of value in ruling out the possibility of another abnormality.

Holman (43) alone mentions the possibility of polycytinemia.
Bullock (16) finds a normal blood count in his eleven operated cases. From an academic view Eppinger (28) finds to constant changes in venous blood pressure, total blood volume or vital capacity. Leech (54) suggests the possibility of comparison of venous and arterial blood to diagnose the presence of a communication between the right and left heart.

Providing the diagnosis of a patent ducts is reasonably established, it is essential to rule out other associated lesions, if the case is to be considered for ligation. Such lesion would be stenosis of the aortic valve, hypoplasia or coarctation of the aortic arch, and stenosis or atresia of the pulmonary valves. Systolic or diastolic murmurs over the aortic area which do not appear to be transmitted from the pulmonic area are highly suggestive of aortic stenosis or insufficiency, particularly if accompanied by a left axis deviation in the electrocardiagram (39). Hypoplasia of the aortic arch can be excluded by proper fluoroscopic examination. Coarctation will show a lower blood pressure in the leg than in the arms, the reverse of normal, and compensatory collateral circulation produces changes in the ribs easily evident by roentgen examination (28). Stenosis of the pulmonary valves may be exceedingly difficult to diagnose because the murmur arising from it are almost identical with those originating from the ductus. However, the patient with an uncomplicated patent
ductus has a loud snapping second pulmonic sound due to the increased pressure within the pulmonary artery, whereas the pulmonic second sound will be absent or diminished if there is an abnormality of the valve (38, 77). Furthermore, pulmonic stenosis is practically always accompanied by some right-sided hyperthrophy in the roentgenogram, by right axis deviation in the electrocardiogram, and by cyanosis due to a right left shunt of blood through a septal defect (38).
TREATMENT

In the early literature no space is devoted to this phase of the subject. Gerhardt (85) quotes Diemar as advocating what appears to be a most barbarous form of treatment. Believing atelectasis to be the cause of persistency of the duct, Diemar recommends keeping the child awake and making it cry continuously, in order to overcome the pulmonary collapse. He claims to have cured five cases but this statement must be taken cum grano salis.

The first individual to propose ligation was Murno(61). On May 6, 1907 in a paper before the Philadelphia Academy of Surgery, he proposed ligation of the patent ductus. He had made dissections on cadavers of new born infants and proposed to split the sternum and to place a tie around the ductus or to crush it. Munro felt that the ductus was largely intrapericardial, and his operation approached it by opening the pericardium. So far as can be ascertained there is no record of his ever having attempted it on the living. Munro was quite a bit ahead of his time, and although various authors mention his suggestion, no active action was taken until 1938. In fact in 1936 Abbott (2) states that the only type of treatment available is the removal of foci of infection in order to prevent the possibility of endocarditis. In May, 1938, Graybiel, Strieder and Boyer (34) report the first, though unsuccessful attempt to ligate a patent ductus in a patient with subacute
bacterial endarteritis. The first successful ligation was performed by Gross and Hubbard (37) in August of 1938. Since the first report there have been no less than 60 cases reports of patients with ligation of the vessel. There is a mortality of 26% with these thirty patients. Gross (39) and Bullock (16) together have a total of 21 patients with a mortality of 10%; Touroff (81), however, has operated upon 4 patients with sub-acute bacterial endocarditis with a mortality of 75%. Therefore, one realizes that the mortality is only about 10% in uncomplicated cases and may run to 75% in those patients with endocarditis.

It is not within the scope of this presentation to describe extensively the operative technic. Briefly, the ductus can be adequately and safely brought into view by an approach through the left anterolateral chest wall, traversing the left pleural cavity, temporarily collapsing the left lung, opening the parietal pleura of the mediastinum and then dissecting down between the great vessels. The cutaneous incision can be made above or below the nipple, and in the adult woman it could be made below the entire breast (39). Entry through the second space gives a good exposure, provided the intercostal muscles are divided well around into the axilla. Great care and patience must be exercised in freeing up and isolating the ductus for fear of injuring it or the regional structures (17). Heavy bailed
waxed silk ligatures have been used in most cases, according to Reid's method (68), and this has been supplemented in two cases by Gross (38) by injection of a sclerosing solution between the ligatures. Torouff (80, 81) advocates section of the vessel between the ligatures whenever possible. Following ligation of the ductus, the left lung is re-expanded with positive pressure, and the chest is closed. The anesthesia in the majority of the cases was cyclopropane. If the operation is carefully done, it is tolerated very well and there is little postoperative reaction (16, 39*). Some of Gross (39, 40) patients have been out of bed on the first or second day, and hospitalization of more than seven to ten days is seldom necessary. Bullock et al (16) advises caution in use of post-operative fluids, because of the sudden increase in diastolic pressure.

Should all patients with a diagnosis of patent ductus be subjected to ligation? All surgeons on the subject agree that not all cases warrant the risk of surgery. The positive criteria for selection of cases for operation may be enumerated as follows:

1. There must be reasonable assurance that the ductus is patent as is determined, by a loud, continuous, machinery murmur in the pulmonic area accompanied by an increased second pulmonic sound and a systolic or continuous thrill which is most intense in the pulmonic region.

2. There should be evidence of congestion in the lung fields by roentgenologic examination.

3. There should be a prominence of the pulmonary artery roentgenologically.
4. There should be roentgenologic evidence of cardiac enlargement, particularly in the region of the left ventricle.

5. There should be a peripheral blood pressure which has an essentially normal systolic level, but a definitely lowered diastolic level. In short, one should have an indication that the ductus is enlarging, or that the heart is carrying an increased burden (38, 39, 40, 80, 81).

Gross (38) considers the complication of bacterial endocarditis to be a contra-indication for ligation. On the other hand Torouff, Graybiel, Strieder, Hubbard, et al (16, 17, 28, 47, 80, 81) consider the mortality rate certainly could not be raised by surgical intervention. They hope to ligate the duct early in the course of the disease, and thereby prevent the spread into the aorta. Out of 4 attempts, Torouff writes, that one patient with a diagnosis of endocarditis is still living 36 weeks after the operation. Hubbard (47) is of the opinion that ligation should be done early before the intima of the ductus and pulmonary artery has been damaged; Bullock et al (17) consider the ligation easier in their youngest patient.

The surgical intervention for this anomaly is still in the embryonic stage. It will require many year of careful study the mortality rate, prognosis, and complications will be fully appreciated (40). The prognosis following ligation in regards cardiac failure and endocarditis is still a matter of conjecture; however, Bullock et al (17) writes of having patients
up and around after having been bedfast for several months, and Torouff apparently has prevented one patient from succumbing to bacterial endocarditis.
CASE REPORT

Miss Bonnie Blubaugh, a white, 17 year old school girl enters the Clarkson Hospital for the first time on 8-7-40:

PRESENT ILLNESS:

Patient relates that 3 weeks after birth, it was discovered that she had a congenital deformity of her heart. Because of this she had been always watched and guarded rather closely. She had led a somewhat restricted life as far as activities and exercise are concerned, but this has been on a voluntary basis until two years ago. At that time she first noticed swelling of her ankles. She went to bed for a week and was on digitalis for a period of one month. At no other time was medication or bedrest necessary. At present she notices some shortness of breath with excessive exercise; however, she dances and skates without suffering any cardiac embarrassment. She has always noticed mild palpitation of the heart.

FAMILY HISTORY:
Mother---Living and well.
Father---Living and well.
Sisters---2; both living and well
Brothers---1; has had murmur since rheumatic fever.
Maternal aunt had diabetes and paternal grandfather died of tuberculosis.
PAST HISTORY
- Whooping cough, measles, and chicken pox were the childhood diseases; no complications. Fractured left tibia in 1933. Tonsillectomy in 1937.

HISTORY BY SYSTEMS:
Head---Occasional frontal headache in the morning.
Eyes---Negative.
Ears---Negative.
Nose---Had frequent epistaxis when a child.
Mouth---Teeth in good condition.
G-R---See P. I.
G-I---Good appetite. Bowel movements regular without laxatives.
GU---Negative.
Catamenia---Began when 14; last 3 days; but irregular, varies every 28-40 days.
N-M---Negative.
Wt.---Loss of 9 pounds since last winter.

PHYSICAL EXAMINATION:
This patient is under developed (5'2") and only fairly well nourished (90 pounds).
Head---Copious brown hair.
Eyes---Negative
Ears---Good hearing.
Mouth---Teeth in good repair.
Throat---No injection or discharge.
Lungs---Equal expansion. Clear to auscultation and percussion.
Heart---Heart is markedly enlarged. Dulness extends to anterior axillary line in 5th intercostal space. The PMI is palpable in the 5th intercostal space slightly lateral to the nipple line. Sounds are loud and clear, although a systolic murmur is heard over the entire heart. This murmur is very loud and a machine-like rumbling is audible over the pulmonic area and in the third intercostal space. Blood pressure 110/60. Pulse rate is 85.
Abdomen---Negative.
Extremities---Normal tonus. Reflexes equal and active.

PROGRESS NOTES:
8-7-40---General diet with fluids. Radiographic study of the chest in the postero-anterior plane shows the heart shadow to occupy 51% of the transverse diameter of the chest and there is a rounded fullness of the cardiac outline in the pulmonic area. The broncho-vascular trunks in both lungs appear moderately widened but the lung fields and pleural sacs appear clear.
RBC---3,080,000.
HB---12.7.
WBC---10,600.
Urine---Negative.
8-22-40---Systolic (2 plus) murmur followed by accentuated second pulmonic at pulmonary area. No suggestion of machinery murmur. (Dr. F. W. Niehaus).

8-23-40---WBC. 12,300.

8-27-40---Dismissal Note: Patient entered with typical findings of a patent ductus arteriosus and with a history of a congenital defect known since birth. The machinery murmur immediately disappeared following the double ligating of the vessel. The lung was inflated under positive pressure and fluid and air aspirated. The patient developed atelectasis of the left lobe post-operatively and fluid was demonstrable in the left pleural cavity. No abnormal changes in pulse, temperature, or respirations were observed. The patient is dismissed in good condition.

9-20-40---Check-up examination shows reduction of the prominence in the cardiac outline of the area of the pulmonary artery. The left diaphragm is elevated about 4 cm. as compared with the preliminary film. This produces a rotation of the heart thrusting the apex toward and the left chest wall. The pulmonary and pleural congestion seen in previous films has practically cleared. The report has been taken practically verbatim from the records of the Bishop Clarkson Memorial Hospital. Permission to use the record was extended through the courtesy of Drs. Niehaus and Bisgard.

This is the first and only attempt at ligation of a patent ductus in this state; to date this case is unreported in the literature.
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