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E. B. M A L H E R B E

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# THE SURGERY OF THE DUCTUS ARTERIOSUS AND THE PROBLEM OF ITS POST-NATAL CLOSURE.

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## INTRODUCTION.

When Gross in 1939 performed the first successful ligation of the patent ductus arteriosus, congenital heart disease, for the first time, became a subject of interest to the surgeon. Up to that time, this subject has been of interest largely to the diagnostician, for there was but little, if any, specific therapy available. After Maude Abbott by her life long work on the subject in particular, James Brown and others, had done so much to enhance our understanding of congenital heart disease, and had placed accurate diagnosis within the bounds of possibility, the time had come for the surgeons to make their contribution. Gross, by his successful operation, has stimulated the interest of surgeons everywhere, so that, today, ligation of the patent ductus is a universally performed operation. Other forms of congenital heart disease - coarctation of the aorta in particular (Gross and Hufnagel, 1945, Blalock and Tausig, 1945) - are being examined anew, this time with a view to surgical correction.

This thesis is concerned solely with the "patent ductus arteriosus". It is felt that an accurate understanding of the nature of the anomaly, its function, or effects upon the circulation and the body's reaction to them, is essential if surgical therapy is to be applied rationally. Many contributions to the "pool" of knowledge have been made by workers from various parts of the world, but there are still many problems which are not clearly understood. The bulk of the knowledge is scattered throughout the medical literature and not a great deal is correlated

in any one paper. This thesis, therefore, attempts to review critically the information which is available and studies certain aspects of the subject. As the problem of post-natal closure of the patent ductus arteriosus is dealt with more extensively than others, it is felt, that, for the sake of continuity and clarity, this aspect should be considered separately. The thesis therefore consists of two parts. The first deals with various aspects of practical surgical interest, including anatomy, physiology, clinical aspects, surgical technique and its results; the second with the rather more academic problem of the post-natal closure.

For this study eleven patients have been carefully investigated, including some aspects that have not received a great deal of attention from other authors. These aspects will be elucidated in their appropriate sections of the text. ~~Four~~ Six of these patients have been subjected to the operation of ligation (not by the writer+). For the second part experimental investigations on guinea pigs have served as the basis.

+ The author wishes to express his gratitude to Professor Saint, who operated on this series, for his permission to investigate these cases and to use the results for this thesis.

# PART I.

## CHAPTER I.

## THE SALIENT HISTORICAL FACTS REGARDING THE DUCTUS ARTERIOSUS.

It is generally said that the ductus arteriosus was first described by Galen in the second century A.D. as a short vessel uniting the aorta to the pulmonary artery. Noback and Rehman (1941) maintain that the first known mention of the term "ductus arteriosus" occurs in Guilio Cesare Aranzi's "De humano foetu liber", published six years after his death in 1595. The name more commonly associated with the ductus arteriosus is that of his contemporary, Leonardo Botallo (1565), for even today, writers, particularly those from the continent, refer to the "ductus arteriosus Botalli".

According to Franklin (1941), who in masterly fashion reviews the classical literature, Botallo never described the ductus arteriosus ! His name has apparently been associated with the ductus arteriosus on account of an illustration by van Horne in his edited edition of Botallo's works (Gilchrist, 1945). This illustration (Fig. 1) was van Horne's own, and subsequent authors have repeated the mistake.

The function of the ductus arteriosus as shunting blood from the pulmonary artery to the aorta before brith was known to Harvey (1628). Senac (1749) must have been aware of the possibility of the ductus remaining patent, for he is credited by James Brown

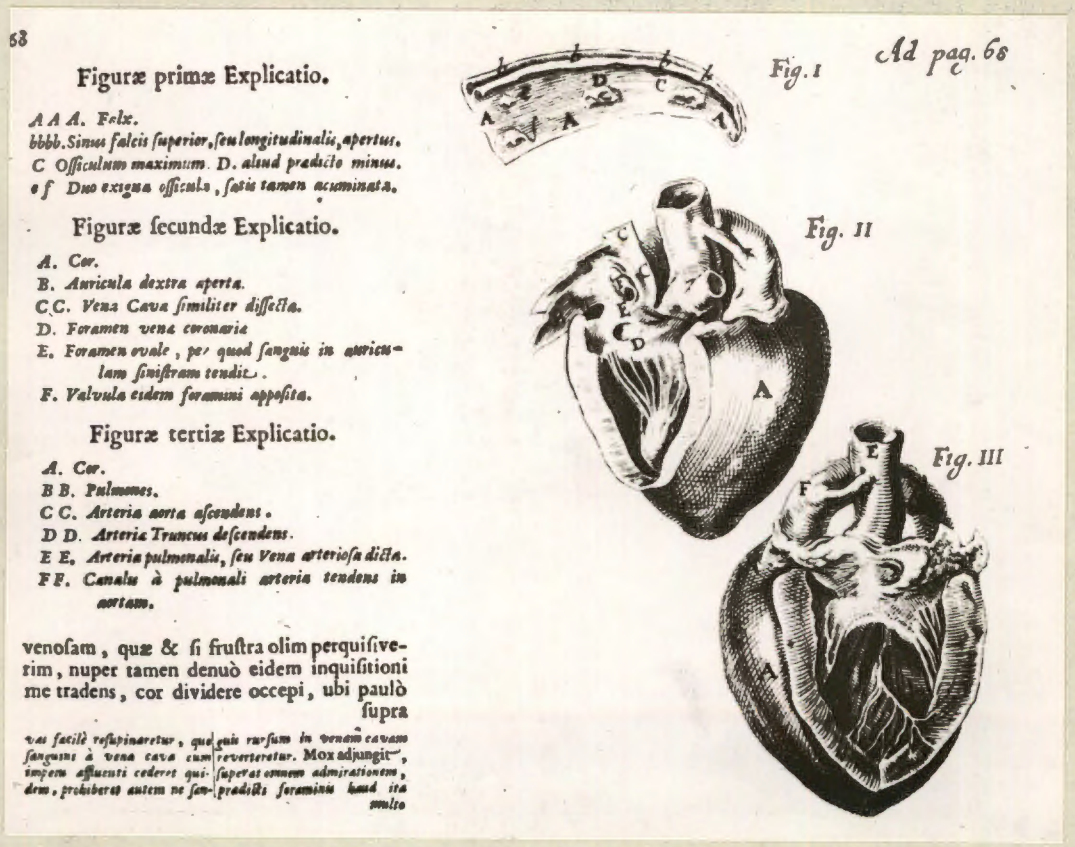
(1939) with observing that the ductus is likely to remain patent in cases where respiration is impeded. Brown also credits Meckel (1812) with observing the association of the ductus arteriosus with other abnormalities. Kilian (1826) gives the first anatomical and topographical description, which, in the light of present knowledge, appears to have been somewhat inaccurate. The nearest approach to the accepted description was given by Strassman in 1894 - although several other descriptions appear in the literature before this. According to Shapiro and Keys (1943), who reviewed the world literature, the first proved case of patency in an adult was described by Chevers in 1845.

Munro in 1907 first suggested the ligation of the ductus arteriosus, and demonstrated the feasibility of the operation on a cadaver before the Boston Medical Society. Nevertheless, for 32 years his suggestion was not acted upon. This was probably due to the fact that thoracic surgery in general developed more slowly than any other, and to the fear that such ligation might be attended by ill effects.

In 1939 Gross performed the first successful ligation after unsuccessful attempts in 1938 by O'Shaughnessy, in whose case the diagnosis did not prove correct at operation, and by Graybiel et al in whose case technical difficulties prevented successful ligation.

The first successful ligation has proved a great stimulus to experimental physiology in this field, and the past six years have seen the addition of a great deal of knowledge, certainly

very much more than that contributed by the 17 centuries preceding them.



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Figuræ primæ Explicatio.

*A A A.* Falx.
*bbbb.* Sinus falcis ſuperior, ſeu longitudinalis, apertus.
*C* Officulum maximum. *D.* aliud prædicto minus.
*e f* Duo exigua officula, ſatis tamen acuminata.

Figuræ ſecundæ Explicatio.

*A.* Cor.
*B.* Auricula dextra aperta.
*C C.* Vena Cava ſimiliter diſſecta.
*D.* Foramen venæ coronariæ
*E.* Foramen ovale, per quod ſanguis in auriculam ſiniſtram tenditur.
*F.* Valvula eidem foramini appoſita.

Figuræ tertiæ Explicatio.

*A.* Cor.
*B B.* Pulmones.
*C C.* Arteria aorta aſcendens.
*D D.* Arteria Truncus deſcendens.
*E E.* Arteria pulmonalis, ſeu Vena arterioſa dicta.
*F F.* Canalis à pulmonali arteria tendens in aortam.

venoſam, quæ & ſi fruſtra olim perquiſiverim, nuper tamen denuò eidem inquiſitioni me tradens, cor dividere occepi, ubi paulò ſupra

*vas facilè reſupinaretur, quo ſanguis rurſum in venam cavam ſanguinis à vena cava cum impetu affluenti cederet quidem, prohiberet autem ne ſanguis reverteretur. Mox adjungit, ſuperat omnem admirationem, prædicta foramina haud ita multo*

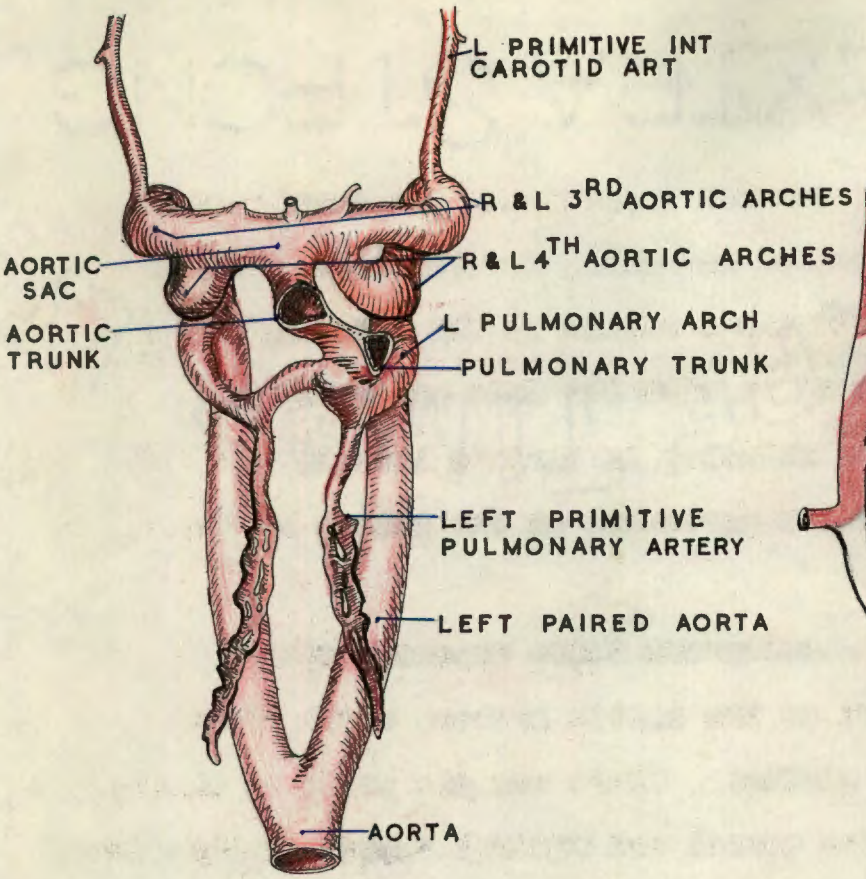
Fig. I

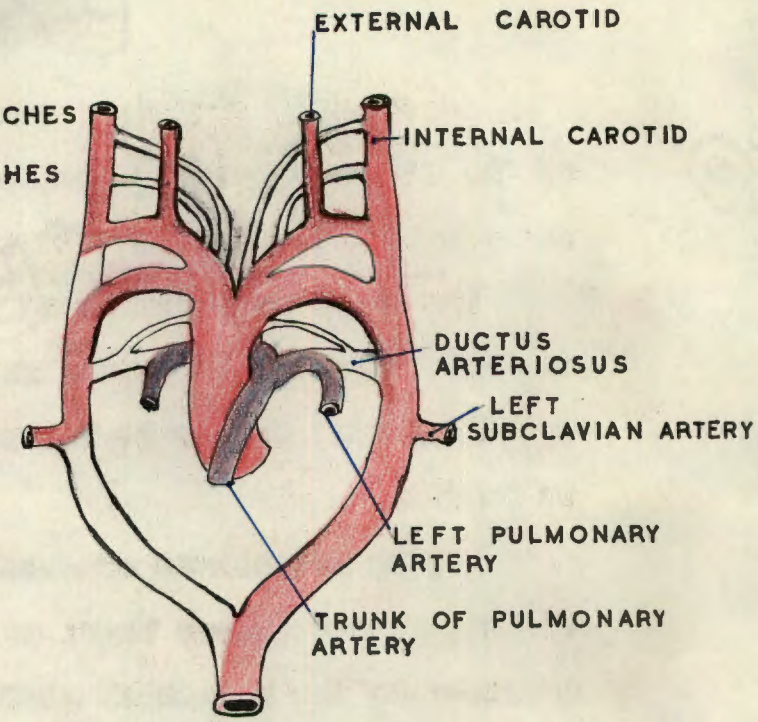
Ad pag. 68

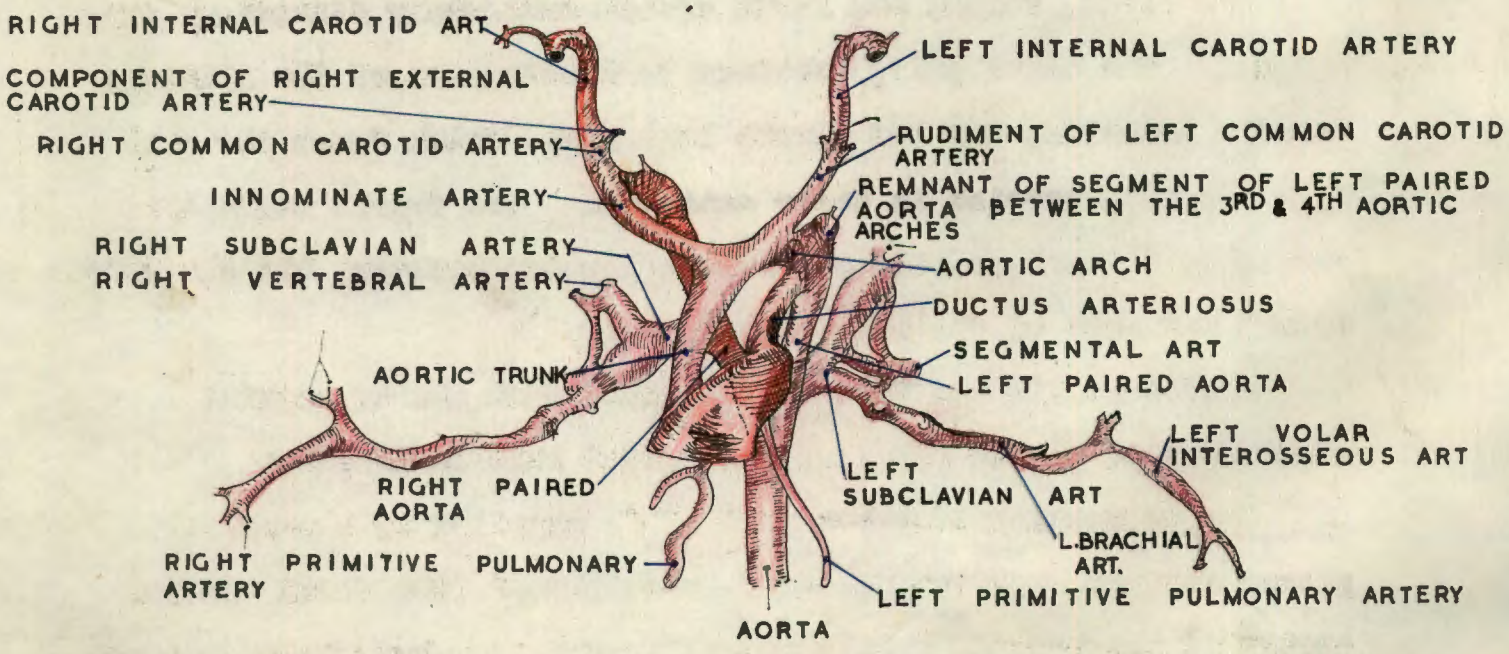
Fig. II

Fig. III

Van Horne's edition of Botallo's complete works (1660) contains this illustration inserted by the editor and not included in Botallo's original text. Botallo did not describe the ductus and the structure depicted in van Horne's illustration is anatomically incorrect.


L PRIMITIVE INT CAROTID ART
R & L 3RD AORTIC ARCHES
AORTIC SAC
R & L 4TH AORTIC ARCHES
AORTIC TRUNK
L PULMONARY ARCH
PULMONARY TRUNK
LEFT PRIMITIVE PULMONARY ARTERY
LEFT PAIRED AORTA
AORTA


EXTERNAL CAROTID
INTERNAL CAROTID
DUCTUS ARTERIOSUS
LEFT SUBCLAVIAN ARTERY
LEFT PULMONARY ARTERY
TRUNK OF PULMONARY ARTERY


RIGHT INTERNAL CAROTID ART
COMPONENT OF RIGHT EXTERNAL CAROTID ARTERY
RIGHT COMMON CAROTID ARTERY
INNOMINATE ARTERY
RIGHT SUBCLAVIAN ARTERY
RIGHT VERTEBRAL ARTERY
AORTIC TRUNK
RIGHT PAIRED AORTA
RIGHT PRIMITIVE PULMONARY ARTERY
LEFT INTERNAL CAROTID ARTERY
RUDIMENT OF LEFT COMMON CAROTID ARTERY
REMNANT OF SEGMENT OF LEFT PAIRED AORTA BETWEEN THE 3RD & 4TH AORTIC ARCHES
AORTIC ARCH
DUCTUS ARTERIOSUS
SEGMENTAL ART
LEFT PAIRED AORTA
LEFT VOLAR INTEROSSEOUS ART
LEFT SUBCLAVIAN ART
L.BRACHIAL ART.
LEFT PRIMITIVE PULMONARY ARTERY
AORTA

## CHAPTER II.

## EMBRYOLOGY.

Accounts in the standard work emphasizing the development of the ductus are few. Keibel and Mall, for instance, make no reference to the ductus arteriosus either in the index or the text.

The development is bound up with the fate of the aortic arches. Sir Arthur Keith, Walmsley in Quain's Anatomy and Congdon (1922) appear to be in agreement on the nature of their evolution.

During the course of development there appear certain transitory structures known as the aortic arches, which lie in relation to the branchial clefts. There are six pairs of these, and they unite the primitive dorsal and ventral aortae. They are not present at the same time and certain of them entirely disappear, while others persist and form the aorta and branches of its arch.

The first, second and fifth arches completely disappear (Figs. 2,3,4). The third pair, destined to become part of the internal carotid arteries, and the fourth left arch, which forms the arch of the aorta, persist in their entirety. The fourth right arch partially disappears, the persistent portion becoming the innominate artery and part of the right subclavian.

As the origin and fate of the sixth arch are of special significance, a more detailed account of this is in place.

The developing lung buds are first supplied by a capillary plexus derived from the so-called "aortic sac" (the fused ventral aortae of the human). This capillary plexus subsequently becomes

connected to the dorsal aorta, and the vascular connection between the latter and the aortic arch constitutes the sixth arch. The continuation of the capillary plexus to the lung bud becomes the pulmonary artery (Fig. 3).

The ventral part of the sixth right aortic arch persists as the proximal part of the right pulmonary artery, but its dorsal part disappears. The ventral part of the sixth left arch is absorbed into the trunk of the pulmonary artery, while the dorsal part persists as the ductus arteriosus.

The relation of the recurrent laryngeal nerves to the aortic arches during development is of interest, for, on the left side this nerve is eventually closely related to the ductus arteriosus, and at operation serves as the chief guide to it.

The recurrent nerves originally pass to the larynx under the sixth pair of arches, and are thus drawn caudally with the descent of these structures. In the mature foetus, therefore, the left recurrent laryngeal will be found hooking around the aortic arch below and behind the ductus arteriosus. On the right side, on the other hand, where most of the sixth and the entire fifth arch disappear, it may be regarded as slipping cranially until it impacts against the structure derived from the fourth arch, namely, the right subclavian artery.

## CHAPTER III.

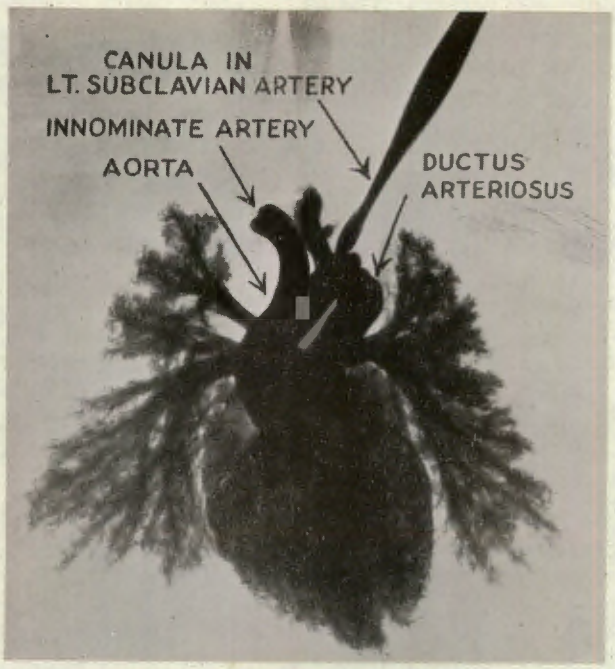
## THE ANATOMY.

A. Normal.

(a) Macroscopic:-

Although Galen described the ductus arteriosus in the second century A.D. as a short vessel uniting the pulmonary artery to the aorta, the first detailed anatomical and topographic description was apparently that of Kilian in 1826 (cited by Rehman and Noback, 1941). This was followed by further contributions and corrections by other writers, who supported or differed from Kilian on various points. Of the many, the most important contribution appears to have been that of Strassman in 1894, who differed somewhat from Kilian. This description more nearly approaches that generally accepted today. The chief points of dispute appeared to be the exact course and plane of the ductus, its point of entry into the aorta as related to the origin of the left subclavian artery, and the diameter.

No useful purpose will be served by relating the various descriptions given, but those of Kilian and Strassman may be briefly remarked upon, with a view to comparison with that accepted today. Kilian states: the ductus slopes upwards from right to left, being slightly bent in its course from before backwards. The angle formed by its entrance into the aorta is acute, and the lumen decreases from the pulmonary artery to the aorta, "admitting a quill". The left subclavian arises three to four "linien"




Radiograph showing the calibre, length and position of the ductus arteriosus at birth. Preparation obtained by filling the heart and large vessels of a full-term stillborn foetus with iodide solution through the left subclavian artery. The aorta has been ligated just distal to the entrance of the ductus. (After Tubbs, 1944).

(1/12th inch) to the right (or proximal) to the point of entry of the ductus.

Strassman, on the other hand, describes the ductus as entering the concave undersurface of the aorta, the diameter as being almost equal to that of the aorta, the course as being almost parallel to the aorta, and the point of entry into the aorta as being distal to point of origin of the left subclavian artery. In addition, he describes a valve-like arrangement - which bears his name - guarding the opening of the ductus into the aorta, and formed from the wall of the aorta.

The most recent contribution to the anatomy of the normal ductus arteriosus is that of Noback and Rehman (1941). They ~~described~~ dissected 100 cadavers of foetuses, new-born and young infants, with the assistance of all modern technical and photographic aids. They add some additional information to the existing store, but one feels, however, that their descriptions are somewhat marred by a desire to explain the phenomenon of closure on an anatomical basis.

It can be said that at the end of foetal life, the ductus arteriosus is a relatively short vessel, about one centimetre long and five millimetres wide, which diverts blood from the pulmonary trunk, and joins the trunk to the aorta at an acute angle, not greater than 30-35° (Roeder, 1902) at a point about one centimetre distal to the origin of the left subclavian artery (Rehman and Noback, 1941). The left, and the right, pulmonary arteries can be regarded as branches of the pulmonary

1 Copy of Strassmann's Figure 2 showing the course of the ductus arteriosus in the newborn human. The valve of the ductus arteriosus (V.D.A.) is placed at the aortic entrance of the ductus.

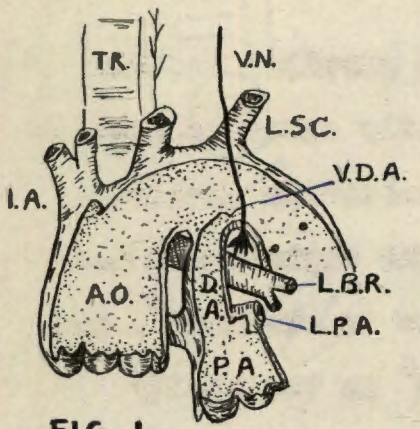


FIG 1

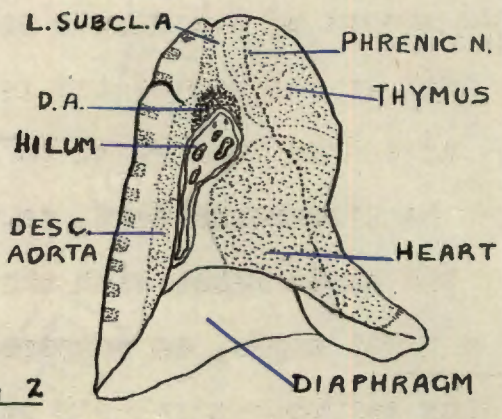


FIG 2

2 The medial surface of the left lung showing the areas in contact with neighbouring structures. Note impressions caused by the thymus and ductus arteriosus (D.A.) in the newborn human.

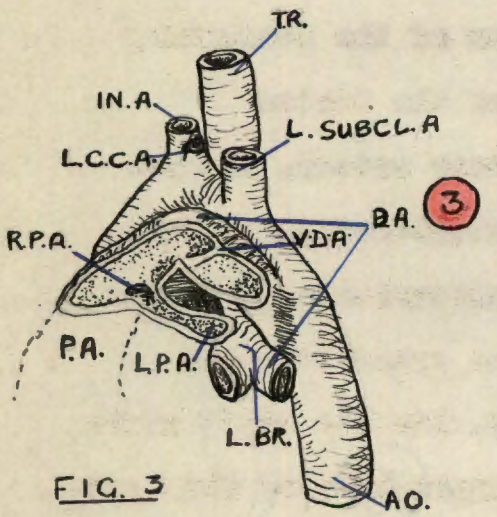


FIG. 3

3 Drawing of the ductus arteriosus placed in the same plane as that of Strassmann (See Fig. 1). The ductus tends to parallel the aortic arch and contains a transverse ridge or valve (V.D.A.) projecting into the lumen of the ductus almost midway between the pulmonary artery (P.A.) and aorta (A.O.)

(After Rehman and Noback)

Fig. 5.

trunk, arising from it latero-inferiorly at the point where it becomes the ductus arteriosus. They are smaller in size than the ductus arteriosus, which at this stage approximates the pulmonary artery and aorta in size.

The course of the ductus arteriosus lies parallel to that of the arch of the aorta, and is almost directly antero-posterior and not ascending from right to left, as is generally imagined. (It must be remembered that, in the foetus, the angle which the arch of the aorta makes with the frontal plane is about 80°, i.e., almost a right angle, as compared with the 50° in the adult) In passing antero-posteriorly it bulges towards the left, and enters the aorta on its antero-lateral aspect, and not into the medial surface.

The ductus is related superiorly to the arch of the aorta, from which it is separated by a space filled with connective tissue and lymphatics. The proximal portion of the descending aorta lies posterior to the distal portion of the ductus. Inferiorly, it is related to the left pulmonary artery, the recurrent laryngeal nerve hooking around it latero-medially, left bronchus and vagus nerve proceeding antero-posteriorly. To the left, the ductus is in relation to the thymus anteriorly and superiorly, while laterally, and posteriorly, lie the vagus nerve and left lung. The medial surface of the upper lobe of the left lung presses against the ductus, and contains an impression formed by the lateral bulge of the ductus. Medially and inferiorly the ductus rests against the left bronchus.

(b) Microscopic:-

The microscopic anatomy is fully discussed in connection with the problem of post-natal closure in the second part of the thesis.

Suffice it to say, that it is agreed by the majority of workers, that its structure is distinctly different from that of the aorta and pulmonary artery - vessels which at this time it approximates in size. This difference lies in the relative amounts of muscle and elastic tissue present. The ductus has a thicker wall in which muscle tissue predominates.

B. Abnormal.

Persistence of the ductus arteriosus after birth constitutes an anomaly. While maintaining the essential features of the foetal ductus arteriosus, there nevertheless are certain variations that are of practical importance.

The Dimensions:- The ease, and indeed, the very possibility of ligation, depend upon the length of the ductus arteriosus, and to a lesser degree upon the diameter. That these measurements vary considerably has been the experience of all surgeons concerned with ligation, and has been seen in the present series. Jager and Wolleman (1942), who dissected 72 cadavers, give the following range of measurements.

| | | |
|---|---|---|
| Length | from 0.5 to 1.3 cm. | mean 0.8 cm. |
| Diameter | from 0.1 to 0.8 cm. | mean 0.3 cm. |

Shapiro and Keys (1943) state that the ductus is generally short and that cases where it is more than 1 cm. are distinctly rare.

Jager and Wolleman describe cases in which there is no ductus, and in which there exists only a window-like opening between the aorta and pulmonary artery. Lenz (1910) describes a similar case with the additional feature of calcification of the window-edge. Ligation in such cases would naturally not be possible; but fortunately they are comparatively rare and Lediberder (1836) regards this state of affairs as being more commonly found in adults than in children.

The shape of the persistent ductus arteriosus, again, is variable. Various shapes have been described and Gerhardt (1893) classifies them as being

(1) cylindrical

(2) funnel-shaped (with the wide part at the aortic end)

(3) window-type

(4) aneurysmal.

The common shape from descriptions by Gross, Jones, Tubbs and others, as well as from personal observations on the cases ligated by Professor Saint in the present series, appears to be cylindrical, with the funnel-shaped next in frequency.

Gebauer (1943) states that the ductus arteriosus gradually widens and shortens with age, as a result of the dilatation of the pulmonary artery. This statement can be regarded as supporting the contention of Lediberder, that the window-type is seen principally in adults.

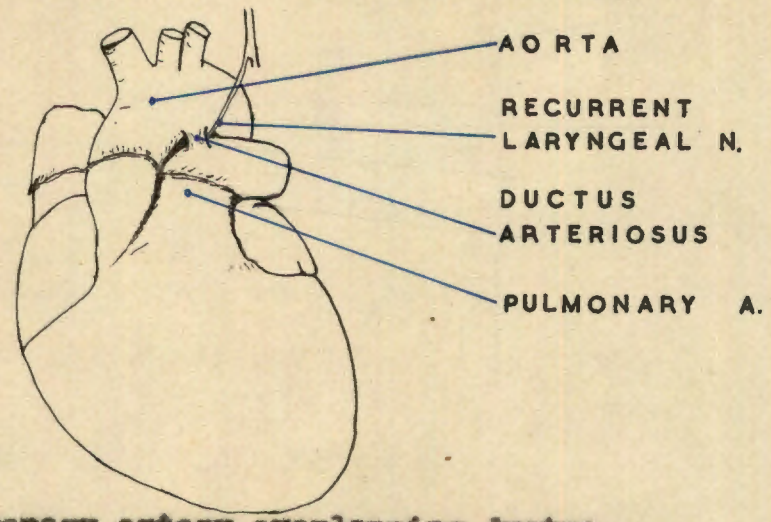
Aneurysmal dilatation has been observed as far back as 1893 (Hebbe). More recently cases have been recorded by

Monckeberg (1924) and Graham (1940). This aneurysmal dilatation may involve the aorta (Altschule, 1937) - but in his case the pulmonary end of the ductus was obliterated. Descriptions of aneurysmal dilatation are few, and as they are more likely to have been reported than the more common cases, this type can be regarded as being rare. They are often the result of subacute bacterial endarteritis of the wall of the ductus.

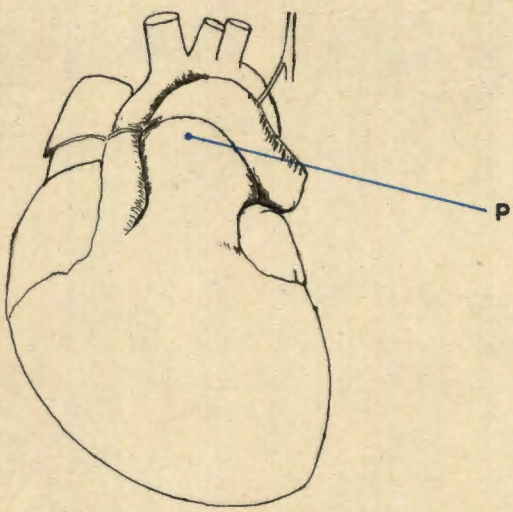
It is obvious that the thickness of the wall of the ductus arteriosus is a very important factor, especially so when statistics of failure of ligation due to the tearing of the wall are studied. Touroff (1940-1944) describes cases of patent ductus arteriosus in which the walls are very thin. His cases were mostly ones associated with subacute bacterial endocarditis.

The medial wall is reputed to be specially liable to tearing (Gebauer, 1943), but ones doubts whether this can be attributed to exaggerated thinness of this side. Observations on the operation of ligation have illustrated that this, more than any other, is the wall, which, for technical reasons, is exposed to the possibility of tearing. Gebauer attributes this to the fact that the connective tissue separating the ductus from the left main bronchus is very dense.

The lumen may contain vegetations, and these may be calcified. The failure to achieve complete obliteration of the lumen by ligation may be attributable, in some instances,




Note pulmonary artery overlapping ductus and aorta.




Note: The two figures should be reversed.

Pulmonary artery retracted to display ductus.

Fig. 6.

to the presence of these.

The relations are essentially the same as those already described in the foetus. However, modifications as the result of pathological changes do occur, e.g., enlargement of the pulmonary artery may be of such proportions as to overlap and obscure the ductus, until the artery is displaced downwards (Fig. 6). This dilatation has been of aneurysmal proportions, as in cases referred to by Holmes (1944). As the ductus is generally short, it enters the aorta on the undersurface of the arch. It usually lies outside the pericardial reflection, but occasionally may be overlapped by this on its anterior and medial aspects (Tubbs, 1944).

Other cardiac and vessel abnormalities associated with the ductus arteriosus are well known. Of these, those of anatomical significance are coarctation of the aorta, which is common, and dextroposition, and reduplication of vessels, which are distinctly rare. The narrowing in coarctation occurs immediately distal to the point of entry of the ductus arteriosus, and not opposite it, as is usually stated.

## CHAPTER IV.

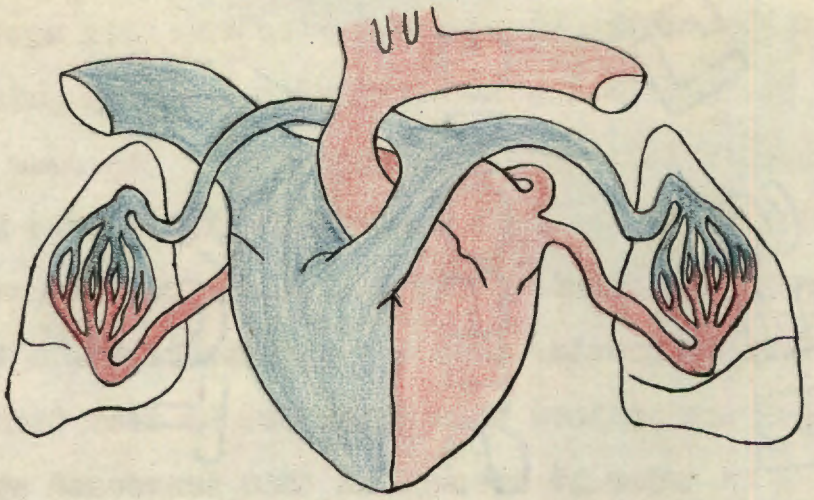
## THE PHYSIOLOGY AND PATHOLOGY.

The physiology of the foetal ductus arteriosus, again, is so intimately concerned with the foetal circulation in general, and the problem of the post-natal closure of the ductus arteriosus in particular, that the whole subject is discussed in details in that section of the thesis. From the clinical point of view, we are concerned more intimately with the physiology of the uncomplicated patent ductus arteriosus (in the sense that there are no other anomalies on account of which the ductus may remain patent as a compensatory mechanism) and its resultant pathological effects. A thorough knowledge of this, it is felt, is essential for the understanding of the condition and the evaluation of the clinical findings, with a view to the application of surgical therapy. Unfortunately, this aspect is not as straightforward and as clear-cut as is generally supposed. In fact, diametrically opposed views have been put forward - those of Eppinger, Burwell and Gross (1940) on the one hand, and of Bettinger (1941), on the other. It is not the intention to give a detailed exposition of these theories, but some reference will have to be made to them and to others, if a reasonable understanding is to be arrived at.

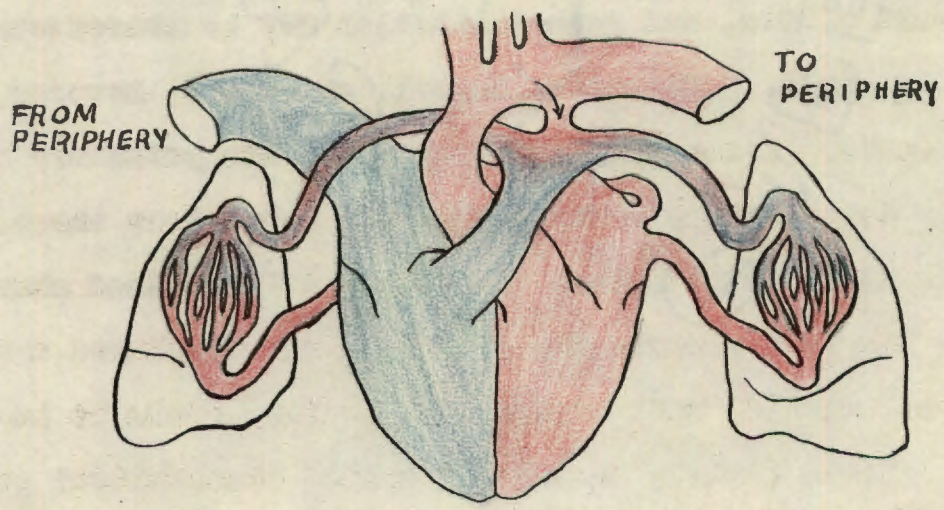
It is generally accepted that, after birth, there is an increase in the pressure in the systemic circulation relative to that in the pulmonary circulation, partly, because of the

increased demand upon the systemic circulation as the result of growth, and partly as the result of the diminution of the peripheral resistance in the pulmonary circulation, consequent upon their aeration. In the presence of a patent ductus arteriosus, therefore, there is a shunt of arterial blood from the aorta into the venous blood of the pulmonary artery - constituting an arterio-venous fistula (Holman, 1925). This state of affairs will persist as long as the pressure relationships, postulated above, are maintained. Consequently, cyanosis, which in these cases may be regarded as indicating the presence of unoxygenated blood in the systemic circulation, would not be expected - a fact borne out by clinical experience. According to Maude Abbott (1936) and James Brown (1939), cyanosis is seen only when the intrapulmonary pressure is raised, as in severe fits of coughing and sneezing; or, as a terminal event, when the pressure in the systemic circulation falls as the result of left ventricular failure. Maud Abbott, in her series of 92 cases, found cyanosis as a terminal event in 25. On account of this possibility of terminal cyanosis, Abbott and Dawson (1924) classified patent ductus arteriosus under the group "Cyanosis Tardive".

What is the effect of this shunting of blood (or this arterio-venous fistula) on the circulatory system, and what compensatory mechanism, if any, does it evoke ? It is in the answering of this question that opinions differ. Eppinger, Burwell and Gross (1941) by taking samples of blood from the pulmonary artery,



DIGRAM OF THE NORMAL CIRCULATION




DIGRAM OF THE CIRCULATION WHEN
THE DUCTUS ARTERIOSUS IS PATENT

the aorta distal to the ductus, etc., in patients subjected to ligation by Gross, before and after ligation, conclude that from 45% to 75% of the blood put out by the left ventricle is shunted by the patent ductus arteriosus into the pulmonary artery. From this it can be inferred that the same quantity of blood returns to the left ventricle without ever having passed through the right. The output of the left ventricle must therefore be greater than that of the right. Eppinger, Burwell and Gross believe this to be two to four times that of the right. In order to accomplish this increased output, the left ventricle would enlarge and hypertrophy, while the peripheral circulation may be reduced as a further compensatory mechanism. The pulmonary vessels, to accommodate the increased volume of blood, must dilate, and such dilatation may be shared even by the left auricle. Eppinger, Burwell and Gross, however, make little mention of any pressure changes in the pulmonary circuit or of any compensatory changes that may take place there.

Keys et al (1943) place the volume of the blood shunted at ± 50% of the left ventricular output. They employed a roentgen-kymographic method, with an error which they claim to be only ± 4.5%. Leeds (1941), from experimental observations in dogs, in which an artificial patent ductus had been made by anastomosing the left subclavian artery to the pulmonary, found the amount of blood shunted to be about 46%. Levy and Blalock (1939), performing similar experiments, did not state the volume of blood shunted, but remarked that it had very little effect on the peripheral

blood pressure, and that the pulmonary pressure was about half that of the systemic - a fact they attribute to the smallness of the pulmonary resistance.

On the whole, the above work can be regarded as supporting in large measure the thesis of Eppinger, Burwell and Gross (1940). Bettinger (1941), on the other hand, is opposed to it, and his views are based on a case described by him. In this case, which was one of uncomplicated ductus arteriosus, there was right ventricular enlargement only, gross dilatation of the pulmonary artery with atheromatous plaques (but not of its branches), a history of cyanosis of lengthy duration, and a paradoxical embolism of the right renal vein to the spleen. From this, he concludes, that in this particular case, at least, there must have been a veno-arterial, as opposed to the usual arterio-venous fistula. He maintains that this was brought about as the result of a compensatory mechanism. The pulmonary arterioles, he alleges, by constricting, can raise the pressure in the pulmonary circuit to a level much nearer that in the aorta than is generally believed, and, by so doing, control and limit to some extent the amount of the shunt. In his case this was developed to a degree that was in fact an overcompensation. The resulting rise in pressure in the pulmonary circuit would, in time, cause the right ventricular hypertrophy. In support of his hypothesis, he states, that only the larger branches of the pulmonary vessels are usually dilated and not the smaller arterioles. This is due to the relative deficiency of muscle

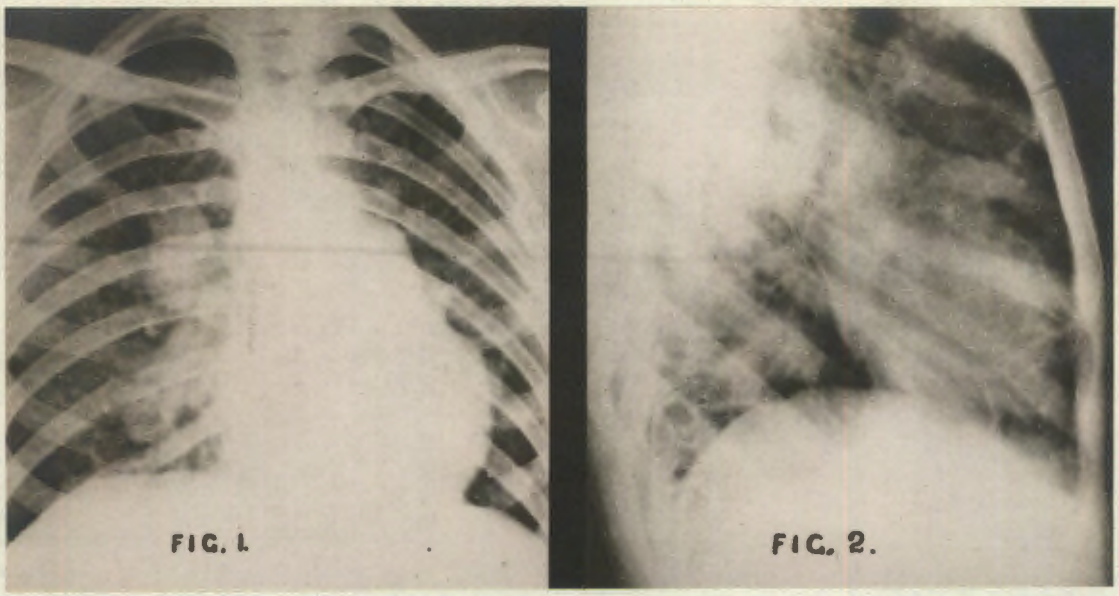
fibres in these vessels. The fact that the retardation of growth is not an essential finding (and this would be unlikely with adequate compensation), he regards as a further support of his theory. Finally he states that cyanosis is a much commoner finding than is generally supposed. The state of affairs as propounded by Eppinger, Burwell and Gross he regards as being a terminal event, being the result of right ventricular failure !

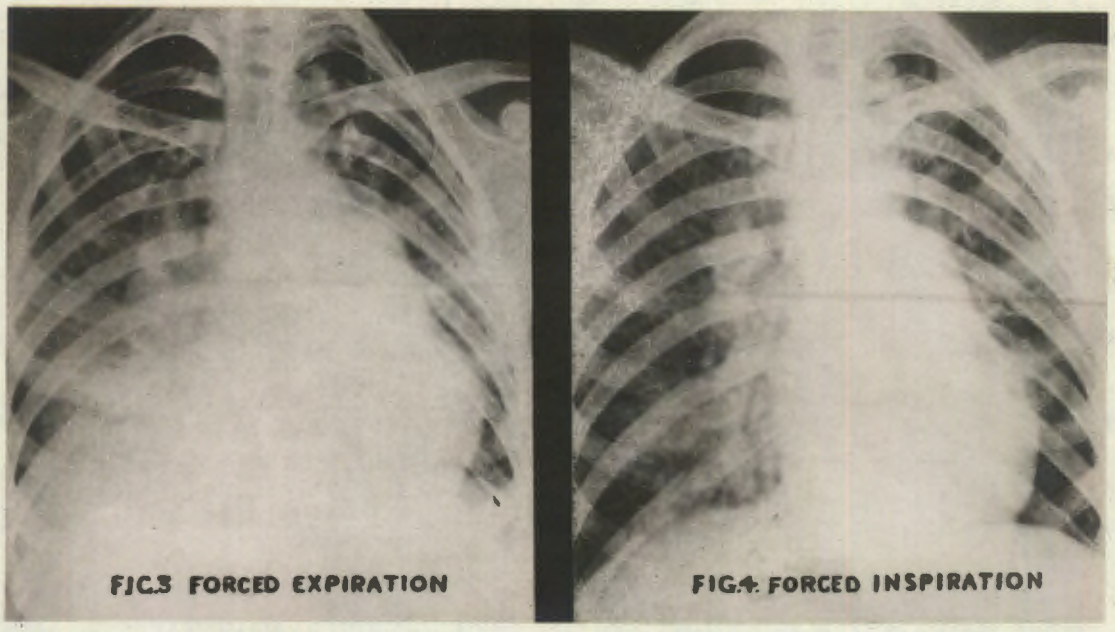
Shapiro and Keys (1943) make the statement that right heart enlargement is the characteristic feature of patent ductus arteriosus. They may have made a mistake of referring to the prominent pulmonary conus as the right ventricle, for Donovan, Neuhauser and Sosman (1943) find left ventricular hypertrophy in 70% of cases.

The main criticism that can be levelled against the work of Eppinger, Burwell and Gross is that there is no satisfactory proof that the samples of blood, which they took from the pulmonary artery, were taken at a point where thorough admixture of the two streams of blood, arterial from the aorta, and venous from the pulmonary trunk, could have taken place. They themselves were dubious of this point until they had experimented with dogs. It is obvious that if the samples should contain a variable amount of arterial blood, the readings of the volume of the shunt based on them, will be inaccurate. This may account for figures which claim a 75% shunt of the output of the left ventricle through the ductus. To any one who

has observed the relative sizes of the ductus and the aorta distal to the ductus, this figure must seem extremely high, and could probably only be possible if there were a great difference in the relative pressures in the two circuits. The roentgenkymographic methods of Keys et al have not been accepted as reliable, and artificial patent ducti, existing for a few months in animals, could not possibly have exactly the same effects as those present in the human from birth. On the other hand, it must be pointed out that the findings of Eppinger and Burwell have been accepted by the majority of observers on clinical grounds.

The views of Bettinger can be criticised on the grounds that they are based on the findings in a case which is unique, and the conclusions drawn from such findings are bound to apply to that case only. Nevertheless, Bettinger has stressed an aspect which apparently had not been considered previously, namely, the possibility of a compensatory mechanism existing in the pulmonary circuit. With our knowledge of the powers of adaptability possessed by the body, it seems reasonable that such a compensatory mechanism should exist. What few authors regard as being of significance is the fact that, if there is a shunt of blood from the high pressure aorta to a lower pressure pulmonary artery, then not only the volume, but also the <u>pressure</u> in this circuit must rise. Bull and Krueger have long since put forward the thesis that vascular changes constitute a physiopathologic response to pulmonary hypertension,




Plates of case of Patent Ductus Arteriosus with aneurysms of pulmonary vessels, taken at rest, forced inspiration and expiration. (This case was proved at postmortem. Holmes, 1944)

Fig. 7.

so that hypertrophy of the pulmonary arteriolar vessels would not be unexpected. Yet, except for very isolated incidental cases, postmortem reports of investigations of the state of these vessels cannot be found. As material for this study is not available in South Africa at present, it will have to remain a point for further investigation. Chapman and Robbins (1944) report a case of patent ductus arteriosus in which medium sized pulmonary vessels showed extensive intimal atherosclerosis. This, not unreasonably, may be regarded as a further result of vascular response to the pulmonary hypertension, for degeneration after hypertrophy is by no means an unusual sequel in surgical pathology. Holmes (1944) and others preceding him, such as Costa (1929), have reported pulmonary aneurysms in association with patent ductus arteriosus (Fig. 7) - again a phenomenon that can be expected under the circumstances cited above. In Holmes' case, the aneurysms involved not the main pulmonary artery, but the vessels of the lung parenchyma. Costa (1929) in 79 cases of pulmonary aneurysm collected by him, cited the patent ductus arteriosus as the cause in 20% of cases. The majority, however, involved the main stem and branches of the pulmonary artery, which may be attributed to the fact that this is a response to increased blood-volume of vessels poorly supplied with muscle fibres, and not due to secondary degeneration following hypertrophy.

Certain clinical observations support the conception that there is some compensatory action on the part of the lesser

circulation. There is, as a rule, no departure from the normal to be detected by the electrocardiogram in cases of patent ductus arteriosus. This seems remarkable, to say the least, in cases in which the left heart is overactive to the degree postulated. If there is no left axis deviation then it must mean that either the left heart is not overactive and hypertrophied, or, that the right heart is also overactive to an almost equal degree. Nor is marked cardiac enlargement a striking feature, although Donovan, Neuhauser and Sosman claim a 70% enlargement of the left ventricle.

In conclusion it may be said that, in the case of the patent ductus arteriosus, as with other matters pertaining to medicine, generalizations are always difficult, and nearly always break down on specific instances. It appears more reasonable to state, that the reaction of the body in cases of patent ductus arteriosus varies within wide limits. On the one extreme, there may be little or no compensatory response on the part of the pulmonary vascular bed - resulting in a large shunt of blood from the aorta to the pulmonary artery (i.e., figures approaching 75% of the output of the left ventricle), while, on the other, compensation may exist to a degree causing the production of a veno-arterial fistula, as in the case of Bettinger. According to Holman (1925), cardiac enlargement will be commensurate with the increased volume of flow and confined to that half through which the greater flow passes. Between these two extremes will be the great majority of cases,

with the majority showing relatively little pulmonic compensation, as is judged by clinical experience, while a minority may show a great deal. One would venture to add the additional hypothesis, that the greater the pulmonary vascular compensation, the longer before cardiac failure will set in, and consequently the better the prognosis. It may well be, that the examination of the postmortem material from those cases who have lived longest, will bear this out.

# CHAPTER V.

## CLINICAL ASPECTS.

### A. Natural History.

The ductus arteriosus may remain patent under two sets of circumstances. In the first instance, it may remain patent as a compensatory mechanism for other defects such as coarctation of the aorta, aortic valvular stenosis, and in particular, hypoplasia or coarctation of the pulmonary artery, and pulmonary stenosis. (In pulmonary stenosis, where the ductus is absent, an artificial one has been created by Blalock and Tausig , 1945, by anastomosing the left subclavian artery to the pulmonary artery.) On the other hand, it may remain patent for reasons not clearly understood, and exist as the sole abnormality - the so-called uncomplicated patent ductus arteriosus. When associated with other abnormalities, the ductus is often essential for the maintenance of the circulation and its ligation would be followed by serious consequences.

It is believed by Bullock, Jones and Dolly (1939) that few cases of multiple defects survive the first year or so of infancy, and in the majority of Maud Abbott's (1936) series of cases, where the ductus existed as a compensatory mechanism, there was cyanosis present. The associated defects, when present in older children and adults, are usually of a minor nature - such as minor degrees of coarctation of the aorta and patent interventricular septum. It is of interest to recall that, according to Versluys, in his comparative anatomy, certain

reptiles such as the chelonia and lacertilia have the association of patent ductus arteriosus with defective interventricular septum as a normal state of affairs.+ When submerging under water, they are able to exclude the lungs from the circulation, by diverting the blood through the ductus arteriosus. As a result of the decreased pulmonary circulation, there is a fall in the pressure in the left ventricle so that blood is forced over the septal defect from the right ventricle to the left. As a result, although the brain and other regions receive more and more unoxygenated blood, these animals are able to remain submerged for a long time.

According to Muir and Brown (1932), Perry, in a review of congenital heart disease, found uncomplicated patent ductus arteriosus to be a rare lesion, namely 8 cases in 121 reported, or 6.5%. Muir and Brown (1932) found the proportion to be much higher - 20 cases in 88 or about 23%. Maud Abbott (1936) reported an incidence of 40%, while Bullock, Jones and Dolley (1939) found 42% of cases (see Table 1). These latter figures appear to be much nearer the correct figure than the earlier ones, as both those of Abbott and Bullock et al were based on postmortem examinations. Grier (1943) found the proportion of uncomplicated cases to be 53%. Maud Abbott found patent ductus arteriosus to constitute 9.2% of congenital heart disease.

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+ The flow of blood in this case would be in a direction which is the exact reverse of that which is usually encountered in pathological patent ductus arteriosus.

## INCIDENCE OF UNCOMPLICATED CASES.

| Author | Total No. of Cases | Uncomplicated | Percentage |
|---|---|---|---|
| Perry | 121 | 8 | 6% |
| Muir and Brown | 88 | 20 | 22% |
| Maude Abbot | 232 | 92 | 40% |
| Bullock, Jones and Dolly | 36 | 15 | 42% |
| Grier | 39 | 21 | 53% |

## SEX INCIDENCE.

| Author | Total No. of Cases | Female | Male. |
|---|---|---|---|
| Shapiro | 62 | 47 | 15 |
| Muir and Brown | 20 | 13 | 7 |
| Donovon et al | 50 | 33 | 17 |
| Gilchrist | 28 | 15 | 13 |
| Present Series | 11 | 7 | 4 |

TABLE 1.

Wilson and Lubschez (1942) place the figure at 10%.

Shapiro and Keys (1943) estimate that there are 20,000 people in the U.S.A., with its population of about 150 million, with patent ducti, or one in 7,000. Bullock, Jones and Dolley place the figure much nearer 6 in 7,000.

Shapiro (1944) finds females involved three times as often as males. Donovan et al (1943), reporting on Gross' series of cases, find the proportion to be roughly two females to one male; Muir and Brown (1936) support this, but Gilchrist (1945) found the incidence to be almost equal in the two sexes. In the present series of eleven cases, seven were females and four males (Table 2).

It has been reported that the condition may be familial, with a fault in the germ plasm as the responsible aetiological factor. Smith (1929) noticed the occurrence of the condition in twins. Of interest in this connection is the fact that one of the cases of the present series was found to be suffering from patent ductus arteriosus (proved at operation), after his sister, who on somewhat equivocal clinical grounds, had been diagnosed as an open ductus, had been subjected to operation, which failed to reveal the ductus.

Extra-cardiac abnormalities may occur in association with patent ductus arteriosus, but not very commonly. Webbing of the toes, clubbing of the feet and undescended testis have been described. Bullock et al (1939) believe accessory nipples to be the commonest associated finding.

B. The Symptoms.

The fact that the vast majority of cases of patent ductus arteriosus are "discovered" during the second decade (Gilchrist, 1945) indicates that symptoms cannot be a striking feature of the condition. This point is emphasized by all authors on the subject, and has been the experience in the present instance. The condition is usually "discovered" accidentally, during routine school medical examinations, or when the cardiac apparatus is checked by a physician called in for some minor ailment. In those cases which do present symptoms, a considerable element of neurosis may prevail. The cases may be described as being "heart-conscious", and their symptoms may date from the time the lesion was brought to their attention.

Generally, then, it is said that symptoms are absent. Gilchrist, however, finds himself unable to agree with this general statement. He feels that often, only after operation, the parents will find that a child which they had previously considered normal, had in actual fact been more listless than they had realised. Adults, too, he feels may be so accustomed to minor disabilities that they regard them to be normal.

The symptoms that are usually complained of are easy fatiguability, dyspnoea on exertion and palpitations. In all the cases examined for this thesis, the original diagnosis was made at a casual examination. Three of them complained of the symptoms mentioned above since that time. "Fear of the night" was a symptom complained of by one patient. This was

apparently due to the disturbance caused by the noisy heart. Activity is frequently restricted in these patients after the discovery of the lesion. Schooling may be interrupted. All of which, undoubtedly, causes some element of neurosis.

Cyanosis, with elevation of the intrapulmonary pressure, as in fits of coughing, has been described by various authors. (Maud Abbott, 1936). Smith (1929) and Leech (1932) state that it may be induced by emotional disturbances. Maud Abbott explains the cyanosis on the basis of unstable intra-arterial pressures. Gilchrist, Gross and others believe that this is not a common finding. It has not been observed in the present series, in spite of attempts to induce it by elevating the intrapulmonary pressure. Clubbing of the fingers was seen in one case.

Epileptiform convulsions are alleged to be an occasional occurrence. Shrotter (1904) and Tilestone (1910) have reported cases with hoarseness due to paralysis of the recurrent laryngeal nerve - presumably by pressure of a dilated ductus.

Attacks of epistasis may occur. Gross (1929) states that this may be profuse and that it occurs particularly commonly between the ages of four and eight. Two patients of the series reported attacks of this nature.

C. <u>The Clinical Signs</u>.

(a) <u>The Bodily and Mental Development</u>:-

Patients with patent ductus arteriosus are usually described as being tall, slender and pale, and as presenting the stigmata

of aortic hypoplasia and arterial depletion. Often they are reputed to be mentally retarded, and physically under developed. Muir and Brown (1932) found subnormal growth in 20% of cases. Shapiro (1944) found stunting of growth inabout 28% and the figures of Gilchrist (1945) agree with the latter. In the present series one child was tall, slender and pale, and two small for their age. The remainder appeared normal, except one who was obese. The reasonable conclusion that can be drawn from this seems to be that there does not appear to be any characteristic bodily and mental configuration associated with patent ductus arteriosus. It may perhaps be said that over-growth appears to be more rare than under development.

(b) The Cardiac Apparatus:-

It is no more than is expected that the essential clinical features are provided by the cardiac apparatus. Yet, it is well known that even these may be entirely lacking in the presence of patent ductus. According to Gross (1939) and others, physical signs may be entirely lacking in the first year of life, and it is usually only after the fourth year that the classical physical signs may manifest themselves.

i) Auscultation:- It is by auscultation that the single most significant sign in patent ductus arteriosus is observed. This is the classical murmur of the patent ductus arteriosus, which was originally described by Gibson (1906). Gilchrist (1945) suggests, and this seems just, that the murmur should be termed the "Gibson murmur". The essential feature of the

murmur is its continuous quality - variously indicated by the terms "machinery", "rolling thunder", "rushing water", or "humming top". This quality appears clearly described by Gibson as follows: "It begins after the commencement of the first sound, and is continued during the latter part of that sound and the whole of the short pause. It persists through the second sound and dies away gradually during the long pause. The murmur is distinctly rough and thrilling. It begins softly, and increases in intensity so as to reach its acme just about, or immediately after the incidence of the second sound, and from that point gradually wanes till its termination. The second sound can be heard to be loud and clanging."

Routier (1937), who analysed phonocardiographically records of the murmur, states that the murmur begins after the first sound and reaches its maximum intensity with the second sound and continues at that pitch during diastole. Reinforcement, according to him, therefore takes place during diastole. This description of the ausculatation agrees with that of Gibson, so that reinforcement occurs during diastole and not during systole, as is generally believed. According to Jones et al (1940), who used auscultation and phonocardiographic methods, the accentuation may vary, sometimes occurring in systole, but more often in early diastole. In view of the fact that Touroff (1943) describes a case in which the murmur persisted after ligation and division, it would appear that the murmur is perhaps not generated in exactly the same way in every

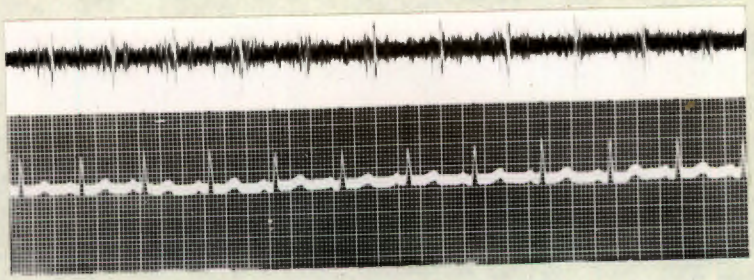


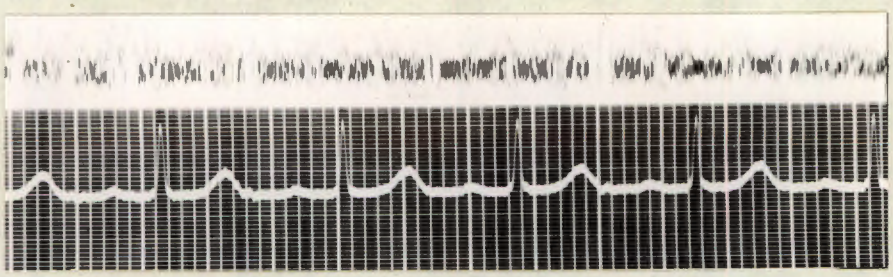
Figure 10. A typical phonocardiogram of case of patent ductus arteriosus.

Note the continuous character of the murmur.

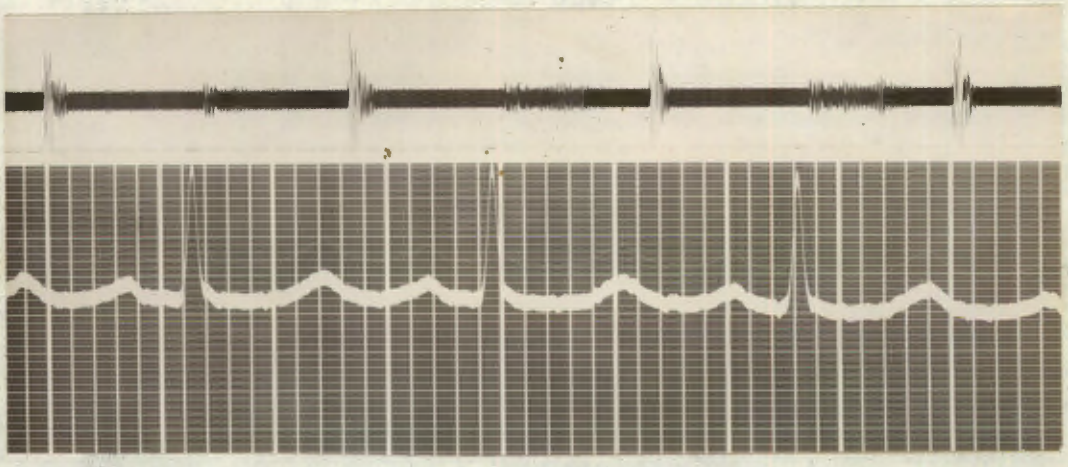
case. This may account for variations such as have been noted. For a typical phonocardiographic tracing see Fig. 10.

The murmur may be systolic in time only. This is seen in young children particularly and is regarded as the earliest manifestation (Gross, 1939). Bettinger (1941), Keys (1943 and others have reported cases of patent ductus discovered at postmortem, in which the murmur was entirely absent.

Of whatever type, the murmur is usually loudest and best in the second left interspace. Jones et al (1940) have found it maximal in some cases in the first or third spaces, whilst Gilchrist (1945) believes it to be loudest at the point where the pulmonary artery lies nearest the surface. This is usually the second interspace, but, in cases where there is considerable enlargement of the pulmonary artery, the murmur may be heard nearer the left anterior axillary line. In some of Gilchrist's cases it was heard "fully a hand's breadth from the sternum". Conduction may take place in many directions. A very loud bruit may be heard all over the praecordium. The common directions of propogation are towards the inner end of the left clavicle and towards the axilla. It may be heard easily at the back, opposite the spine of the left scapula. In all cases of this series the murmur radiated to the inner end of the left clavicle and was clearly heard at the back. The systolic element may be conducted to the apex, where also a diastolic murmur may be detected. Two cases of Jones et al (1940) subsequently proved to have patent ductus, had previously been



Typical phonocardiogram in a case of patent ductus arteriosus.



Phonocardiogram in same patient after operation.

Note slight systolic murmur that is still present.

Fig. 11.

diagnosed as mitral stenosis. Usually, however, the two sounds at the apex may be heard clearly, apart from the conducted murmur.

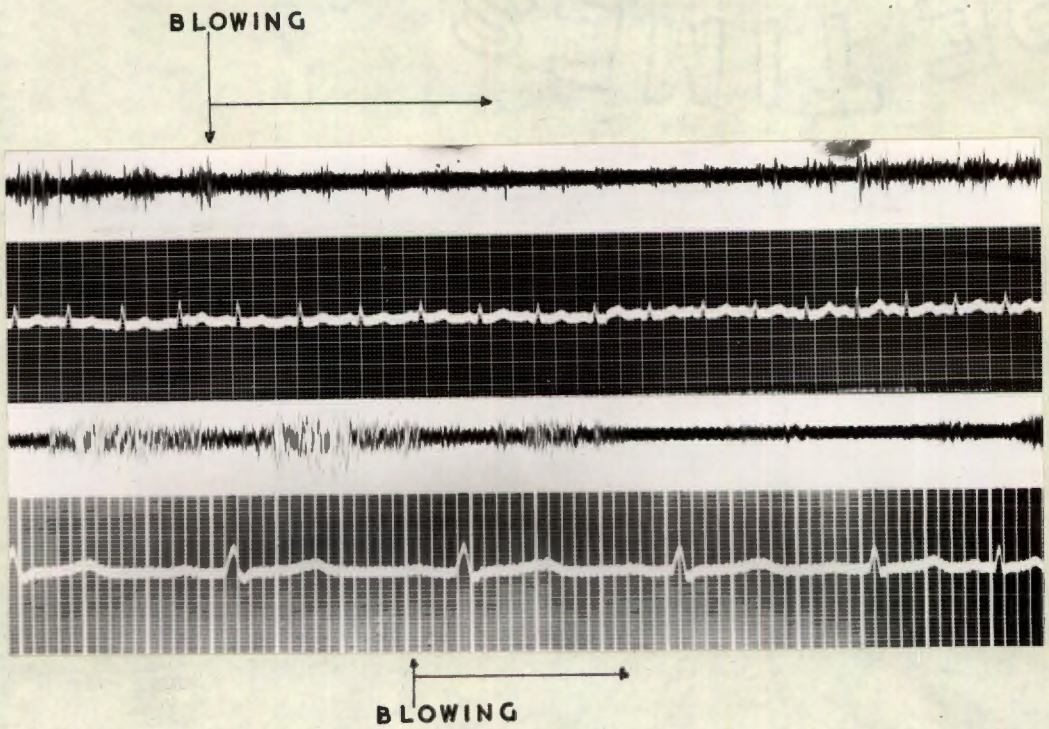
The intensity of the murmur varies. According to Gross (1939) the very loud and harsh murmurs are found in the long and narrow ducti. Wider and shorter ducti, apparently, are responsible for the softer, humming-top murmurs. Bettinger (1943) described a case of patent ductus discovered at postmortem in which there had been no murmur elicited by the previous cardiovascular examination. Keys (1943) reports a similar case and cites two from the literature. Gilchrist (1945) states that in some adults the murmur may be so soft as to escape notice, unless particularly searched for. These soft murmurs appear to be particularly prevalent in cases in which heart failure is setting in. Brown and Muir (1932) maintain that the murmur is often best heard during deep inspiration, while Burch (1944) asserts that it is best heard with the patient leaning forward and the breath expired to the maximum.

It is gnerally accepted that the murmur is generated by the passage of blood through the ductus. In the vast majority of cases this must be so, as the murmur is abolished by ligation in most instances. However, Bourne, Keele and Tubbs (1941), Gross (1944), Shapiro and Keys (1943), Gebauer (1943) and others have reported the persistence of the systolic element after ligation, and this was seen in the present series too (Fig. 11). Laubry and Pezzi (1921) attribute the diastolic element to the

dilatation of the pulmonary artery with pulmonary incompetence. Incompetence, however, is unlikely as the pulmonic second sound is usually accentuated and sometimes reduplicated. This is a very significant feature, as it serves to differentiate the condition from cases of pulmonary stenosis. It may easily be missed unless sought for immediately below the point of maximum intensity of the Gibson murmur (Muir and Brown, 1932). In all the cases in their series, this feature was observed. Additional murmurs may be heard, particularly in cases of subacute bacterial endocarditis. Touroff (1943) believes that this may indicate extension of vegetations to the heart valves.

ii) The Blowing Test:- In the course of the present series of investigations, a test was devised, suggested by Professor Goetz, termed the "blowing test", which, it is hoped, will prove of real value in the diagnosis of patent ductus arteriosus, and may yet come to be regarded as a pathognomonic sign. The test is based on the hypothesis; as the murmur is produced by the shunt of blood through the patent ductus arteriosus from the aorta to the pulmonary artery, any factor which will reduce the volume of the blood shunted, or decrease the rate of flow, such as elevation of the intrapulmonary pressure, will reduce the intensity of the murmur.

In order to raise the intrapulmonary pressure, the patient is instructed to blow into a bottle, or manometer, the opening of which can be sealed off by the lips. The maximum pressure must be exerted, and must be sustained for as long as possible.




**The Blowing Test.**

Phonocardiographic tracings from two patients with patent ductus arteriosus showing the almost complete disappearance of the murmur in the top tracing, and a marked fading in the lower tracing.

The murmur is listened to continuously, at the point of maximum intensity, before, during, and after the blowing. It has been found that in every case of patent ductus arteriosus so tested, THE MURMUR FADES OR DISAPPEARS DURING BLOWING, AND RETURNS WITH INCREASED INTENSITY ALMOST IMMEDIATELY AFTER CESSATION. This has been confirmed by phonocardiographic tracings (see example).

It was obviously necessary to observe the effect of this test on other murmurs. Table 3 shows the results of the test on various patients. Hitherto, it has not been found positive in any other type of heart lesion, with the exception, perhaps, of mitral stenosis. In aortic regurgitation, a condition which is often difficult to exclude in the differential diagnosis by the quality of its murmur, the test has been negative in several cases, the murmur being either unaffected or accentuated.

This observation in connection with aortic regurgitation may be regarded as being very significant, for, a to-and-fro murmur at the base presents the most difficult problem in the differential diagnosis. If it can definitely be stated that the murmur of aortic incompetence is unaffected by the blowing test while the murmur of patent ductus arteriosus fades or disappears, the solution of the problem will be facillitated.

With mitral stenosis there does appear to be fading of the murmur to a slight degree in the majority of cases. In addition there appears to be an alteration in the pitch of the murmur. This is not unexpected, as the murmur is dependent

TABLE 3.

BLOWING TEST PERFORMED ON SERIES OF HEART CASES AS CONTROL.

| Name | Age | Type and Site of Murmur | Nature of Lesion | Result of Blowing. |
|---|---|---|---|---|
| Hendrik Vermeulen | 23 | To & fro murmur 4th left space | Aortic regurgitation with S.B.E. | Slightly increased. |
| George Colley | 26 | Pre-systolic at apex | Mitral stenosis | Murmur disappears, 1st sound sharp and small |
| Johanne Brown | 47 | To & fro all over | Aortic regurgitation (Luetic) | unaltered. |
| Lazarus Brown | 49 | To & from base | " " | " slightly++ |
| Adam Danielz | 57 | Soft diastolic left sternum 3rd space | " " (hypertensive) | unaltered. |
| Willem v.d.Merwe | 13 | Rumbling early diastolic | mitral stenosis | slight diminution elevation in pitch |
| George Ryneveld | 54 | To & fro all over | Aortic Regurgitation (specific) | No change |
| J. de Klerk | ? | Rumbling diastolic | Mitral +? S.B.E | No change. |
| Kitty de Jong | | To & fro at base | Aortic Regurg. | No change. |
| William Hodgson | 47 | Musical systolic + soft diastolic at apex | Mitral stenosis | Diminishes slightly. |
| Blanche Rutge | 28 | To & fro at base. Rumbling diastolic at apex. | Mitral stenosis + aortic regurg. | Basil murmur increased. Apical murmur slightly decreased. |
| Jessie Clough | ? | Short pre-systolic | Mitral stenosis | Slight diminution. |

S.B.E. = Subacute bacterial endocarditis.

upon the pulmonary circulation for its generation. Acceleration of filling of the left ventricle may cause the diminution of the murmur. Mitral stenosis, however, with its murmur maximal at the apex, does not produce nearly the same problem of differential diagnosis, and it may well be that the blowing test may prove of value in excluding murmurs occurring in the mitral area, resembling those of mitral stenosis, from the true murmurs of mitral stenosis.

Thus, while the blowing test has yet to be extensively tested before final conclusions can be drawn, it is tentatively offered as a sign of value in confirming the diagnosis of patent ductus arteriosus.

The murmur is frequently accompanied by a <u>thrill</u>. This thrill may be continuous, systolic or diastolic in time, and is usually felt at the point of maximum intensity of the murmur. Shapiro (1944) found the thrill to be present in 80% of cases. Maud Abbott (1936) found it present in about 30%, while James Brown asserts that it is present in about 50% of cases. In the present series, it was observed in ten out of eleven cases.

<u>Gerhardt's "ribbon" dullness</u> may be elicited in patients with patent ductus arteriosus. This is an area of dullness in the second and third left intercostal spaces next to the sternum. It is attributed to enlargement of the pulmonary artery. Muir and Brown (1932) maintain that the sign may nearly always be found in adults, but is often absent in children. This statement is supported by Shapiro and Keys (1943), who

state that in adults dilatation of the pulmonary artery is an almost invariable finding, but that this is not so in the case of children.

iii) The Blood Pressure:- According to Gilchrist (1945) detailed studies of the blood pressure in patent ductus arteriosus are comparatively rare. Yet, it has often been remarked that the most characteristic feature shown by blood pressure readings in patent ductus arteriosus is a large pulse pressure. This, in cases of wide ducti, where the shunt is considerable, closely resembles that seen in aortic regurgitation. The systolic pressure reveals little that is abnormal, but the diastolic is often low. Many proved cases of patent ducti, however, have shown perfectly normal blood pressure readings; so that a high pulse pressure, again, is not an essential finding.

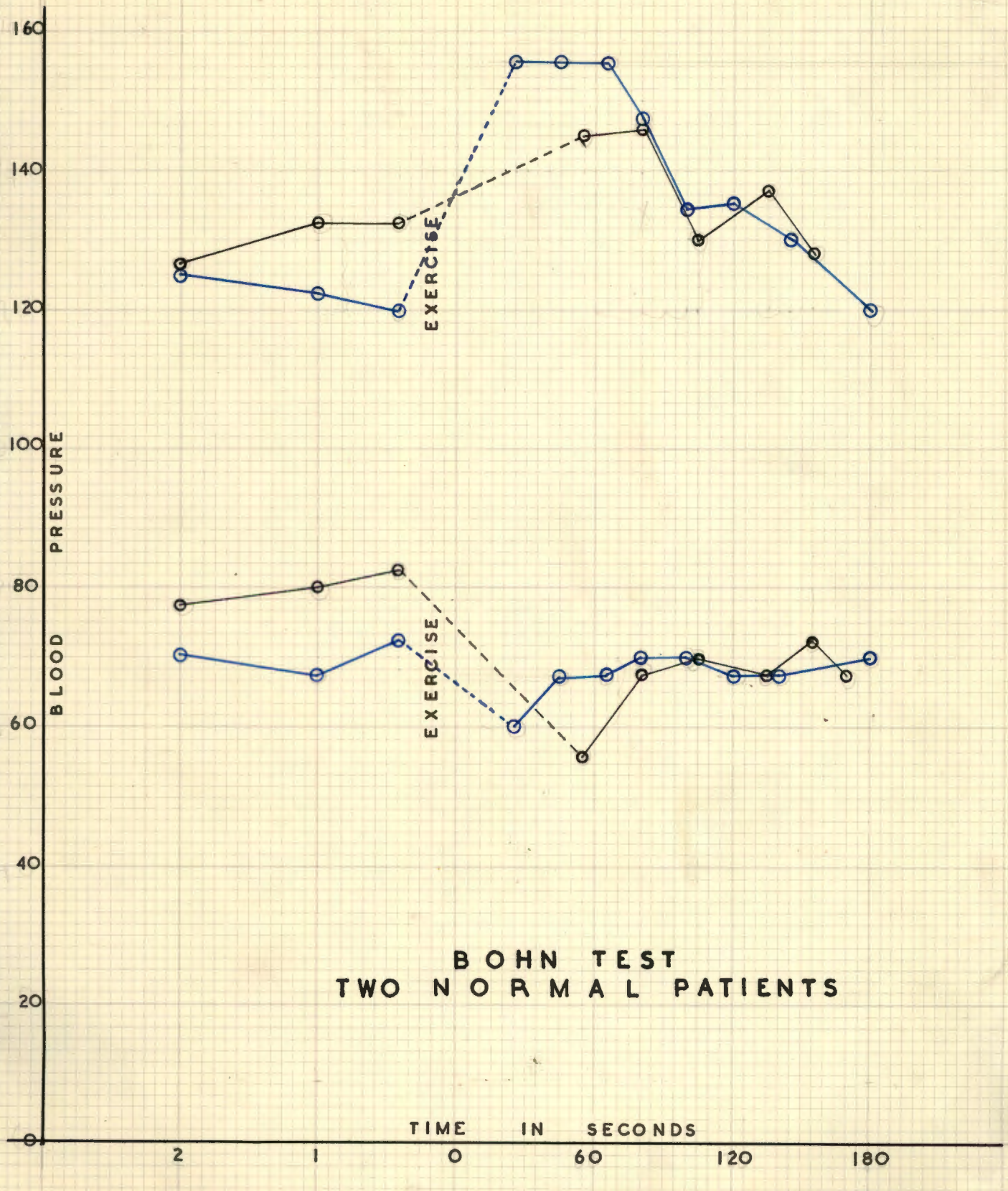
iv) The Bohn Test:- Bohn in 1938 described a test, which he considered to be of great value in the diagnosis of patent ductus arteriosus. The test consists of taking the blood pressure readings at rest - several readings being taken. The patient is then asked to perform 10 or more squatting exercises at fair speed. Blood pressure readings are then taken immediately after completion of the test at rapid intervals. According to Bohn, in patent ductus arteriosus the systolic pressure rises after exercise and the diastolic falls. In one of his cases this fell to zero. Gilchrist (1945) and Vesell (1944) have found this test of value. Gilchrist in-

## TABLE 4.

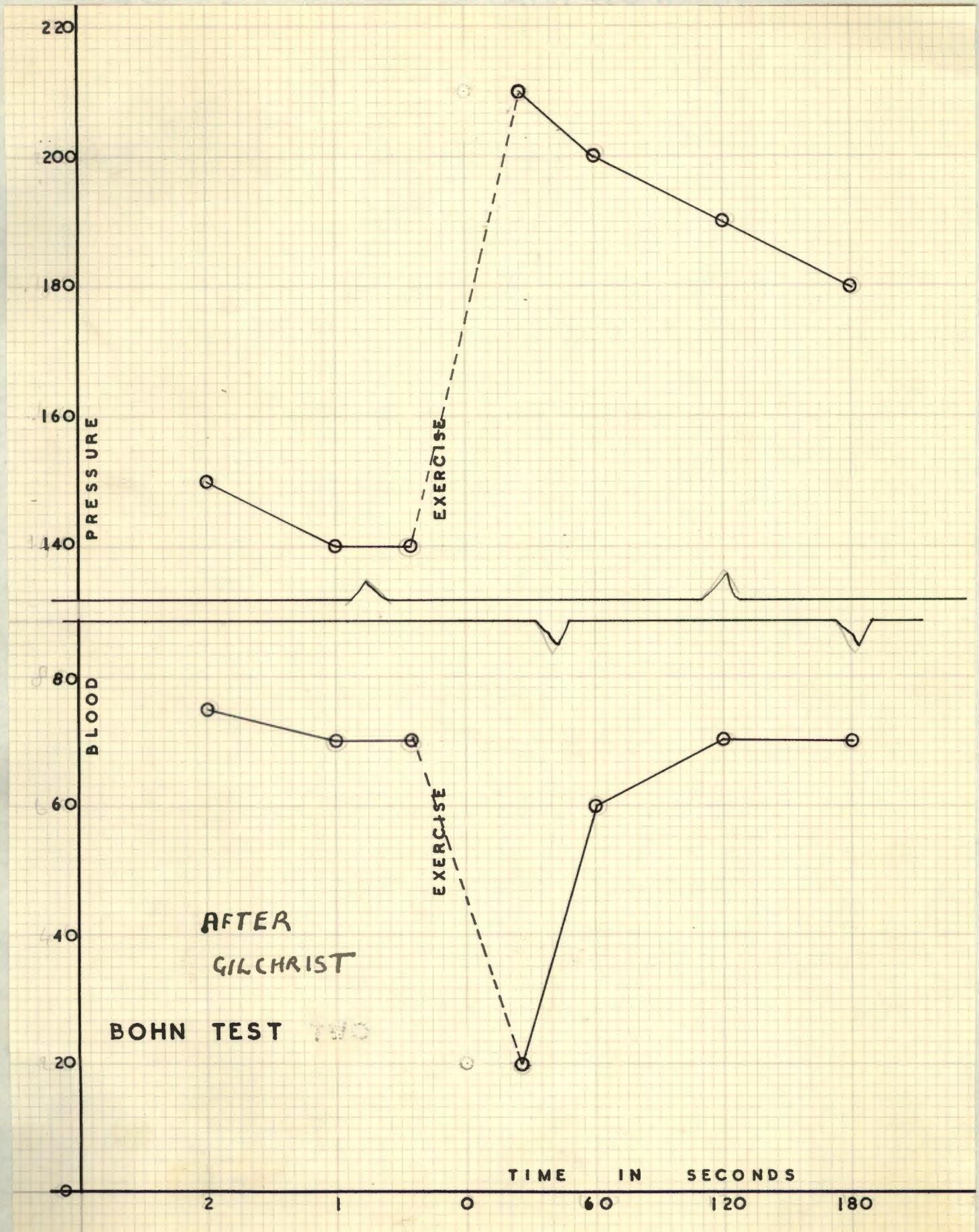
## BOHN EXERCISE TEST.

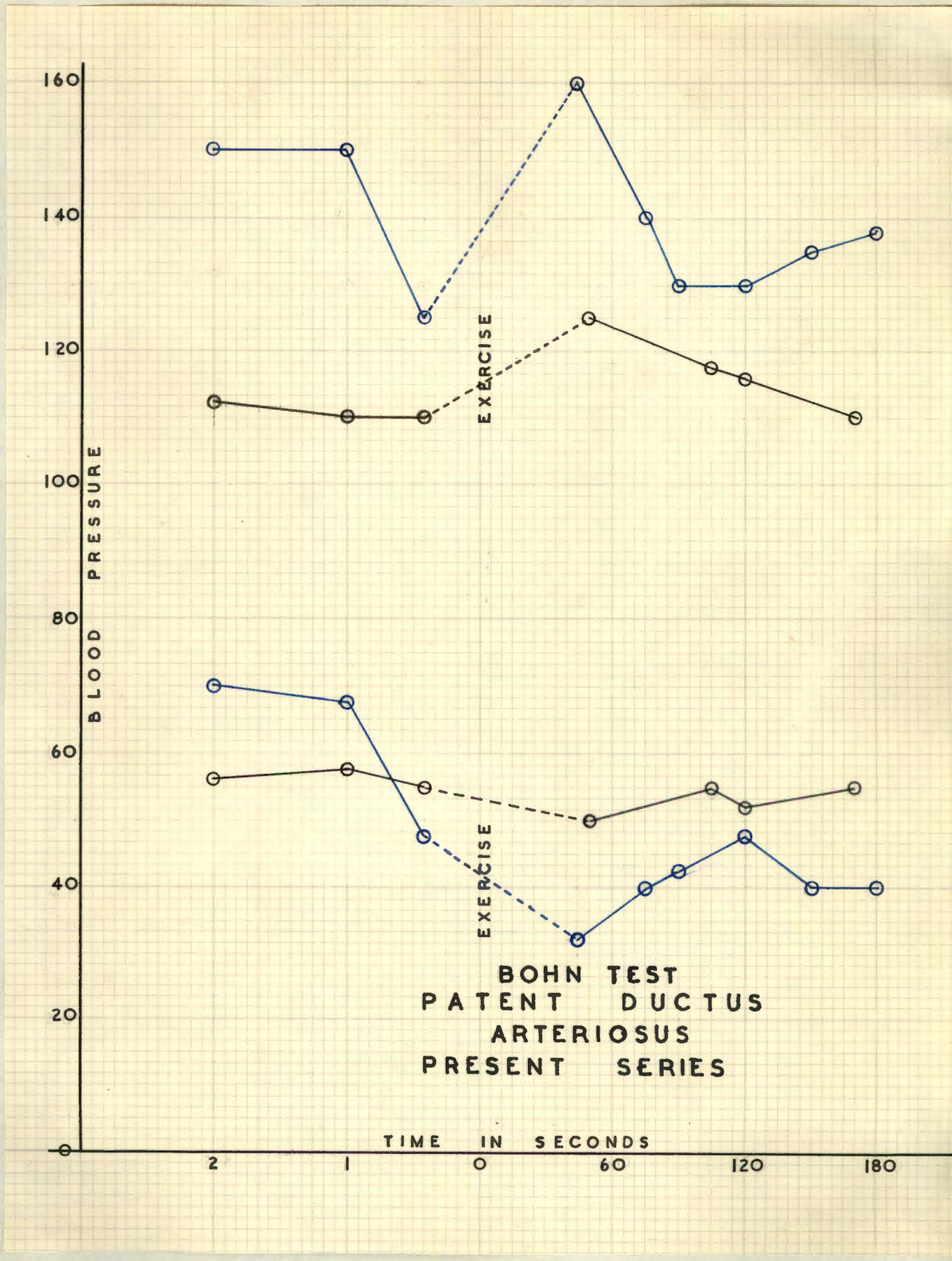
## Patent Ductus Arteriosus.

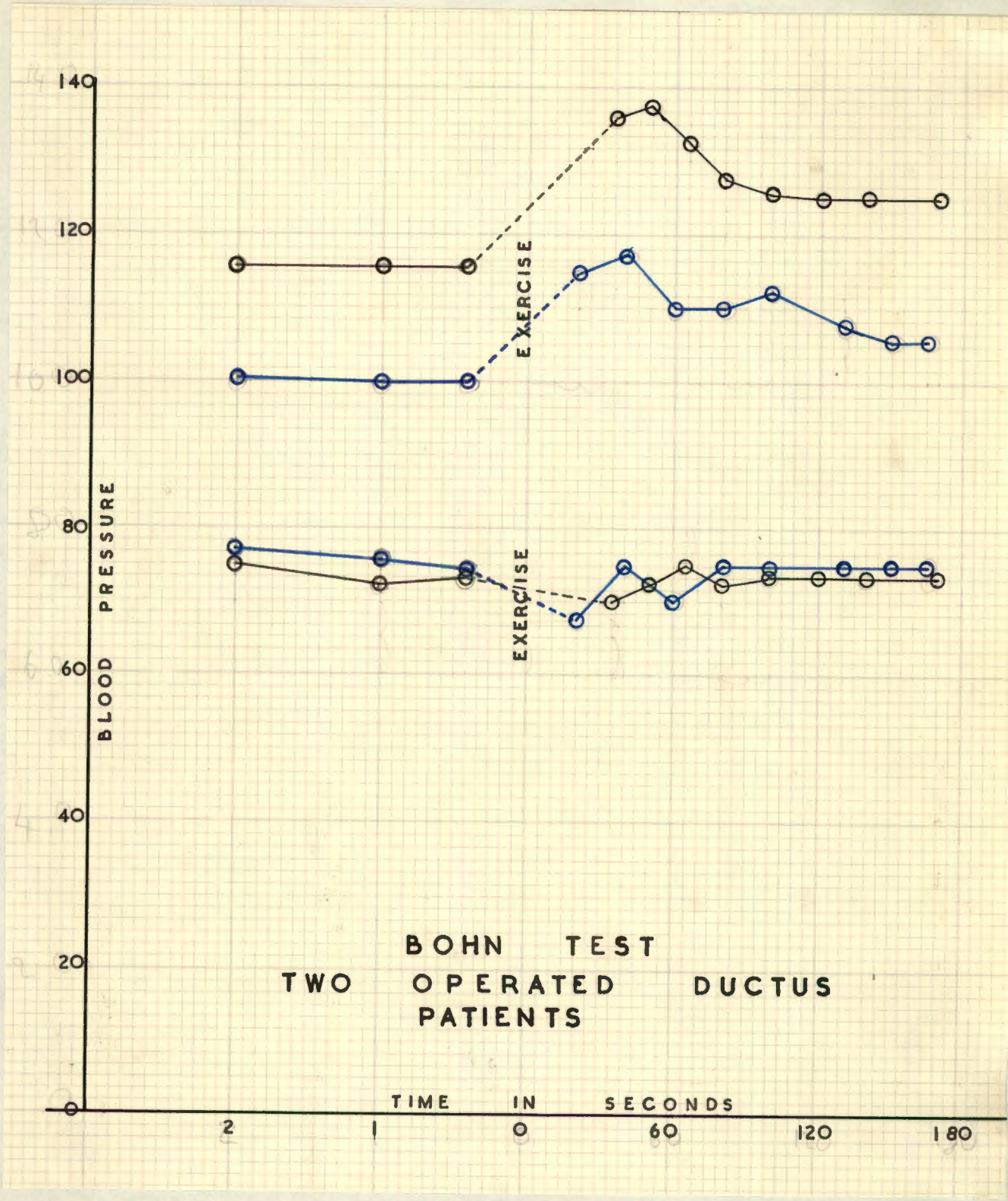
| Name & Age | Pressures Before Exercise | | | Pressures After Exercise | | | Rise in Pulse Pressure |
|---|---|---|---|---|---|---|---|
| | Systolic | Diastolic | Pulse Pressure | Systolic | Diastolic | Pulse Pressure | |
| S.H. 20 | 126 | 68 | 58 | 138 | 56 | 82 | 24 |
| J.G. 12 | 96 | 48 | 48 | 120 | 48 | 72 | 24 |
| T.H. 12 | 124 | 46 | 78 | 130 | 32 | 98 | 20 |
| J.L. 12 | 120 | 68 | 52 | 140 | 66 | 74 | 22 |
| E.F. 8½ | 115 | 65 | 50 | 130 | 65 | 65 | 15 |
| F.B. 31 | 120 | 64 | 56 | 150 | 66 | 84 | 28 |
| A.B. 4½ | 110 | 64 | 46 | 126 | 70 | 56 | 10 |
| Mean | 115 | 60 | 55 | 133 | 57 | 75 | 20 |
| **Normal People.** | | | | | | | |
| P.C.M. 29 | 122 | 80 | 42 | 130 | 60 | 70 | 32 |
| A.J.L. 27 | 124 | 70 | 54 | 156 | 60 | 96 | 42 |
| M.C.B. 23 | 132 | 88 | 44 | 152 | 88 | 64 | 20 |
| E.B.M. 28 | 126 | 80 | 46 | 146 | 56 | 90 | 44 |
| K.H. 21 | 112 | 76 | 36 | 130 | 62 | 68 | 32 |
| M.C.B. 23 | 126 | 72 | 54 | 134 | 64 | 70 | 16 |
| Mean | 127 | 77 | 46 | 141 | 65 | 76 | 30 |
| **Aortic Regurgitation.** | | | | | | | |
| Name not recorded | 154 | 76 | 78 | 166 | 70 | 96 | 18 |
| " | 114 | 54 | 60 | 120 | 54 | 66 | 6 |
| " | 144 | 68 | 78 | 168 | 80 | 88 | 12 |




BOHN TEST
TWO NORMAL PATIENTS


220
200
180
160
140
PRESSURE
EXERCISE
80
60
40
20
0
BLOOD
EXERCISE
AFTER
GILCHRIST
BOHN TEST TWO
TIME IN SECONDS
2
1
0
60
120
180


160
140
120
100
80
60
40
20
0
BLOOD PRESSURE
EXERCISE
EXERCISE
BOHN TEST
PATENT DUCTUS
ARTERIOSUS
PRESENT SERIES
TIME IN SECONDS
2
1
0
60
120
180


140
120
100
80
60
40
20
0
BLOOD PRESSURE
EXERCISE
EXERCISE
BOHN TEST
TWO OPERATED DUCTUS PATIENTS
TIME IN SECONDS
2
1
0
60
120
180

sists that the exercise (in his cases running up-stairs) should be performed briskly, and that one or more readings should be taken within the first minute after the exercise. (See tracing after Gilchrist)

Personal experience with this test (Table 4) cannot support the claims of Bohn, Vessell and Gilchrist. In none of the patients was a large increase in the pulse pressure observed. The test was repeated several times with each patient, with different observers. Readings were obtained within 25 seconds of the completion of the exercise. A glance at the tables will reveal the result of the test in the present series.

A difficulty which was experienced in carrying out this test, and which has not been stressed by other authors, has been the determination of the diastolic pressure reading. This is frequently difficult, even with the patient at rest, and is more so after exercise, because after exercise the sounds become louder, while the change in note becomes more gradual. In other words, there is no abrupt transition from the clear note to the "muffled" one. The sound may be heard to a point on the manometer considerably below the point of transition, and it may be that other workers have used a different indication of the diastolic pressure.

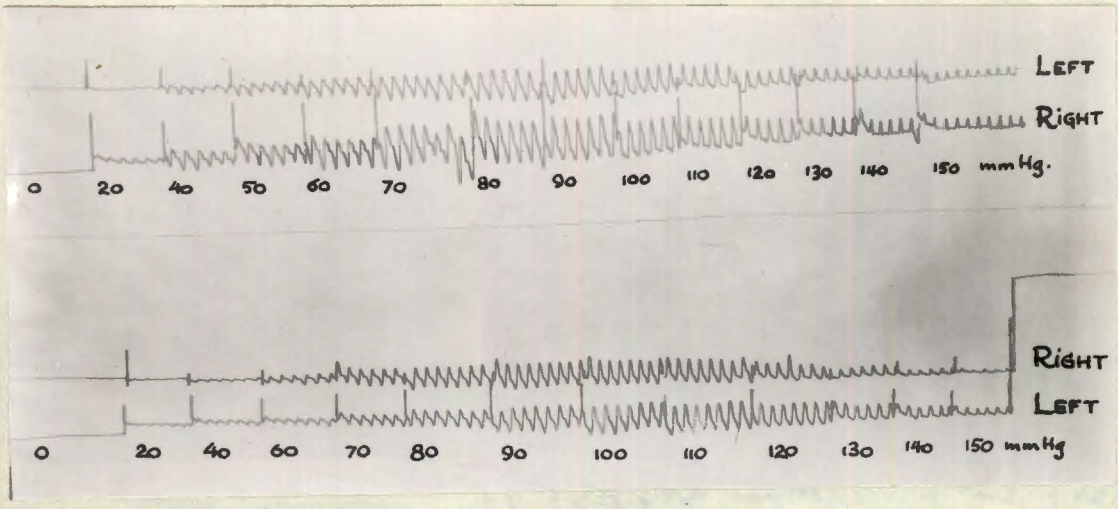
In view of the unsatisfactory nature of the test in present hands, it was decided that further investigations were required. As no information about the effect of the test on

normal people was provided by Bohn, Gilchrist or others, it was obvious that this was the first question to be decided. A number of normal individuals were subjected to the test and readings recorded. Some of these appear in Table 4. When this is compared with the readings of the patent ductus patients, it will be observed that there is little, if any, difference between the readings. In fact, it would appear that there is a relatively greater increase in pulse pressure in normal individuals than in patent ductus patients, when one considers that in the latter the pulse pressure at rest is already larger than in the normal individuals. As a matter of interest, a few readings were taken from people with aortic incompetence, with similar results. The same difficulty was experienced in observing the alteration in the note when reading the diastolic pressure, as had been the case with the patent ductus cases. In many the sound could be heard to zero, after exercise.

It can be concluded, therefore, that as in present hands, at least, the Bohn test has not been found to be of diagnostic value, the claims of Bohn and others cannot be substantiated.

(c) <u>The Peripheral Vessels</u>.

The peripheral pulses in patent ductus arteriosus may be of the collapsing or Corrigan type. This is obviously more likely to be the case where the shunt is large, as in wide, short ducti. Franck (1878) stated that pulsus paradoxus may be encountered. This was not observed in any of the cases of




Oscillograph tracings taken from the same patient before and after operation. Before operation the amplitude of the pulse wave is greater in the right arm than in the left. After operation the amplitude is equal in both tracings, or perhaps slightly greater in the left arm.

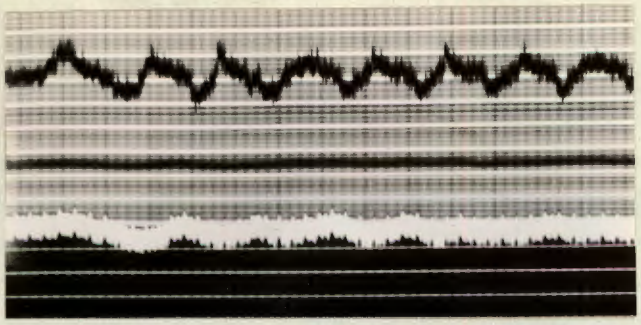
the present series. Hochsinger (1891) observed inequality of the pulses of the two sides. Some of the cases of the present series were tested by the oscillograph. In one patient (see tracing) there was a definite increase in the amplitude of the right pulse as compared with the left. It is felt that this cannot be attributed to coaretation of the aorta, because the narrowing occurs usually beyond the origin of the left subclavian artery. It may be that the shunt of blood through the ductus, which lies almost opposite the origin of the left subclavian, may affect the volume of blood conducted by the latter. Laubry (1930) maintained that a diminution of the femoral pulses as compared with the radial is indicative of slight coaretation. In all the present series the leg pulses were very clearly felt, nor was coaretation observed in any of the cases at operation. Gilchrist (1945) believes that this is the only sign whereby coaretation may be detected in the first decade, as the characteristic radiological features, such as rib erosion, usually manifest themselves at a later age.

(d) Plethysmography.

For reasons already discussed under the chapter on physiology, the peripheral blood flow in patients with patent ductus should be impaired. Study of this aspect was therefore indicated, and was carried out in six patients by means of skin temperature measurements and the plethysmographic methods of Goetz (1940-1945).

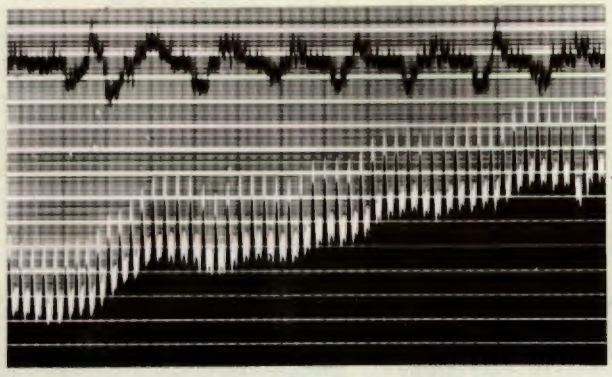
It was found that the peripheral blood flow during rest was

Fig. 12



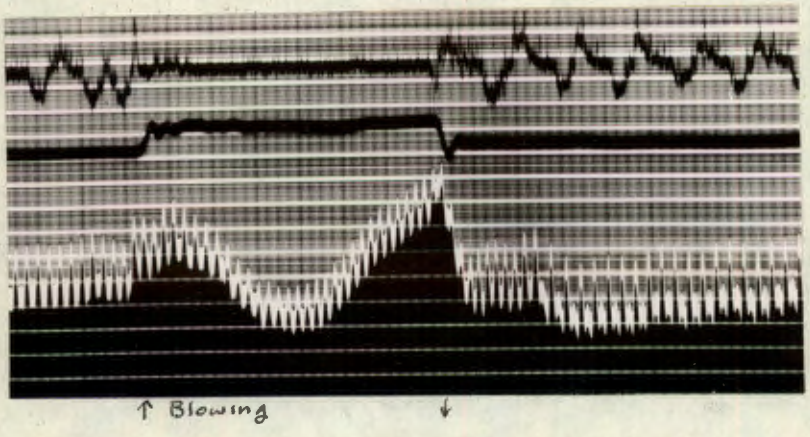
Plethysmogram with patient at rest.
Note small amplitude of pulse wave.

Fig. 13.



Plethysmogram with vessels fully dilated.
Note typical water-hammer pulse.

Fig. 14




Plethysmogram taken during blowing test.
Note return of dicrotic wave after blowing.

markedly diminsihed in all cases. The pulse volume, as indicated in Fig. 12, was just registrable, the shape, however, being in no way abnormal. The rate of blood flow, as calculated by the venous congestion test, was accordingly diminished, being only 4 cc per minute for 100 cc of tissue on the average. With the release of the vasoconstrictor tone, as achieved by body heating, there was a prompt increase of all the values, and the normal vasodilatation level was reached. This was found in all the subjects tested. As the vasoconstrictor tone diminished, a typical water-hammer pulse was registered (Fig. 13). It is true that in the normal individual the pulse, with the release of the vasoconstrictor tone, loses much of typical dicroty and becomes more monocrotic, but the degree seen in these cases is definitely abnormal and is only otherwise seen in cases of aortic regurgitation and arterio-venous aneurysm. It can therefore be said that plethysmography may be of value in the diagnosis of patent ductus arteriosus.

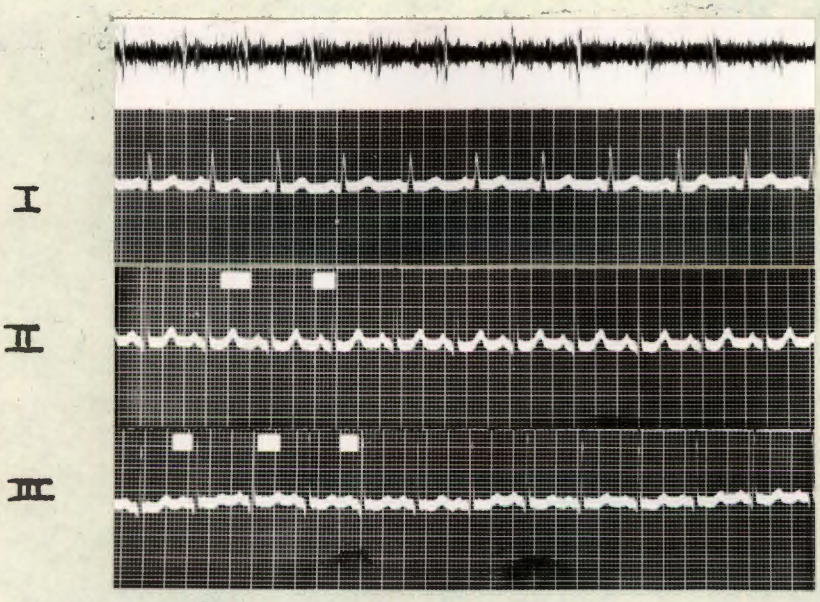
A plethysmographic tracing taken during the blowing test is reproduced in Fig. 14. Although a complete analysis of the tracing cannot be given at this stage, nevertheless, there are some findings which are of interest. It was argued that with the increase of the intrapulmonary pressure, there may be a decrease in the flow through the ductus from the aorta to the pulmonary artery. If this is so, and it is the only change in the haemodynamics, one would expect the peripheral blood flow to increase. However, as is seen in Fig. 14, this apparently does

not occur. But it must be remembered, that the blowing test will also affect the heart output, so that the physiology is not as simple as it appears at first sight. One point that was observed, which is of interest, was the fact that following the blowing, the pulse, which was monocrotic in shape, assumed the normal dicrotic shape. This is never seen in other circumstances in the plethysmogram of patients with patent ductus arteriosus, when fully dilated, and the explanation is not quite clear.

(e) The Electrocardiogram.

Electrocardiographic studies on the patent ductus arteriosus have been extensively performed by various workers, Schnitker (1940), Shapiro (1944) and others. The conclusion that can be drawn from their work is that there is no characteristic tracing that can be attributed to the patent ductus arteriosus. The majority of tracings obtained were physiological ( as in the present series), but a small number of the older people showed some left axis deviation. Right axis deviation is encountered still more rarely. This fact, according to Gilchrist (1945) is of great value in differentiating patent ductus arteriosus from pulmonary stenosis, in which it is the rule (Alexander, Knight and White, 1925).

Gilchrist (1945) failed to observe right axis deviation in any of his series, and left in a few of the adult cases. Schnitker (1940), reporting on 70 cases, found right shift in one only. Shapiro (1944) discussing 62 cases, observed a




The electrocardiogram of a typical case of patent ductus arteriosus showing a normal tracing.

physiological tracing in 52 cases, while there were 5 cases each of right and left axis deviation. Jones, Dolley and Bullock (1940) describe some of the minor variations which may be encountered. These are: prominent Q waves in leads II and III, notching of the R wave in lead I, depression of the S-T interval in leads II and III, etc., etc. They are of no significance and extremely variable.

It may therefore be concluded with Shapiro and others, that the electrocardiogram is of value from the negative point of view - an abnormal tracing being evidence against the diagnosis of patent ductus arteriosus.

(f) Laboratory Findings.

Laboratory findings are not significant in patent ductus arteriosus. Gilchrist (1945), who does not find any significant blood picture changes, states that compensatory polycythaemia is not seen and counts of 5½ million red cells, or more, are rare. In the present series there was slight normocytic anaemia in one or two cases, but otherwise little of note was observed in the blood picture, urinalysis, etc. It is possible that the vital capacity may be impaired but statistical studies are not available, and this matter is still being investigated. The B.M.R., according to Stewart and Jack (1940), as in other forms of congenital heart disease, is not affected. The blood urea was normal except in one case, in which, on one occasion only, it was slightly elevated - but no significance was attached to this.

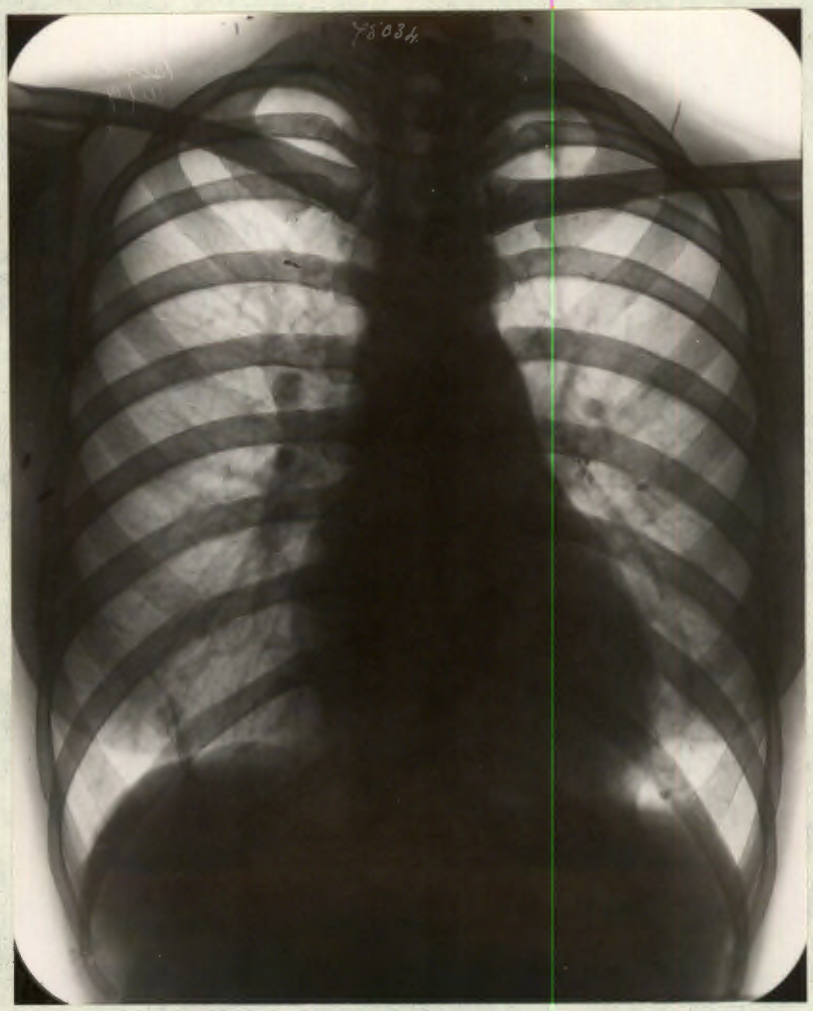
## TABLE OF SYMPTOMS AND SIGNS AS FOUND IN PRESENT SERIES.

| Name | Race, Age & Sex | Dyspnoea Tiredness | Epistaxis | Convulsions | Clubbing and Cyanosis | Accidental discovery | Pallor Build | Murmur | Thrill | Gerhardt Dullness | B.P. | Leg Pulses | Blowing Test | Bohn Test | Frank Sign | Hochsinger Sign | Plethysmograph | Electrocardiogram. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| * S.H. | E.F aged 20 | - | +++ | - | - | + | Normal | Gibson | +to & fro | + | 126/68 | ++ | Not Done | 138/56 | -ve | -ve | Not done | Not done |
| * M.A. | C. F" 18 | - | - | - | - | ++ | Normal | Gibson | +to & fro | ++ | 130/80 | ++ | Not done | Not done | -ve | -ve | " | " |
| * J.G. "F" | E. M" 12 | Easily tired | - | - | - | + | Thin Pale | Gibson | +to & fro | - | 96/48 | ++ | ++ | 120/48 | -ve | -ve | Water Hammer Pulse | Normal |
| T.H. | E. F" 12 | Dyspnoea | ++ | - | - | - | Obese | To & fro slight pause | Slight ?? | - | 124/46 | ++ | --- ++ | 130/32 | -ve | -ve | " | " |
| * R.M. | Co.M" 7 | Dyspnoea | ++ | Clubbing of Fingers | → | - | Small underdeveloped | Gibson | ++ | - | 104/58 | ++ | Not done | Not done | -ve | -ve | Not done | Not done |
| * B.H. | C M" 8 | - | - | - | - | ++ | Slight Pallor N.B. | Gibson | ++ | - | 120/50 | ++ | Not done | Not done | -ve | -ve | " | " |
| * J.L. | E F" 12 | Slight | - | - | - | + | Small but normal | Gibson | ++ | - | 120/68 | ++ | ++ | 140/66 | -ve | +ve | (Water (Hammer (Pulse | Normal |
| E.F. | E F" 8½ | Nil | - | - | - | ++ | Normal | Gibson | ++ | - | 115/65 | ++ | ++ | 130/65 | -ve | -ve | " | Not done |
| F.B. | E F" 31 | Fatigue Dyspnoea | - | - | - | originally | Slight | Gibson | + | + | 120/64 | ++ | ++ | 180/66 | -ve | -ve | " | Normal |
| N.P. | E F" 7½ | Listlessness | - | - | - | School Exam. | Normal | Harsh systolic | Systolic | - | 90/60 | ++ | | 115/55 | -ve | -ve | unsatisfactory | " |
| A.B. | E M" 4½ | - | - | - | - | Accidental | Normal | Harsh systolic | + | -ve | 110/64 | ++ | unsatisfactorily done | 126/70 | -ve | -ve | Not done child too small | Not done. |

* indicates patient who has been operated on.

"F" Note: Since this compilation another patient J.G. has been operated on.

=



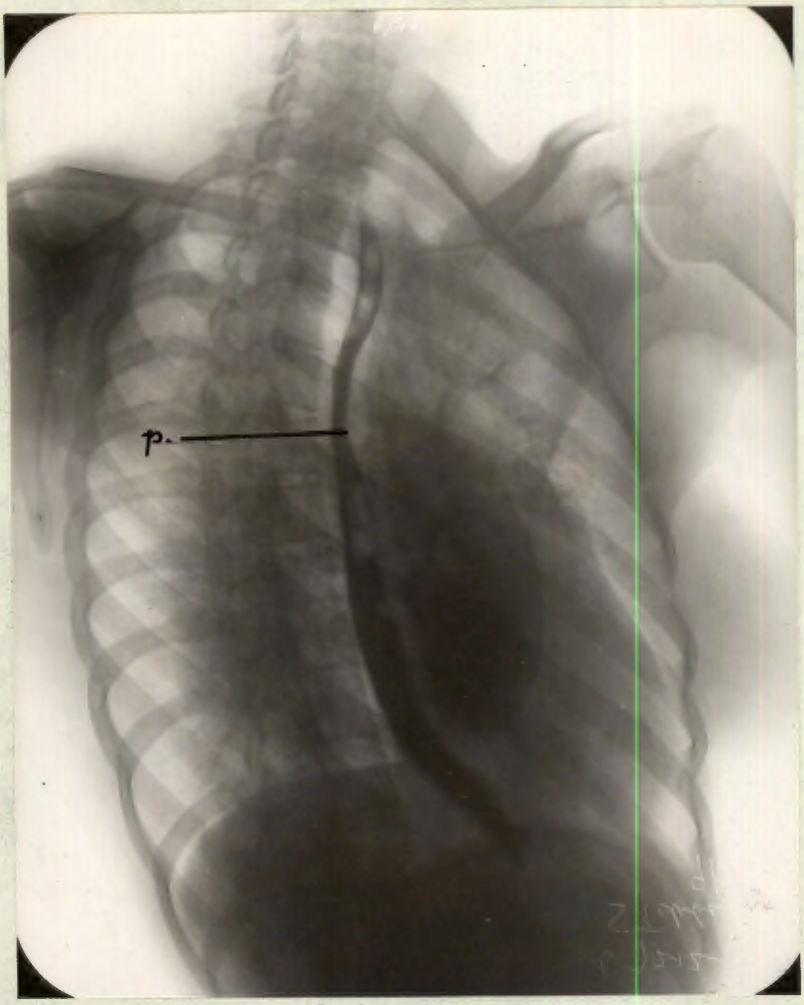
P.A. view of a typical case of Patent Ductus.

Note enlarged pulmonary conus and prominent pulmonary vessels.

(g) The Radiology.

In the patent ductus arteriosus, as in other forms of heart disease, the value of radiology cannot be over emphasized. While all are in agreement that the diagnosis cannot be made by radiology alone, its exact value is perhaps best expressed by Eppinger and Burwell (1940). They state that radiology may "suggest the diagnosis, constitute important confirmatory evidence, and bear witness as to the effectiveness of cure".

The most common radiological sign is a filling in of the "waist", on the left border of the heart, immediately above the bulge of the left ventricle, as seen on the P.A. silhouette. This, erroneously, is often attributed to the pulmonary conus (which cannot be seen on the ordinary P.A. film), but actually it is due to the enlargement of the pulmonary artery. The original observation was made by Zinn (1898), so that this bulge of the pulmonary artery is often referred to as the x-ray cap of Zinn. "British Authors" (1938), which is the standard work employed by many radiological departments, described the increase in size of the "cap" with expiration and its decrease on inspiration. This sign has been ascribed to Roesler, but none of Roesler's books make reference to it. The enlargement of the pulmonary artery, which can often be detected even more clearly by the right anterior oblique view (Muir and Brown, 1932, Donovan et al, 1943) is not necessarily present (Gross, 1940), but it is the commonest finding in patent ductus arteriosus. The enlargement may reach aneurysmal proportions (James

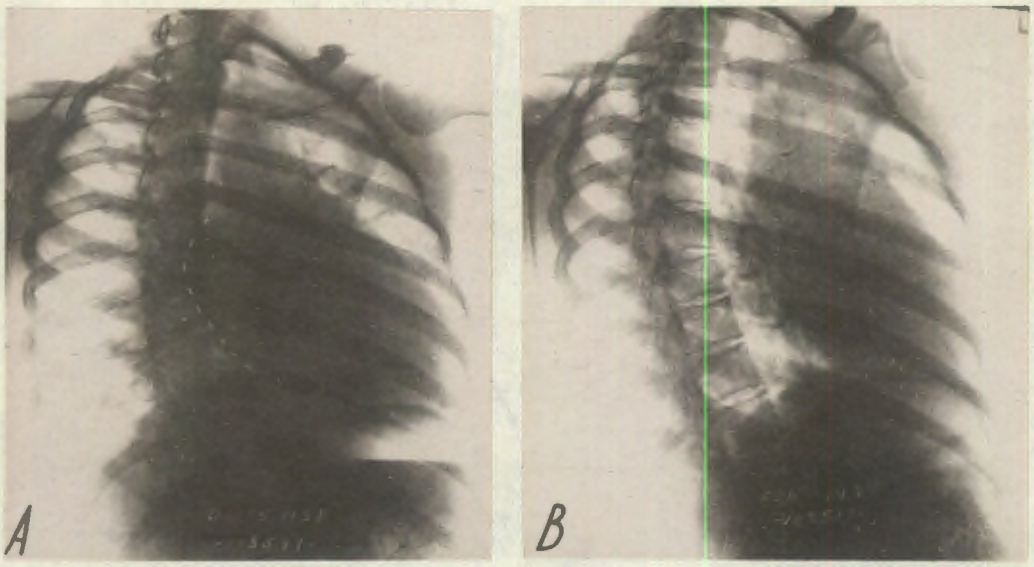



Right oblique view of case of patent ductus arteriosus showing bulge of pulmonary artery marked "p".

Brown, 1939). It was present in 82% of cases of Donovan et al (1943) and has been observed in every case of the present series (Table 5). The pulmonary artery enlargement is varyingly described as being very prominent (Grier, 1943) and not excessive (Donovan et al, 1943). The latter regard excessive enlargement as suggesting other associated congenital anomalies such as pulmonary stenosis. The term used by the authors may not necessarily be regarded as being contradictory, as some believe, that a straightening out of the normal cardiac "waist" already indicates considerable enlargement of the pulmonary artery. It would, therefore, depend upon whether reference is being made to the pulmonary artery itself or to the bulge ascribed to it on the silhouette.

James Brown (1939) emphasizes that the x-ray appearances are considerably affected by the age of the patient and the volume of the shunt permitted by the ductus arteriosus. To these may be added the factors impending failure and subacute bacterial endocarditis. Gross (1940) states that in the first 2 years there may be no abnormalities to be detected radiologically, but that after the third and fourth year the appearances may be characteristic.

Marked cardiac enlargement in the absence of complicating factors (subacute bacterial endocarditis and failure) is considered to be the exception rather than the rule (Roesler, 1937). Slight enlargement as indicated by a cardio-thoracic ratio of more than 0.5 was seen in three cases of the present series.




Two plates copied from the article by Donovan et al. Plate B is supposed to demonstrate the diminution in the size of the left auricle after operation. Note: the position of the patient in the two plates is not the same. The retrocardiac space in plate B, even away from the auricle, is considerably greater than in plate A.

Fig 15.

Donovan et al (1943), who studied 50 cases operated on by Gross, maintain that left ventricular enlargement was discernible in their series in 76% of cases. These figures have not been substantiated by others, and, in addition, the criteria they employ for indicating left ventricular enlargement are not clear. Wessler and Bass (1913) regard left ventricular enlargement as indicating the association of aortic stenosis or coaretation.

Eppinger, Burwell and Gross (1941) have stated that should the mitral valve be too small to accommodate the increased flow of blood into the left ventricle, left auricular enlargement may result. That left auricular enlargement is encountered radiologically, is an unquestionable fact, but there is considerable difference in the incidence encountered by various workers. Roesler (1937), Sussman, Orishman and Steinberg (1943) find left auricular enlargement to be rare. The latter could find definite oesophageal displacement in only one case in 34. Donovan et al (1943), in opposition to all other views, regard left auricular enlargement as being one of the commonest findings in their experience. They record an incidence of 71%. This figure is so remarkable and so different from the experience of others, that there is hesitation in accepting it. The figure, reproduced as Fig. 15, in which they illustrate diminution in the size of the left auricle after operation, does little to encourage acceptance of their figures. The two plates are not comparable, as the patient is not in the same position in the postoperative plate as in the preoperative one. The latter is such, that the

posterior border of the heart, including the alleged left auricle, overlaps the vertebral column, while in the former the rotation is much more, thereby increasing the retrocardiac space as a whole. It would be unjust to condemn their technique on one figure, perhaps carelessly inserted, but until confirmation by other workers takes place, left auricular enlargement may be regarded as being comparatively rare. In the present series, where every known method was used to illustrate possible left auricular enlargement, including the recumbent barium swallow, definite enlargement was observed in two out of eleven cases only, and suspicious evidence seen in another.

Engorged or congested pulmonary vessels are frequently seen. In the present group it was observed in all but one case, being the second most common finding.

Fluoroscopy has been regarded as the most valuable part of the radiological examination, and kymographs, although valuable, are regarded as being an unsatisfactory substitute. Wessler and Bass (1913) remarked that excessive pulsation could be observed in the pulmonary artery, while Hubeny (1920), reviewing the literature, concluded that the most valuable radiological sign was the exaggerated beat of the left ventricle and pulmonary artery. Excessive pulsation of the hilar vessels - referred to as the "Hilar Dance", or Assman's sign, may also be observed. Donovan et al found it present in 35% of cases, while in the present series, it was observed in 4 cases, or 36%. Kymography illustrates excessive pulsation too, but in one plane

Typical kymogram of patient with patent ductus arteriosus.

Note exaggerated pulsation of pulmonary and left venticle.

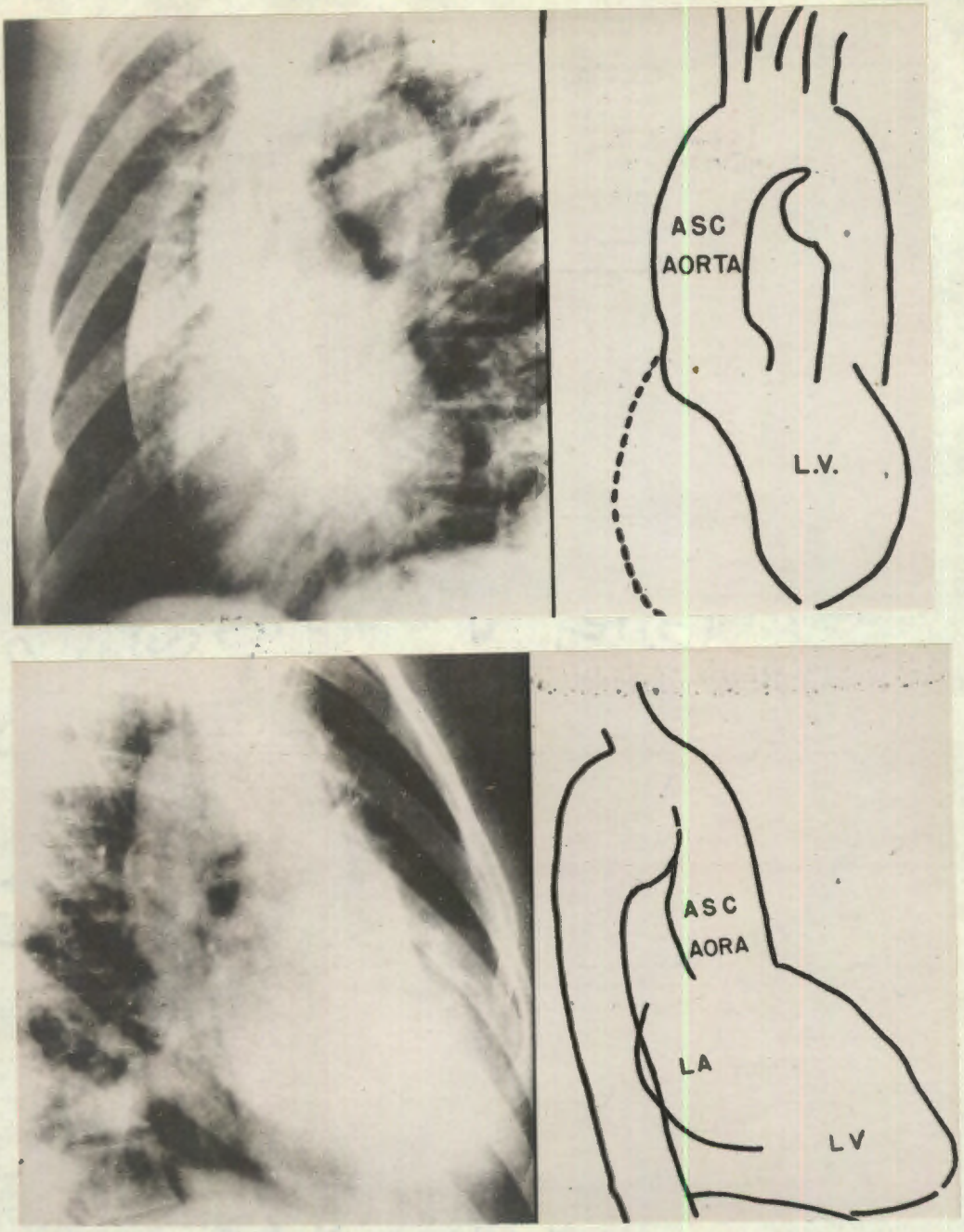
Fig. 16.

only. The pulsation of the pulmonary artery (see Fig. 16) is naturally of the vascular type.

To the armamentarium of the radiologist a new method of investigation has been added by the advent of angiocardiography. This was attempted in one case of the present series, but as 70% diodrast was not available, 50% had to be used. The concentration obtained with this was unsatisfactory, so that attempts have been temporarily suspended.

By this means the outline of the chambers of the heart and the great vessels (but not the patent ductus) can be demonstrated (see Fig. 17). Sussman, Grishman and Steinberg (1943), who have used the method extensively, maintain that valuable information for the differential diagnosis of congenital heart disease can be obtained. In patent ductus arteriosus cases, it provides proof that the prominent so-called "pulmonary conus" is due to the pulmonary artery, not other mediastinal swellings, but it is of particular value in differentiating other causes of enlarged pulmonary artery, such as Eisenmenger's complex, patent interventricular septum. It is particularly in the doubtful cases, therefore, that this examination may be valuable.

The more important radiological evidences are summarized in the table (5) and their incidence in the present series indicated.




Two plates with explanatory diagrams illustrating the value of angiocardiography. A traction aneurysm of the aorta is seen at the point of origin of the ductus arteriosus. This is a postoperative picture, and the patient had superimposed subacute bacterial endocarditis. (After Steinberg et al)

Fig. 17.

## RADIOLOGICAL FINDINGS IN PRESENT SERIES.

| Name | Age | Cardiac Enlargement Total | L. Ventricle | Enlarged L. Auricle | Enlarged Pulm. Art. | "Roesler's Sign" | Hilar Dance Assman's sign | Pulm. Vessel Engorgement |
|---|---|---|---|---|---|---|---|---|
| F.B. | 31 | -ve | +ve | -ve | ++ve | -ve | +ve | ++ve |
| M.A. | 18 | -ve | -ve | -ve | ++ve | ++ve | +ve | +ve |
| S.H. | 31 | -ve | -ve | -ve | ++ve | ++ve | -ve | +ve |
| J.L. | 12 | -ve | -ve | +ve | +ve | -ve | -ve | +ve |
| E.F. | 8 | Slight | -ve | -ve | +ve | +ve | ++ve | ++ve |
| H.B. | 4 | -ve | -ve | -ve | ++ve | ++ve | ++ve | ++ve |
| R.M. | 6 | Slight | -ve | -ve | ++ve | ++ve | ? | ++ve |
| B.H. | 8 | Slight | -ve | +ve | ++ve | ++ve | ? | +ve |
| N.P. | 7 | -ve | -ve | +ve | +++ve | ++ve | -ve | +ve |
| J.G. | 12 | -ve | -ve | -ve | +ve | -ve | -ve | +ve |
| T.H. | 12 | -ve | -ve | -ve | +ve | +ve | -ve | -ve |
| Total | 11 | 3 | 1 | 3 | 11 | 8 | 4 | 10 |

# CHAPTER VI.

## THE DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS.

### A. Diagnosis.

One of the reasons for the long lapse in time between Munro's (1907) original suggestion and Gross' (1939) actual successful operation, had been the difficulty in absolute diagnosis. Since the work of Maud Abbott, James Brown and others, this is no longer the case. Gross (1944) maintained that the diagnosis can be made with 100% certainty and in his series of 50 cases, only four had complications at operation which made surgery inadvisable. Shapiro and Keys (1943) record 2 cases of mistaken diagnosis out of a total of 140 cases. The most single, useful of diagnostic features is the Gibson's murmur, maximal at the second left interspace, but, although this may be absent, the diagnosis can still be made. Gross had operated successfully on two cases who presented a systolic murmur only.

The criteria for diagnosis have been summarized by Shapiro (1944) as being

(a) The machinery murmur

(b) Thrill in the pulmonic area

(c) Enlarged pulmonary artery

(d) Enlarged pulsating pulmonary vessels

(e) Enlarged heart

(f) Increased pulse pressure

(g) Stunting growth

(h) Absence of cyanosis

(i) Normal electrocardiogram

(j) History of heart disease from early childhood.

This comprehensive list includes practically all the clinical features of the condition. Many of them, however, may be absent in any one case, so that Gilchrist (1945) maintains that the criteria, other than the Gibson's murmur, which are of value, in order of their importance, are increase in size and excursions of the main trunk of the pulmonary artery, increase in the pulse pressure aggravated by exercise, and long, harsh systolic murmur heard below the inner end of the left clavicle. (It has already been pointed out that the exercise test has not been found of value in the present investigation.) Perhaps the diagnosis can be made most easily from the criteria given by Muir and Brown (1932), who feel that the essential criteria are:

(a) Machinery murmur

(b) Rough, long systolic bruit in 2nd left space, with conservation, accentuation or reduplication of the 2nd sound

(c) Gerhardt's ribbon dullness

(d) Enlarged pulmonary artery

(e) Complete absence of symptoms

The diagnosis, according to them, may be made on the association of any three of the above.

B. <u>Differential Diagnosis</u>.

The patent ductus arteriosus, usually, presents itself

clinically by virtue of the murmur which it produces at the base of the heart. It is obvious, therefore, that the condition must be differentiated from other lesions producing similar murmurs. These are certain haemic or functional murmurs, rheumatic heart disease and other congenital anomalies. Discussion of the differential diagnosis from one single feature, such as the murmur, alone would entail a discussion of the whole subject of congenital heart disease, which is not in place in this thesis. The discussion will therefore be confined to those anomalies which present in addition to the murmur also superficial radiological resemblances to the patent ductus, that is, those which present an enlarged pulmonary artery. These, according to Sussman et al (1943) are the inter-atrial septal defect, idiopathic dilatation of the pulmonary artery, isolated pulmonic stenosis with a dilated pulmonary artery and Eisenmenger's complex.

The <u>haemic or functional murmurs</u> are sometimes continuous and observed chiefly at the base. They, however, do not present the harsh note characteristic of Gibson's murmur, but, on the contrary, are soft and blowing. Haemic murmurs may be excluded on the haematological findings, but one which gives rise to some difficulty in young children is the so-called "venous hum" (Shapiro, 1947). This, generated by the neck vessels, is observed over the base principally, and is soft and blowing. It may be abolished by rotation of the head from side to side, or by digital

compression of the neck vessels.

The murmur of aortic incompetence is one which sometimes provides considerable difficulty in differentiation, for, not uncommonly, a rheumatic history may be obtained in cases of patent ductus arteriosus (two cases of the present series had such histories). In addition, the peripheral blood findings and the site of maximum intensity of the murmur may be similar to that in the patent ductus arteriosus. However, a break in the continuity of the murmur, due to a pause between the systolic and diastolic components, is nearly always obtainable. Radiologically, left heart enlargement may be obtained, while the pulmonary artery segment will not be affected. It is in connection with this murmur that the blowing test, evolved during the present investigation, has proved of great value (see table 3).

Mitral stenosis does not, as a rule, enter the differential discussion, as the murmur is heard best at the apex, and is usually so very characteristic. In patent ductus arteriosus, in spite of the fact that either or both the systolic and diastolic elements may be conducted to the apex, the closed heart sounds can usually be discerned quite clearly through the conducted murmur. Difficulty may occur when, as the result of subacute bacterial endarteritis, complicating the patent ductus arteriosus, vegetations have extended to the cardiac valves (Touroff, 1943). It must be emphasized that an enlarged left auricle does not exclude patent ductus arteriosus, as is often alleged.

It is when the continuous nature of the murmur is absent, as is sometimes the case, that the most difficulty is experienced with the diagnosis. A harsh systolic murmur at the base, such as is occasionally seen in patent ductus arteriosus, may be observed in several other conditions, such as pulmonary stenosis, and others already referred to above. Some, it has been said, may present an enlarged pulmonary segment, on radiological examination. There are, however, usually other additional features which make the diagnosis clear. The absence of an accentuated or reduplicated second sound, such as is the rule with patent ductus arteriosus, is in favour of pulmonary stenosis. Conditions other than patent ductus arteriosus which present an enlarged pulmonary segment, usually show marked general cardiac enlargement, - a feature distinctly rare in patent ductus cases. The emphasis is usually on the right ventricle, as in pulmonary stenosis, Eisenmenger's complex, etc., and this is associated with right axis deviation on the electrocardiogram. Inter-auricular ventricular septal defect usually has a small pulse pressure and enlargement of the left ventricle and both auricles, which is often considerable. This is particularly striking in the left auricle, when the defect is complicated by mitral stenosis (Lutembacher's syndrome). With the exception of Eisenmenger's complex, in which the aorta is normal, conditions which produce an enlarged pulmonary arterial segment, and which have to be differentiated from the patent ductus arteriosus, usually have relatively small left heart chambers and the normal aortic

knuckle is not seen on the P.A. film.

The systolic murmur of the patent interventricular septal defect is usually situated low down, in the 3rd and 4th left space parasternally, and, as a rule, does not radiate to the left clavicle or to the apex. (Muir and Brown, 1932, have emphasized that the murmur of congenital heart disease is remarkably constant in character and localization.) Radiologically, the pulmonary artery may be enlarged but there is associated enlargement of the right ventricle, which frequently lifts the apex of the heart away from the diaphragm, giving a "wooden-shoe" type of effect (Grier, 1943).

Other forms of congenital heart disease, such as Fallot's tetralogy (which in addition to its characteristic polycythaemia, does not produce enlargement of the pulmonary artery) are excluded from this discussion on this ground.

It has already been observed that in cases where the ductus remains patent as a compensatory mechanism, cyanosis is almost an invariable feature.

Sussman et al (1943) have stressed the value of angiocardiography in the differential diagnosis of various congenital heart diseases, and particularly in showing minor defects associated with the patent ductus arteriosus, such as slight coarctation and patent septa.

## CHAPTER VII.

## COURSE, COMPLICATIONS, PROGNOSIS AND INDICATIONS FOR SURGERY.

Although actual observations of a large number of patients with the patent ductus arteriosus over a long period of time has not been reported by any medical clinic, information as to the course and prognosis of the condition have been provided by post-mortem studies (as in the case of Maude Abbott, 1936) and studies of case reports in the literature (Shapiro and Keys, 1943, Bullock et al, 1939). It has been contended, and for this there may be grounds, that figures obtained from specialised reports of this nature do not give an accurate indication of life expectancy. Wilson and Lubschez (1942), by devising tables from the living, calculated to reflect the life expectancy, give a very much more sanguine prognosis than is generally accepted. They themselves, however, metnion that their series of 38 cases observed are small, and in addition it must be noted that there were only 2 patients in their series who had reached the age of 30. While there is no doubt that some cases of patent ductus arteriosus may survive the strains of multiple pregnancies, may show excellent physical development and capacity for hard work, and may reach an age of 60 or more, this, in the opinion of the great majority of authorities, is the exception rather than the rule. Gilchrist (1945) reports a case of spontaneous closure. The outlook, as presented by the postmortem studies of Maude Abbott

and the reviews of the literature by Bullock et al, is very much more grave. Maude Abbott finds that in the series of 92 cases of uncomplicated patent ductus arteriosus, 26% died from cardiac failure, 23% from subacute bacterial endocarditis and 2% from rupture of aneurysms of the ductus. The average age of the group at death was 24. No more optimistic are the findings of Keys and Shapiro, who find that of the 62 cases over the age of 17 collected by them, the ductus was the direct cause of death in over 80%. Of the deaths, heart failure was responsible for 30% and subacute bacterial endocarditis for more than 40%. The average age of the group was 37 with a maximum of 66. Bullock et al (1939) reviewing 80 fatal cases, find that 14% had died by the age of 14, 50% by 30, and 7% by the age of 40. In contrast to these figures, Wilson and Lubschez (1942) state that in a series of 38 cases which had been observed by them for an average period of 9 years, they had not observed a single death by subacute bacterial endocarditis. Gilchrist (1945), on the other hand, believes that the figures obtained at post-mortem may not give the true reflection of the incidence of subacute bacterial endocarditis, because the condition often masquerades under other erroneous diagnoses, such as miliary tuberculosis. Perry (1933) reports a case of this nature. Gross (1944) believes the incidence of subacute bacterial endocarditis to be about 25%.

It may, therefore, be said that untreated cases of patent

ductus arteriosus may expect a much shorter span of life than the normal individual. Shapiro and Keys (1943) believe this reduction in life expectancy to be in the neighbourhood of 25 years. The cases are exposed to all the risks which threaten the normal individual, but have special hazards peculiar to their condition. Of these, premature cardiac failure, the result of excessive strain on the heart, and subacute bacterial endocarditis, are the important ones. Surgical treatment by removal of the cause of strain in the former will obviously lessen the tendency to failure, but its role in the treatment of subacute bacterial endocarditis requires further elucidation.

The organism responsible for subacute bacterial endocarditis is, as a rule, the streptococcus viridans. The predisposing cause for the endarteritis of the pulmonary artery, as in other forms of subacute bacterial endocarditis, is trauma to the endothelial lining. In this case the trauma, according to Maude Abbott and others, occurs at a point in the pulmonary artery opposite the orifice of the ductus, and may therefore be attributed to the effect of the swirling of blood currents emerging from the ductus arteriosus. From this site the vegetations may extend to the pulmonary valves and other valves of the heart, and to the ductus itself, eventually reaching the aorta. Trimble and Larsen (1931) have pointed out that it is extremely rare for the ductus itself to be the primary seat of the vegetations. These vegetations are constantly being traumatised by the force of the blood stream through the ductus,

resulting in the dissemination of emboli. The prognosis for subacute bacterial endocarditis, with few striking exceptions, is invariably fatal. The course, according to Blumer (1923) is one of remissions and intermissions with death between the end of the 3rd month and the 8th month in 75% of cases. Chester (1937) reported one case of spontaneous cure, as did Touroff (1942), but such cases must be extremely rare. Nor has modern treatment, such as combined intravenous heparin and sulphapyridine therapy (Kelsen and White, 1939), proved as successful as was originally claimed. The results, with exceptions as reported by Leach et al (1941), and Winn, Hughes and Saunders (1943) have been disappointing. Tubbs (1944), Touroff (1940) have reported the appearance of sterile blood cultures after sulphonamide therapy and Neuhoff (1944) after large doses of penicillin, but this does not appear to be permanent. While ligation of the ductus cannot remove the vegetations already present, reports by Touroff, Tubbs, Gross and others, appear to offer new hope for a condition which had previously been regarded as being hopeless. Touroff obtained sterile blood cultures within days of ligation of the patent ductus arteriosus. This is remarkable, when one remembers that vegetations are still present in the pulmonary artery. The explanation given by Touroff is as follows: After ligation, vegetations inside the pulmonary artery cease to be violently traumatised, so that dislodgement is reduced. No infective material can enter the aorta via the ductus (which he believes

does happen otherwise), and the pressure, volume and rate of flow in the pulmonary artery is restored to normal. This relieves the over-distension and consequent dilatation of the small pulmonary vessels, preventing the passage of emboli, and restores the efficiency of the pulmonary protective mechanism. (Touroff, 1942b, by blood culture studies, has shown that the lungs have the power of removing or neutralizing infective emboli.) The reduction of the high oxygen content of the pulmonary blood which follows ligation, and which may favour the growth of organisms and the development of vegetations (Boldero and Bedford, 1925) will permit healing to take place. Experience has shown that in those cases in which vegetations have extended to the cardiac valves or to the aorta, the results of surgery are not as favourable as in early cases.

It would appear, therefore, that surgery is definitely indicated in cases showing signs of cardiac incompetence and cases of subacute bacterial endocarditis. With this statement no one can quarrel. Gross (1944) adds to this list, "retardation of growth and development" as another absolute indication. It is when the early cases are considered that there is difference of opinion. Experience has not yet shown that ligation or division of the patent ductus arteriosus will prevent subacute bacterial endocarditis, although the arguments in favour are considerable. Indeed, it has been reported by Shapiro and Keys (1943) that 2 patients developed subacute bacterial endocarditis as a direct result of surgical interference. According to

Gebauer (1943) it is in the early years (before complications have added difficulties by distorting the anatomy) that the operative risk is minimal. Yet, this is the time when the condition appears to be most innocuous, for it must be remembered that according to Hubberd, Emmerson and Green (1939), the ages of maximum incidence of subacute bacterial endocarditis lie between 16 and 25, and cardiac failure usually supervenes a little later. It is at this time, too, when it is most difficult to advise that a child which is apparently in perfect health, should be subjected to an operation which carries a small, but definite, operative mortality. Experience is reducing the mortality, so that there may be less hesitation in future in recommending the operation as a preventative measure.

Gross (1944) believes that while coercion should be employed in recommending the operation in cases of subacute bacterial endocarditis, impending failure or cardiac embarrassment, and in cases showing impairment of development, the question of preventative treatment should be left entirely to the free choice of the parents, after laying before them the merits of the case.

## CHAPTER VIII.

## THE OPERATION.

### A. Pre-Operative Treatment.

Pre-operatively the patient should be treated as for any operation involving the opening of the pleural cavity. Artificial pneumothorax is induced 3 days before the operation to prevent any undue disturbance following the opening of the pleural cavity. This is controlled by radiographs and repeated if necessary. Too early an induction of the artificial pneumothorax may produce a reative hyperaemia of the pleura, which may obscure the landmarks. The question of the administration of blood by transfusion has been the subject of dispute. Jones et al (1940) have maintained that transfusions are not indicated, as ligation in itself produces a relative increase of the blood volume. Tubbs (1944), on the other hand, doubts whether this increase of blood volume actually takes place, and in his experience has found transfusions of considerable value in certain cases. The majority of surgeons advise a compromise. Transfusions are administered immediately before or during the operation, in case haemorrhage should occur, but ceased when the ligature is tied or the clamps applied.

Welch and Thompson (1940) advise the withdrawal of fluids 8 hours pre-operatively, and use nembutal, morphia and atropine as pre-operative drugs.

### B. The Anaesthetic.

Cyclopropane is the anaesthetic of choice in America and

# FIGURE 18.

Technique after Gross.

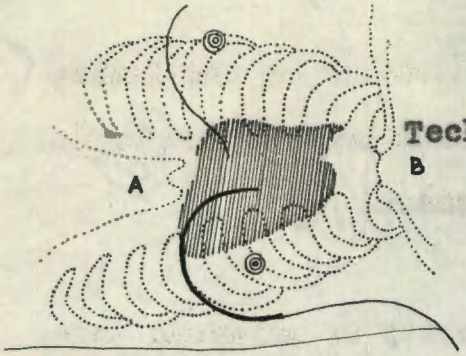



FIG. 1.

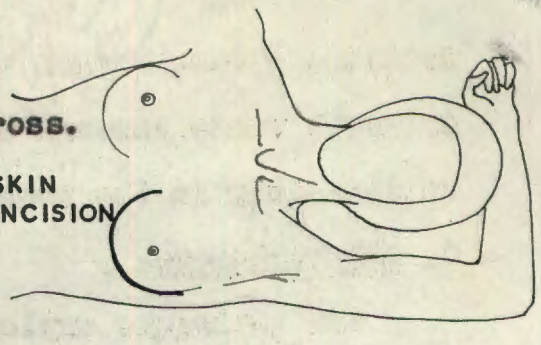



FIG. 2.

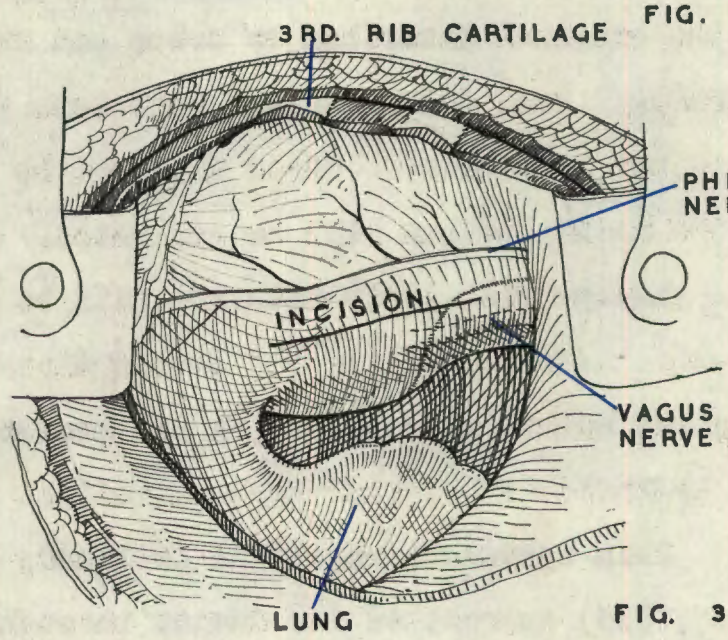



FIG. 3.

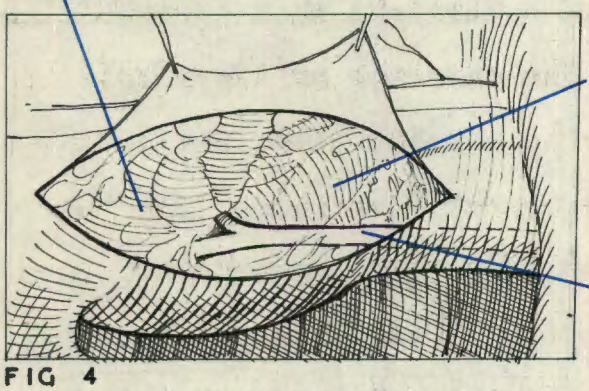



FIG 4

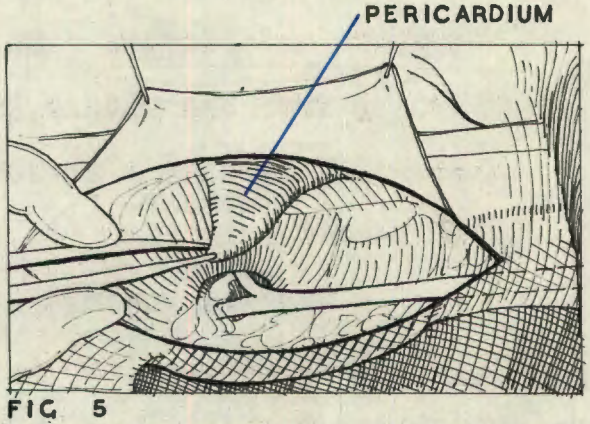



FIG 5

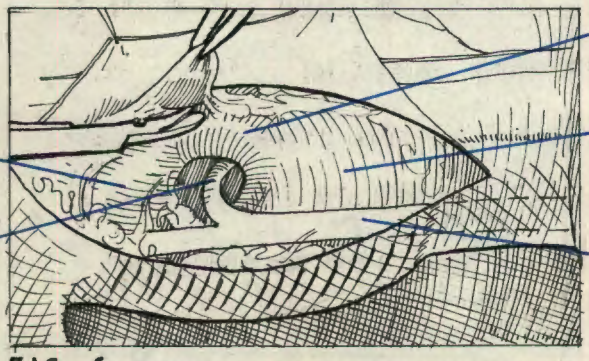



FIG 6

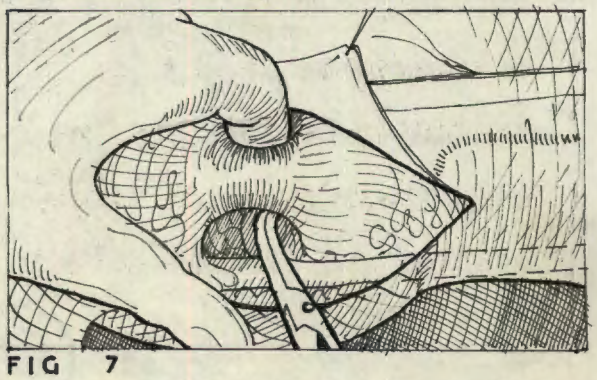


FIG 7

Britain. Gas, oxygen and ether, administered by the intra-tracheal route through a Boyle machine has been found perfectly satisfactory in the present series of cases.

C. The Technique.

The technique employed by the majority of surgeons today is based on the original described by Gross and Hubbard (1939) and Gross (1940). Some modifications have been introduced by Gross himself, and by others. These will not be discussed in detail, but the modifications will be indicated. The diagrams found in this chapter with their citation will be found of particular value in understanding the description.

The original method of approach to the ductus arteriosus as indicated by Munro (1907) was the longitudinal splitting of the sternum. This approach, as far as is known, has not been used. Gross (1939) approached the ductus through the 2nd left interspace anteriorly. He employs a straight skin incision extending from the middle line to the anterior axillary line in males. In females a curved incision carried along the breast fold is used (see Fig. 18 ) and the breast elevated. The incision is carried through the superficial muscles and the intercostal muscles are divided. Division of the adjacent costal cartilages facillitates retraction, but Gross does not find it necessary to divide the internal mammary vessels. Other surgeons, including Professor Saint, who operated on the present series, form their division between ligatures. Touroff (1943) has pointed out that in certain individuals the aortic arch, as

seen on the x-ray film, is situated more inferiorly than usual. In these cases he advised exposure through the 3rd space. Harrington (1943) finds the exposure outlined above inadequate, particularly when dealing with complications such as haemorrhage from the ductus as the result of tearing. He maintains that a much better exposure is obtained by using the ordinary postero-lateral approach of lobectomies, and advises it in particular in those cases in which there are lung adhesions.

After exposure of the mediastinal pleura, the left phrenic and vagus nerves are identified. This causes no difficulty unless there is hyperaemia of the pleura, as obtained by a premature induction of the artificial pneumothorax. The mediastinal pleura is grasped and incised behind and parallel to the phrenic nerve and in front of the vagus. The incision is carried well across the arch of the aorta. The left recurrent branch of the vagus is identified and carefully observed throughout the operation to prevent injury to it. This nerve passes under the arch of the aorta, and behind and immediately adjacent to the ductus arteriosus latero-medially. It serves as the guide to the ductus, which enters the undersurface of the aorta almost directly opposite the left subclavian artery. Although a thrill is usually obtained in this area, it is often transmitted to the great vessels so that it is not always a useful guide to the ductus, unless exploratory digital compression of the latter should abolish it. Careful blunt dissection of this area, avoiding injury to the recurrent laryngeal, should display the

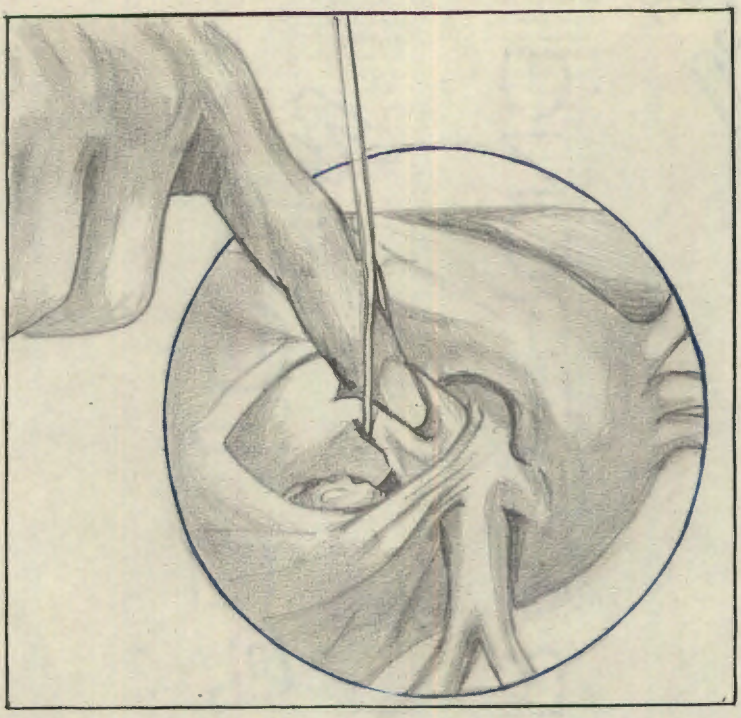


Figure 19a.

If the patent ductus is torn, the pericardial sac may be opened and a hernia tape placed around the pulmonary artery to stop bleeding momentarily in the event of a threatened exsanguinating haemorrhage.

(After Johnson et al)

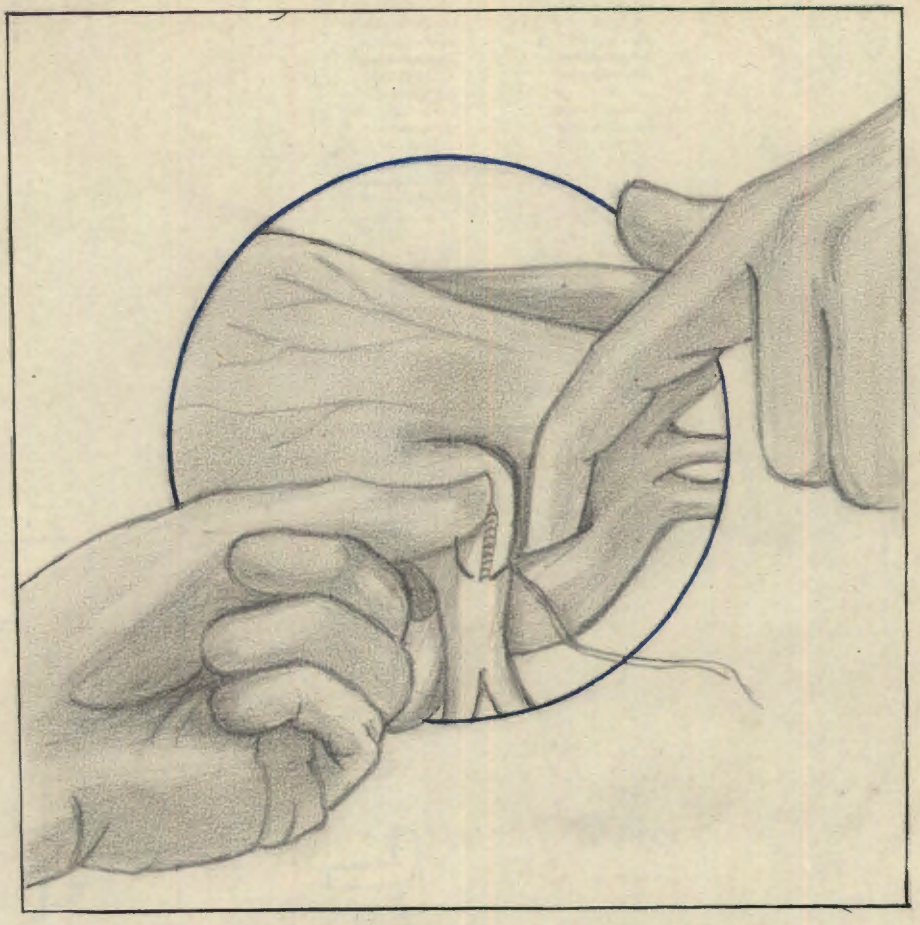


Figure 19b.

If the ductus has to be completely divided the opening in the aorta may be closed by an assistant's finger. The left pulmonary artery may be compressed between the thumb and forefinger so as to allow the circulation to continue through the right pulmonary artery, while the pulmonary end of the ductus is sutured.

(After Johnson et al)

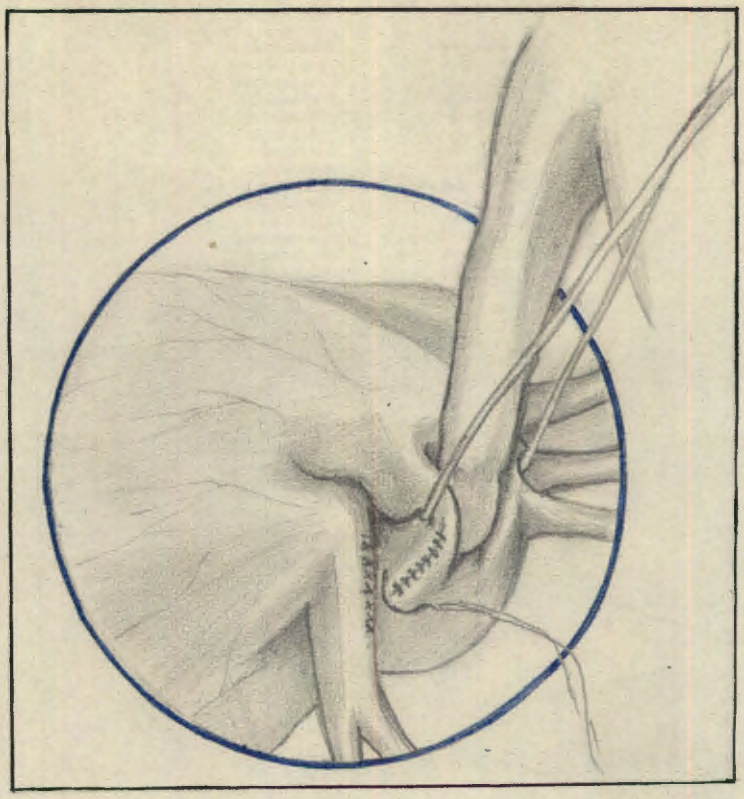


Figure 19c.

When the aortic end of the ductus is being sutured, haemorrhage may be controlled by pressure with a hernia tape around the aorta between the left carotid and the left subclavian arteries. The circulation to the brain is not interrupted.

(After Johnson et al)

ductus. The pulmonary artery, which is often large, and overlaps the ductus and lower border of the aorta, may have to be retracted. A flap of pericardium frequently overlies the antero-medial aspect of the ductus. This should be grasped by forceps and gently dissected away so as to prevent opening the pericardium if it is possible. Freeing the postero-lateral surface of the ductus usually does not provide great difficulty, but the antero-medial aspect may require a great deal of patience. Gebauer (1943) attributes the difficulty on the medial side to the tough nature of the fibrous tissue between the ductus and the left main bronchus - a site of origin of the pericardium. Gross advises the use of curved haemostats for finding a plane of cleavage between the pulmonary artery and aorta. Johnson et al (1942) feel that, while this is in order in simple cases, it may prove disastrous (as it did in their hands) in infected or sclerotic cases. They advise the use of the finger. The finger is inserted between the aorta and the pulmonary artery and by burrowing close to the relatively tough posterior wall of the aorta above and pulmonary artery below, a plane of cleavage, above and below, may be ascertained from both sides of the ductus, along which an aneurysm needle may be passed, without actually coming in contact with the ductus. They go so far as to say that in difficult cases or in cases in which haemorrhage occurs, or is anticipated, the pericardium should be incised and the great vessels exposed in such a way that hernia tape for their temporary intermittent occlusion may be passed

# TECHNIQUE.

Figure 20.

(after Touroff)

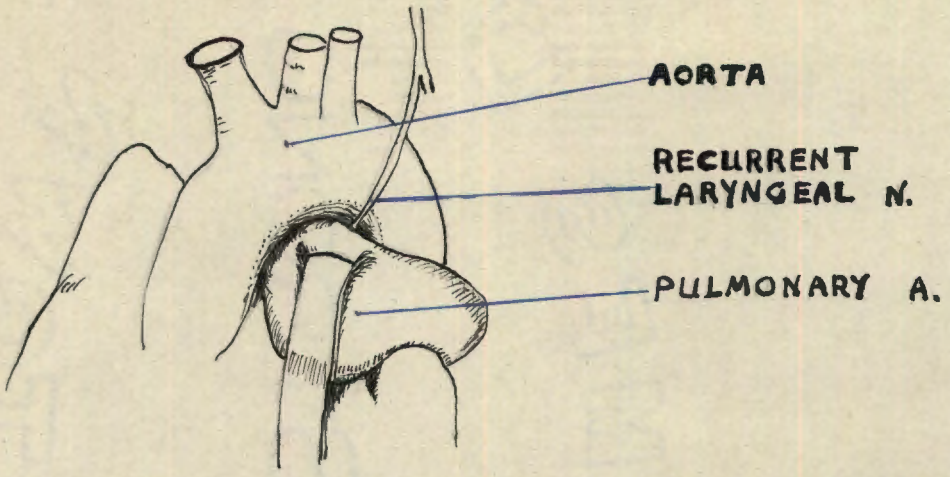



FIG. 1.

The Pulmonary artery has been dissected from the aorta and is displaced downward by a retractor. After removing areolar tissue and lymph nodes from the region of the concavity of the aortic arch, the ductus arteriosus comes into view.

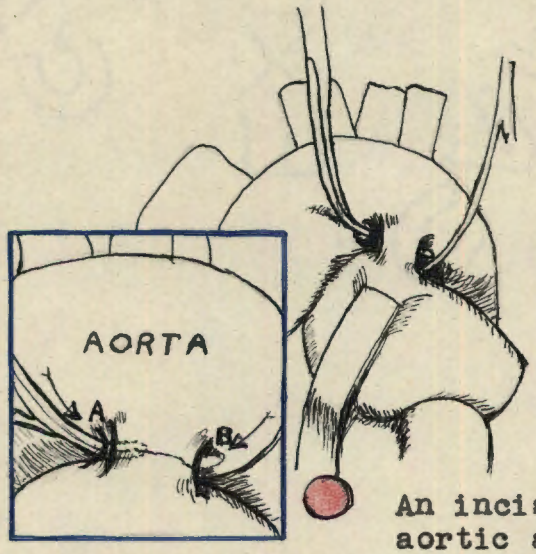



FIG. 2.

An incision is made in the aortic adventitia at "A". A fine curved cystic duct clamp is introduced into the adventitial incision and gradually passed downward and laterally (upon the aorta) as far as possible. A similar dissection is begun at "B" and carried upward until a "tunnel" has been completed (beneath the adventitia of the aorta) behind the aortic end of the ductus.

TECHNIQUE
CONTINUED

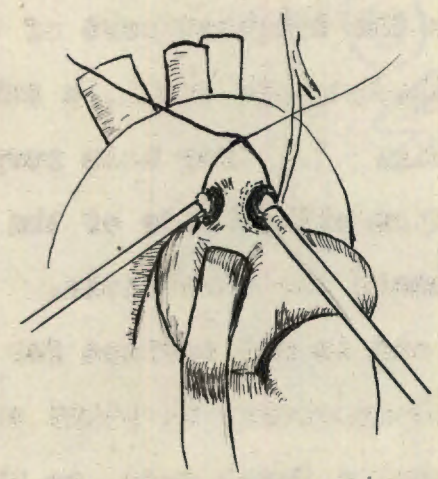


FIG. 3.

After the tunnel within the adventitia of the aorta has been completed the plane of dissection is carried on to the posteromesial surface of the ductus. Note that the retractors within the adventitia hold aside the right branch of the pulmonary artery and the recurrent laryngeal nerve without actually coming into contact with either of those structures the ligature has been passed behind the ductus.

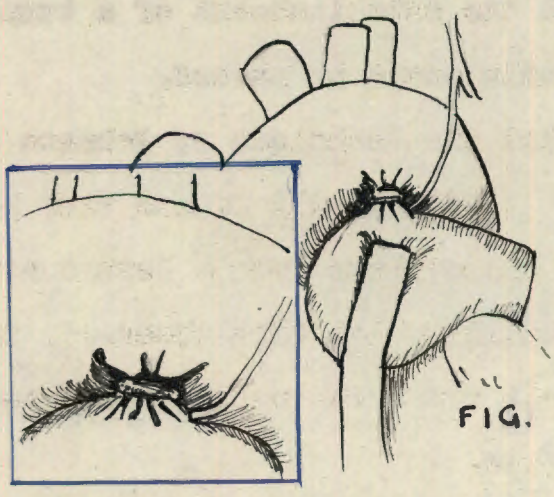


FIG. 4.

Double ligatures are tied about the ductus as close to aortic end as possible.

around them for control of the haemorrhage until the ductus is dealt with (see Figs. 19 a.b.c.). Touroff (1943), on the principle that the aorta is the strongest structure (and therefore the most resistant to injury) in the immediate operative field, and that the aortic end of the ductus is the toughest part of the ductus, believes that in infected or atheromatous ducti, a subadventitial tunnel should be established (Fig.20). For this purpose he incises adventitia of the aorta on either side of the ductus and finds a plane of cleavage; beneath the adventitia. This must be a very skilled performance, and is not advised for general use ! In this connection it is necessary to point out that Miangolorra and Hall (1941) report a fatal case, as the result of haemorrhage from the aorta itself - due to a friable area in the wall of the aorta adjacent to the ductus ! In the present series, careful dissection with the finger and blunt dissecting forceps, eventually permitted the establishment of a tunnel through which an aneurysm needle could be passed.

It may be pointed out that the technique of Johnson et al - as seen in Figs. 19 a,b,c. is the only method that has been put forward for dealing with haemorrhage from a torn ductus. In the majority of cases reported, in which this occurred, the outcome was fatal. Bourne, Keele and Tubbs controlled a small leak with a muscle graft with success.

After exposing the ductus satisfactorily, it may now be ligated in continuity, ligated and divided, or divided and sutured. Ligation should be performed with thick material, such as tubular

woven silk, or hernia tape - material which is strong enough to occlude the ductus without cutting through it. Gross, Jones et al, all advise a temporary occlusion - to observe the effects, before ligation is done. If no ill-effects are observed, the two ligatures may be permanently tied.

Because ligation by itself has proved unsuccessful in some instances, Gross (1944) advises division with suture of the divided ends as the treatment of choice. He has employed this method with success in his latter cases. Four artery clamps are placed on the ductus - a manouvre which, according to Gross, can always be carried out with patience and manipulation, and the ductus divided between the middle two. The distal clamp is removed and the free edge of the divided ductus sutured with a continuous oiled silk artery suture - starting one end and eventually returning ot it, producing a double suture. The proximal clamp is removed and the adventitia sewn over the first suture line.

Gross, sutures the mediastinal pleura, but many surgeons prefer to leave it open. The intercostal muscles are sutured with chromic cat-gut and the ribs approximated by passing strong chromic around them at several places. The muscles and skin are closed in layers. Many surgeons obtain expansion of the lung before final closure by positive pressure. Gross prefers to obtain expansion by aspirating the pleural cavity through a tube, as he believes that this produces less postoperative disturbance. In the present series the positive pressure method

was used, with no disturbance of note. Gilchrist (1945) reports a case which developed a septic mediastinitis. He advised the introduction into the region of the ductus of sterile sulphonamide powder.

D. The Postoperative Care.

These patients, like all patients subjected to intrathoracic surgery, should be carefully observed for the first few days. Respiratory embarrassment particularly should be watched for. Gilchrist (1945) advises the use of an oxygen tent in the first 24-48 hours postoperatively, but it has not been found necessary in the present series of cases. Repeated carbon dioxide inhalations may be employed, to assist the expansion of the lung. Respiratory complications are difficult to assess and control radiography is always employed. This gives the only satisfactory guide as to the expansion of the lung and also indicates the accumulation of fluid. Pleural effusion, a not uncommon sequel, can be aspirated on the second or third day postoperatively. Welch and Thompson (1940) report an occasional high pyrexia, as observed in cases operated on by Jones et al. The reason for this was not apparent. Codeine and nembutal are recommended as postoperative sedatives.

The special postoperative complications that may be expected after ligation, according to Nixon (1942) are:

(1) haemorrhage from the ductus

(2) sepsis

(3) pneumonia

(4) perforation, as the result of the erosion by the ligature

(5) injury to the recurrent laryngeal nerve

(6) postoperative thrombosis.

In the present series of cases the postoperative course has been remarkably smooth and uneventful. Patients are given the usual nursing care for chest cases, and most were fit for the discharge by the tenth day. It is usually recommended that activity should be restricted for a few months, and after that a normal life should be advised.

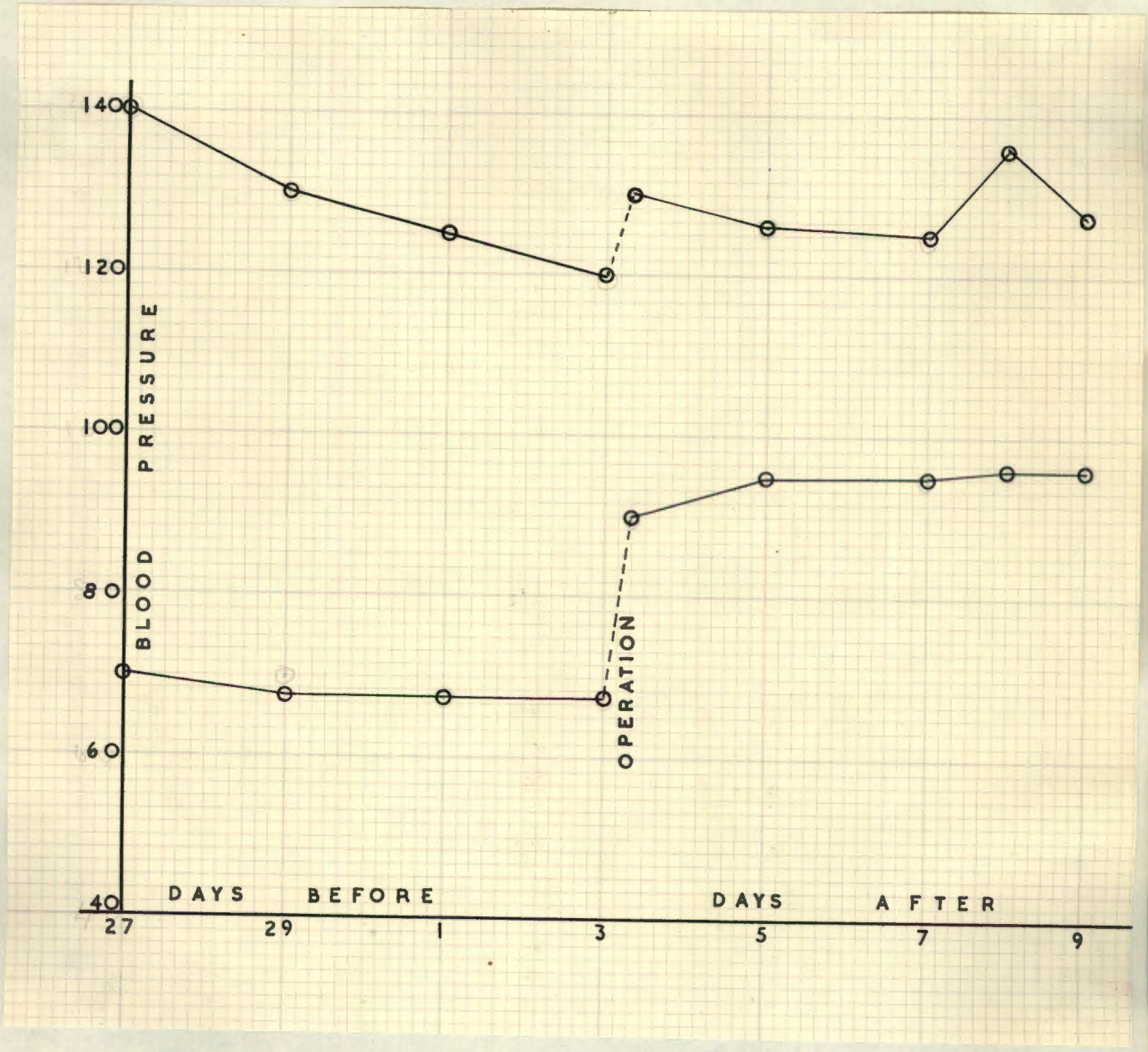



Figure 21.

Note Effect of Operation on Diastolic Blood Pressure.

# CHAPTER IX.

## THE EFFECTS AND RESULTS OF SURGERY.

The immediate effects of occlusion of the ductus arteriosus as observed at the operating-table are a disappearance of the thrill and the Gibson murmur and a prompt elevation of the diastolic blood pressure (Fig.21). This has not been shown to have any adverse effects in the present series of cases.

The diastolic pressure has remained elevated in all but one of the cases, which will be discussed below.

Bourne (1941) described an interesting phenomenon observed in one of the cases with superimposed bacterial endocarditis which had been ligated by Tubbs (Bourne, Keele and Tubbs, 1941). In this case, as a result of the obliteration of the ductus there resulted a temporary but striking and prolonged impairment of renal function associated with a marked increase in the blood pressure. There were no abnormal urinary findings, but the blood urea was elevated to the region of 72 mg %, and the urea clearance was impaired. Bourne advances an ingenious theory to explain the phenomenon. He states that the peripheral vessels - including renal, preoperatively are in a state of permanent partial dilatation, associated with a lowered diastolic blood pressure. He suggests that the increased output per beat of the heart following operation would result in a reflex over-reaction on the part of the arterioles, which persists until the vasomotor system adjusted itself to the new circumstances. The events

which occurred in this case have not been reported by others and have not been seen in any of the present group of cases, although the blood urea and blood pressure have been kept under observation.

Gilchrist (1945) believes that obliteration of the ductus should not only produce an arrest of the dilatation of the pulmonary artery and other cardiac or central vascular changes, but a retrogression. He suggests that this should be seen particularly in older people, as in young children the reaction may be merely an arrest of the growth of the heart and vessels until the bodily brewth has caught up with them. Experience in the present series has not borne this out. Two cases aged 18 and 20 show, a year after ligation, very little alteration in the contour and size of the heart and pulmonary vessels, although the Gibson murmur has disappeared or only a faint systolic murmur is present, and the diastolic blood pressure has remained elevated. One of the children, on the other hand, has shown retrogression of the so-called "pulmonary conus" and size of the pulmonary vessels. It is not unexpected that the more resilient vessels of the children should show more ability to return to normal than those of adults.

The question of possible recanalization of the ductus arteriosus after ligation is a most interesting one. Incredible as it may seem, it has been proved on many occasions by a second operation (Gilchrist, 1945) or at post-mortem examination, and has been the experience of all surgeons performing the operation

What mechanism causes loosening of the ligature it is difficult to understand, particularly when one has personally observed the care and exactitude with which the ligatures were tied, triple knots being used in every case.

Assessment of the results of operation is obviously difficult, as the operation has only been practised for 6 years. Of its long-term results, it can only be said that while prolonged observation will be the only true gauge, all our knowledge seems to indicate that the life expectancy of these people should be greatly increased. The excessive strain on the heart is abolished, which should avoid early failure. Whether subacute bacterial endocarditis is going to be prevented remains to be seen, but, if the trauma of the intima of the pulmonary artery is avoided, it seems reasonable to hope that this complication should no longer supervene.

Statistics of the more immediate results are available. These are again not entirely satisfactory, because assessments of this type are based on isolated reports. Such reports are inclined to reflect successful cases only. Nevertheless, Shapiro and Keys (1943), by communication with most of the American surgeons, concerned with the operation have found the following:- Of 140 collected cases operated on up to that time, 107 were uninfected, while 33 had subacute bacterial endocarditis. Of the 107, 81 were successful (gauged by the disappearance of the Gibson murmur, and thrill and elevation of diastolic pressure); in 14

that this does indeed take place. The problem appears to be the old question of the ligation of large vessels in continuity, and an infallible ligature material has not yet been found. Pearse (1940), by experimental studies on animals, has shown that cellophane produces an intense fibrous tissue reaction and that this may be successful in occluding vessels. The original suggestion that cellophane may be used for the ligation of patent ductus was first made by Holman (1940), when discussing Pearse's work. Cellophane has since been used in addition to ordinary ligatures by Gross and Jones, Bolley and Bullock, Harper and Robinson Rohman (1944), Gross (1944) and Gebauer (1943) report recanalisation even with cellophane, although the incidence was less, so that Gross to-day divides and sutures the ductus instead of ligation. In the present series, too, one case, after showing complete disappearance of signs, clinical and radiological, developed a soft systolic murmur towards the end of the second week post-operatively. This gradually became louder and eventually became continuous. A year later the murmur is a typical Gibson murmur and the patient has all the radiological evidences of deterioration (Figs. 22)

It must also be recorded that Touroff (1943) reports a case of persistence of the Gibson murmur even after ligation and division of the ductus arteriosus, so that in some cases, at least, the murmur may not be indicative of recanalization. Other clinical and radiological indices may have to be used.

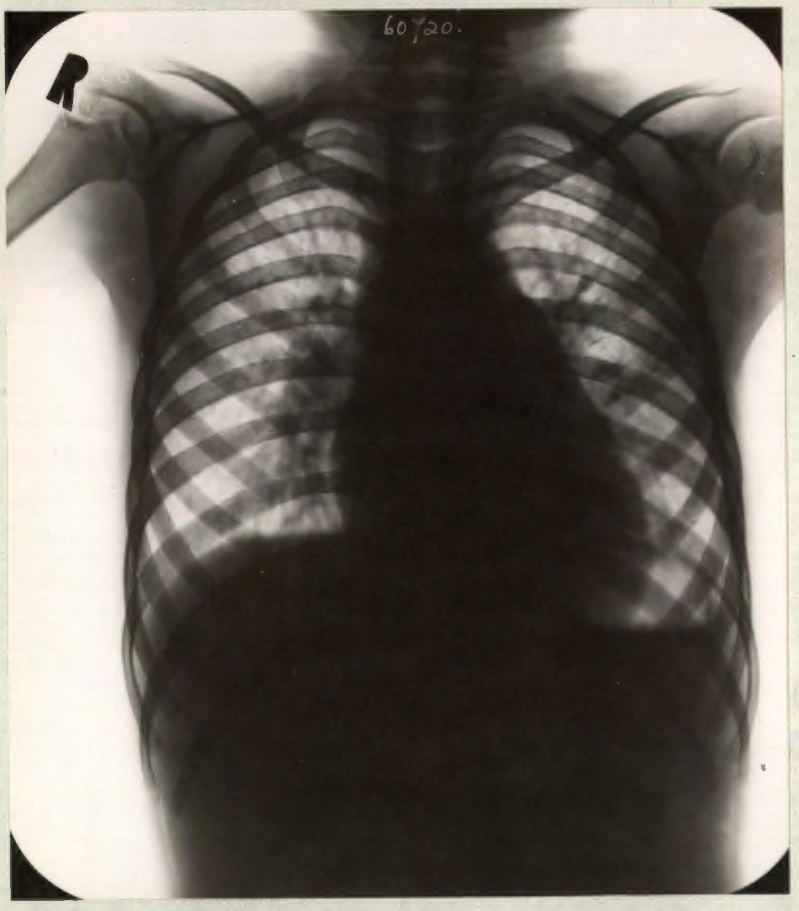
the Gibson murmur returned after operation, and 9 died as a result of rupture of the ductus at operation, 2 from subsequent bacterial endocarditis and one from septic mediastinitis. In 3 the structure ligated was not the ductus. Of the 33 with subacute bacterial endocarditis, 20 were completely cured, 8 were not improved and 5 died from rupture.

It must be pointed out again that these figures show a cure of 50%, as opposed to the almost 100% mortality rate before surgery.

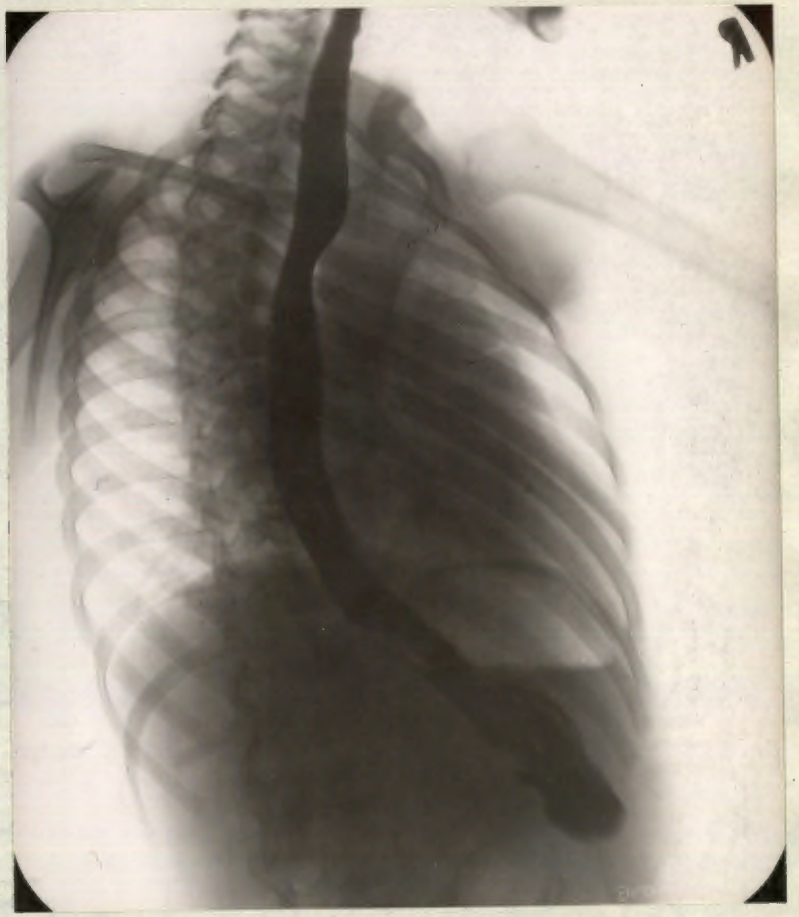
The uninfected cases, therefore, show an operative mortality in the hands of many surgeons of about 8.5%. Buch (1944), making a similar study of case reports finds a similar figure for the operative mortality. Although the mortality as reported by Shapiro and Keys is not extremely high, more than 20% of the uninfected cases were not markedly improved. Gross attributes this relatively poor result to:

(1) Failure to find the ductus,
(2) Ductus too short to ligate,
(3) Ligation of the wrong vessel,
(4) Haemorrhage from the ductus,
(5) Incomplete obliteration or recanalization,
(6) Wound sepsis,
(7) Post-operative pneumonia, mediastinitis, etc.

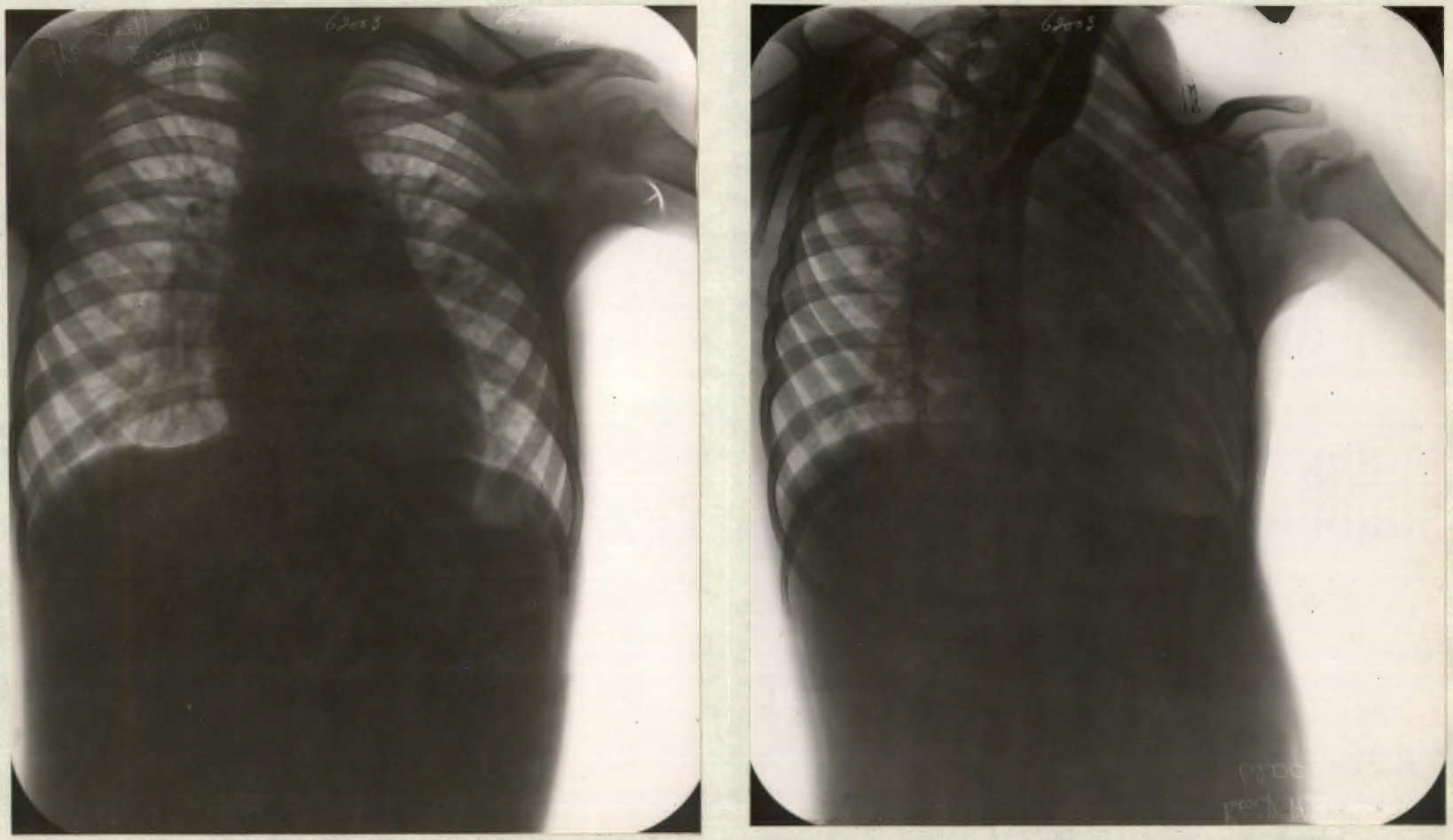
Several of these are avoidable. In the hands of Gross (1945) and others who have done a large number of operations, and of others who have not had the same experience, benefiting from past mistakes, there has been a reduction of the mortality figures.



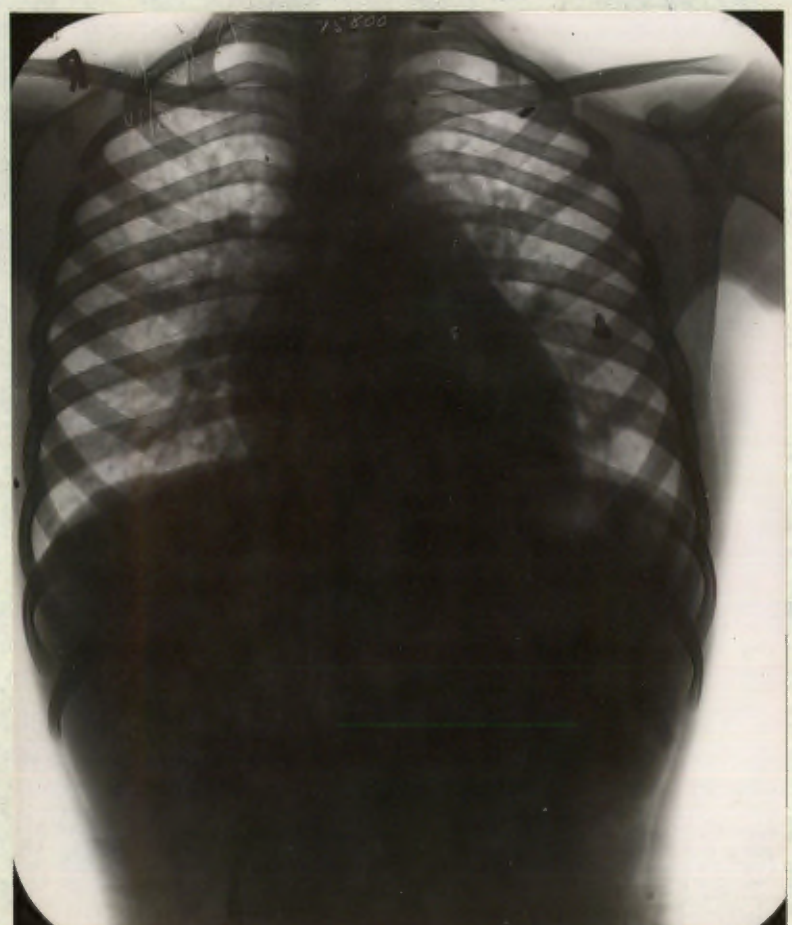

P.A. view of case of patent ductus arteriosus before operation.

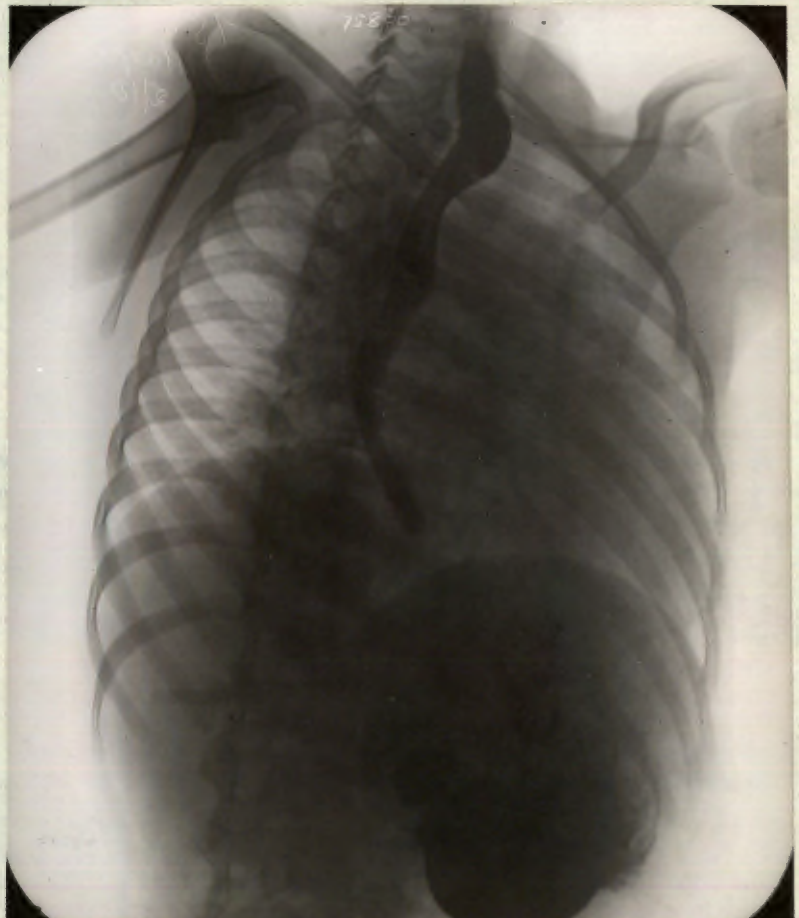


Left oblique view of same case. Note slight indentation of oesophagus by left auricle.



Plates of same case as depicted in previous Figure taken about two weeks after operation. Note "waist" appearing on left border on P.A., also normal outline of oesophagus in oblique film.





Gross (1944) has a total mortality in all cases performed by him of 2 in 80, or 4%, and both of these were early cases. In the present series of 5 cases subjected to operation there was no operative or post-operative mortality, and 4 patients were improved, while one appears to have recanalized (See Figures and citation).

Improvement in technique, increased understanding of the indications, knowledge of the hazards and evasion of avoidable mistakes have and will considerably improve the figures, not only of mortality but also of cases that have benefited.

## PART II.

## THE PROBLEM OF THE POST-NATAL CLOSURE OF THE DUCTUS ARTERIOSUS.

No aspect of the ductus arteriosus has given rise to more speculation and experimental investigation than the question of the mechanism of its post-natal closure, and the reasons for its occasional failure. In spite of extensive investigations, both anatomical and physiological, no satisfactory explanation has yet been advanced. The problem has interested scientific observers for a considerable time, so that it is not surprising that many theories have been advanced and discarded, only to be revived in perhaps a slightly altered form. During the nineteenth century and before, these theories were mainly speculative, as experimental studies were not carried out. The twentieth century, on the other hand, has seen the development of more and more elaborate experiments in an attempt to seek the solution.

### A. The Foetal Circulation.

For a thorough understanding of the problem, it is necessary to give a brief account of the function of the ductus during intra-uterine life. Before birth, the ductus arteriosus serves to divert blood from the pulmonary artery to the aorta, as had been observed by Harvey as far back as 1628. As the lungs are not functioning before birth, a large circulation through them is not required, so that blood is in part shunted away from them to the systemic circulation. The exact quantity of blood diverted in this way is a subject of dispute. Some workers believe that

the greater portion of the output of the right ventricle is diverted in through the ductus, while others, including Patten (1930) maintain tha there is no evidence of any sort to support that contention. Patten holds "that it has the unmistakable odour of teleology to postulate a capacious but virtually unused vascular plexus in growing lungs ready at the instant of birth to receive a suddenly rerouted current of blood carried to the lungs". He maintains, further, that it is unlike anything known about the development of the vascular system to think of vessels growing beyond a capacity consonant with their present requirements. His contention has received support from experimental work by Abel and Windle (1939), who found that there was no "s i g n i f i c a n t" increase in the amount of blood flowing through the lungs after birth, as compared with that circulating before birth.

The exact proportions of superior and inferior vena caval blood which was transmitted by the right and left ventricles respectively, is another matter which for 150 years had been a subject of constant dispute. The so-called Galen-Harvey theory, which, according to Barclay et al (1944) had quite erroneously been associated with the name of Harvey, postulates that thorough mixing of the two caval streams takes place in the right auricle, before it is transmitted, in part via the right ventricle to the lungs and ductus arteriosus, and in part through the foramen ovale to the left auricle and then via the left ventricle to the head and neck. On the other hand, Sabatier (1791) is credited

with expressing somewhat contrary views. He believed that there was practically no mixing of the blood from the two caval streams. The blood returning from the head and neck and upper limbs, via the superior vena cava passed directly to the right ventricle and from there to the lungs via the pulmonary vessels, and to the descending aorta via the ductus arteriosus. The inferior vena caval stream, rich in oxygen from the placenta, on the other hand, passed through the foramen ovale to the left auricle and via the left ventricle eventually reached the head and neck.

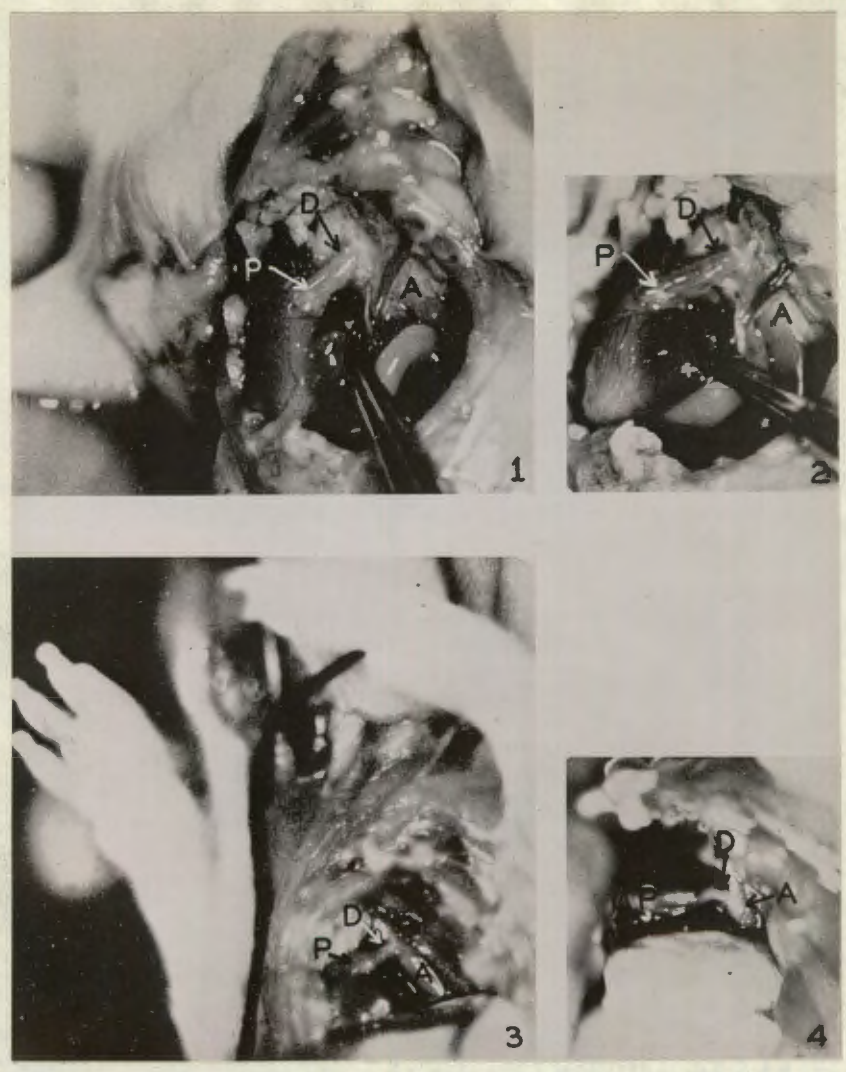
These two theories have each had their champions and for many years the matter was in dispute. At the beginning of the present century, experimental aids were invoked to support the various arguments. The Galen-Harvey theory was supported by Pohlman (1907), Kellogg (1928) and Patten (1930). The Sabatier theory received support from many of the older observers such as Kilian, Wolff, Ziegenspeck, etc. (cited by Barron, 1944), but more recently observations by Amoroso et al (1942), Windle and Becker (1940), Whitehead (1942) and last of all by Barclay, Barron and Franklin (1940-1944). It would be out of place in this thesis to give a detailed account of the various experiments that were made and the conclusions that were drawn. It may be suggested that the experiments of Pholman, Kellogg and Patten were probably performed on animals that were moribund, because Whitehead has shown that mixing of the caval streams does occur when the pressures which are responsible for their remaining separate begin to fall. Suffice it to say, then, that it seems

to have been established, fairly conclusively, by the brilliant studies of Barclay et al (1940-1944) at Oxford, that in the main the theory of Sabatier was correct. They actually directly viewed the course followed by radiopaque materials injected into the veins, through the heart and great vessels, by cinemaradiographical methods.

Present knowledge, then, appears to show that the inferior caval stream divides, a part going to each auricle, but the bulk passes through the foramen ovale, following the course as outlined by Sabatier. The superior caval stream, on the other hand, passes through the right ventricle and finally to the pulmonary vessels and the ductus arteriosus. At term, the ductus arteriosus and the isthmus of the aorta contribute about the same quantities of blood to the descending aorta. Much less well established, but nevertheless generally accepted, is the contention of Pohlman (1907), that the capacities of the two ventricles are equal before birth and that the pressure in them is equal. (The latter has also been demonstrated by Hamilton et al, 1937) Prior to this it had been supposed that the pressure in the right ventricle was greater than that in the left. These experiments are open to criticism (vide infra).

B. <u>The Changes in the Ductus Arteriosus that follow Birth</u>.

After birth the ductus arteriosus and other channels (which do not concern this thesis) close, and the blood which had passed through them is rerouted along the ordinary physiological pathways. The exact time at which this occurs is not definitely established,




1. and 2. Open ductus arteriosus. Thoracic viscera as seen through an opening in the left side of the chest. The open ductus (D) appears as a continuous vessel from the pulmonary artery (P) to the aorta (A). The aorta near the point of entrance of the ductus is not clearly seen as it is covered by overlying tissue, but is visible caudalward, being crossed by a dark vein. A small part of the pulmonary artery beyond the ductus can be seen going posteriorly and inferiorly in Figure 2. From fetal guinea pig near term. Photograph (X2).

3 and 4. Closed ductus arteriosus. View and lettering similar to Figure 1. The ductus has closed following inflation of the lungs with air, and appears much narrower than the trunk of the pulmonary artery.

Fig. 23.

but it has been shown by Kennedy and Clark (1942) in guinea pigs (Fig.23), and Barcroft, Kennedy and Mason (1938 and 1940) in sheep, that a functional closure occurs within a few minutes of the onset of inspiration. This functional closure is a reversible process and the ductus opens if respiration ceases. Permanent occlusion develops subsequent to this, the ductus arteriosus being converted into a purely ligamentous structure - the ligamentum arteriosum. These observations by Kennedy and Clark, and Barcroft et al, appear to confirm the original thypothesis of Gerard (1900) that there are two stages to the phenomenon of closure - "Physiological occlusion which occurs shortly after birth, having the ductus patent in all its length but preventing the passage of blood, and secondly, anatomical obliteration". Whether exactly homologous events take place in the human foetus is not definitely known, as experimental observations are not possible, but there are indications that this may be so. Scammon and Norris (1918) cite Billard (1828) as saying that of 128 cases observed by him, who had died in the first 8 days of life, there were cases in which the ductus was occluded on the first day, and 50% were closed by the 8th day. Scammon and Morris themselves compiled statistics from the literature, which showed that of 1095 children who had died in the first year of life, the ducti were closed as follows: 1st week, 0.3%, 2nd week, 2%, by the end of the 8th week, 50% and by the end of a year, 94%. Christie (1930), reviewing 558 consecutive autopsies, found the ductus patent as follows:

64.7% by the end of 2 weeks, 12% at the end of 8 weeks and 1.2% at the end of a year. Postmortem tests of patency are never satisfactory, particularly in very young infants. The usual test consists of passing a probe down the ductus. In those cases where only a functional closure has taken place, the probe would naturally pass through, even with slight force. Histological section would be the only accurate method, and this, to the knowledge of the author, has not yet been extensively carried out. The fact that Billard found cases in which the ductus appeared to be closed on the first day, suggests that in the human, too, closure occurs in the first instance as the result of a physiological process, whih comes into play very shortly after birth.

C. The Mechanism of Closure.

At the present stage, therefore, we know the nature of the prenatal circulation, and we know that the ductus closes shortly after birth by a functional mechanism, and that subsequent to this it becomes obliterated. However, exactly how and why closure takes place is still not known. Many theories have been advanced, and they are perhaps best summarised by Wells (1908):-

(a) The first expansion of the large bronchi by air compresses the ductus arteriosus.

(b) Bending of the arch of the aorta, by increased pressure after birth, causes closure.

(c) Beginning of respiration causes a change in the position of

the thoracic viscera, and thus causes tension and collapse of the ductus.

(d) Fibrous bands passing over the ductus are connected with the diaphragm, and upon descent of the diaphragm with respiration, the bands are pulled down and occlude the ductus.

(Theories explaining closure of the ductus arteriosus on a change in the disposition of the thoracic contents following respiration emanate mainly from the 18th and 19th centuries and even the early part of the present, when anatomical studies were the main means of research. The names associated with them are of Schanz, Linsemeier, Strassman and others. More recently, Rehman and Noback (1941) have revived the anatomical concept of closure.)

(e) A concentric fold of tissue present at the aortic end, which acts like a valve preventing the flow of blood from the aorta into the ductus, was described by Strassman (1898).

It has been shown by Barclay et al (1944) that in the vast majority of mammals, this fold is of little consequence, and in man is almost negligible.

(f) Thrombosis in the lumen and subsequent adhesion of the walls to close the ductus.

(g) Fibrous growth in the intima leads to occlusion.

(h) Active contraction of the layers of the ductal wall close it. Graper, von Hayek, Swenson, Kennedy and Clark, etc.)

Many of the above theories were advanced before it was appreciated that there were two phases to the phenomenon of

closure, so that only those which imply an immediate complete action need be considered. The only mechanism whereby the ductus can be closed off within minutes, is by the contraction of its wall, and the fact that Kennedy and Clark and others have shown that this contraction may be reversed, tends to show that the action of the muscle in the wall is sphincter-like. Histological studies by Craper, von Hayek and others, and also by the author (vide infra) have shown that the structure of the ductus arteriosus is different from that of the pulmonary artery and aorta - vessels which at this time it approximates in size, and that it is such, that a sphincter-like action is not unlikely. If this is accepted - and all the evidence tends to point that way - then the question of the mechanism which initiates and maintains the contracture of the ductus until it is finally obliterated must still be answered. Barron (1944) indicates that there are three possible mechanisms, namely

i) nervous action,

ii) blood-borne stimuli,

iii) mechanical forces.

i) Nervous Action:-

The presence of nerve endings in the wall of the ductus has again been a matter of dispute. Boyd (1941) demonstrated nerve endings in the wall of the ductus. These were mainly sensory, but a few motor fibres were probably also seen. Kennedy and Clark (1942) and Barron (1941) have failed to repeat this. Kennedy and Clark (1942), after cutting every known nervous pathway,

still produced closure of the ductus by rhythmical inflation of the lungs. It would appear, therefore, that nervous action is not the mechanism.

ii) Blood-Borne Stimuli:-

Similar conflicting reports have been given out about the action of blood-borne stimuli. Kennedy and Clark maintained that they were able to bring about closure by the injection of oxygen into the umbilical vein, but not by nitrogen. Barron could not substantiate this. Other bio-chemical substances have not been extensively used. Thus, while it appears essential that this question still needs very much more investigation, at present, at least, blood-borne stimuli do not appear to be the essential factors in initiating contraction of the ductus.

iii) Mechanical Forces:-

Theories (see above) which may be regarded as implying a mechanical action, which had been discarded during the initial stages of the experimental era, are being revived (e.g., Noback and Rehman, 1941). Nevertheless, anatomical considerations based on the principle of compression, stretching and rotation of the ductus, appear to be too uncertain to account for a phenomenon which, with few exceptions, invariably takes place. On the other hand, observations on the structure of the ductus and its anatomical relations, as seen in guinea pig foetuses, during the present experimental investigations, seem to suggest the possibility that forward displacement of the pulmonary vessels, which results from the expansion of the lungs, may assist

in altering the relative haemodynamic relationships existing in the large vessels.

After careful review of the theories propounded and the experimental work that has been done, one is inclined to conclude with Barron (1944) that the solution, when found, may be based on simple haemodynamic considerations. The theory of Ziegenspeck (1905), so far not thoroughly put to the test, that the ductus is in a tonic state and that the lumen is kept open by the pressure of the blood in it (implying that the removal of the pressure will result in its closure) may still prove to be near the truth. Consideration of the principles that apply to blood vessels in general suggests to one that perhaps it is not so much that the ductus empties because it contracts, but that it contracts because it is empty !

It was with a view to studying the haemodynamics of the heart chambers and great vessels before and after birth, that certain experimental studies have been initiated. These, for reasons beyond control, such as a seasonal shortage of pregnant guinea pigs, and technical difficulties that have had to be overcome, are in their initial stages, but sufficient progress has been made to warrant a brief record in this thesis.

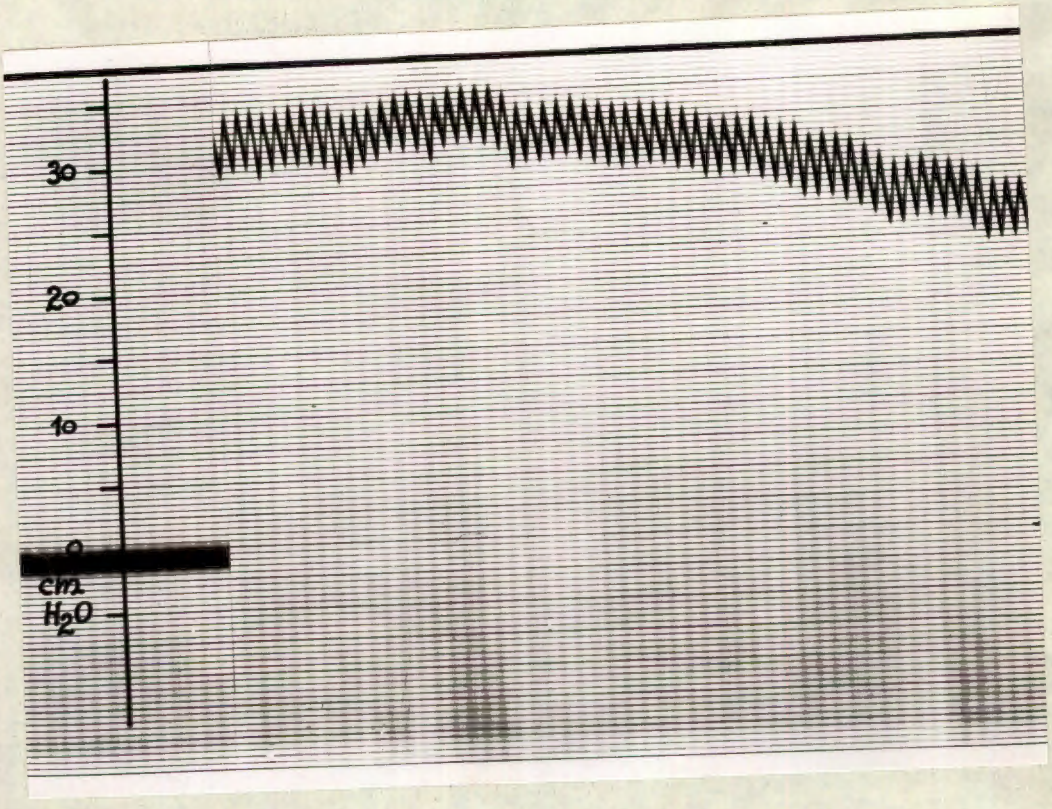
D. Experimental Observations.

The Methods:- The apparatus depicted in Fig.24 was constructed for the purpose of measuring intracardiac and arterial pressures. It consists of a narrow bore intravenous needle, specially shortened and rebevelled for the purpose. The needle is connected

to a system of water and mercury manometers, for direct reading of the pressure and to a Frank capsule for obtaining a camera tracing. The apparatus was duplicated to enable simultaneous readings in both ventricles or two different vessels. Considerable trial was required before the correct bore needle, and the correct fluid for the tube system, were obtained. A saline-heparin solution appears to be the best. Pure saline permits of too rapid a clotting in the needle and citrate solution appears to affect the animals adversely.

The animals employed for a start were pregnant guinea pigs near full term (period of gestation, according to Ibsen, 1928, being 68 days). A suitable anaesthetic had to be searched for. Urethane was not suitable, nor was chloroform, or chloroform-ether mixture. Pure ether gave the most satisfactory results. It did not seem to affect the foetuses adversely, for if permitted to do so, they breathed perfectly well after delivery.

The pregnant guinea pigs were placed in a saline bath at body temperature in such a way that the lower half of the body was submerged. After anaesthetising the mother, the foetuses were delivered one at a time through a small incision in the uterus, at the point furthest from the placenta. After some failures, a technique was developed for performing this, without causing separation of the placenta. The opening in the uterus was closed with skin clips, the foetus being kept under the surface of the saline all the time. Great care was taken during all this to prevent occlusion of, and traction on the cord during




Typical tracing obtained from the ventricle by the apparatus depicted in Fig. 24

Fig. 25

the above performance. The left chest of the foetus was then opened and the heart and great vessels displayed. The heart, in all cases used for readings, was beating vigorously and steadily. The thinness of the walls enabled one to observe the different colours of the venous and arterial blood in the two ventricles. The needles could be inserted into either ventricle with ease. This method avoided the serious objections to the methods of Hamilton et al, who inserted needles through the chest wall, and subsequently dissected the heart to see whether the needles had been in the ventricles.

Readings were successfully obtained in the last two foetuses. It was shown that the pressure in the left ventricles rose in both cases to the height shown in the tracing (Fig. 25 ) and that the pressure in the right ventricle was equal to this.

Although insufficient a number of cases have yet been done to be of statistical significance, it appears that by this method it will be shown, to the satisfaction of all, that the pressures in the two ventricles before birth, are equal. Subsequent to that, the study of the changes, if any, in pressure of the ventricles after inflation of the lungs - with a direct observation of the ductus at the same time, may yield results that will eventually enable one to decide on the nature of the mechanism that initiates the phenomenon of closure. This record may, therefore, be regarded as a preliminary report on this aspect of the phenomenon.

E. The Histology.

The ultimate anatomical obliteration of the ductus has also been investigated. Serial sections have been cut of the ductus arteriosus in guinea pigs at various stages of browth. The ages of the guinea pigs were: 2 full term, still born guinea pigs, one two-hour old guinea pig, and the guinea pigs at the ages of 3 one day days, 6 days, 13 days and 21 days.

The results obtained are depicted in the microphotographs (Figs. 26 to 39 ). It can definitely be agreed with von Hayek, Kennedy and Clark (1941), Jager and Wolleman (1942) that at the end of foetal life the ductus is different in structure from the aorta and pulmonary artery - vessels which its equals in size. The ductus is thicker-walled and has definitely less elastic tissue and more muscle fibres than those vessels. It can also be shown that opposed to the view of Dry (1921) and others, the ductus, after birth, is more closed in the centre than at the ends.

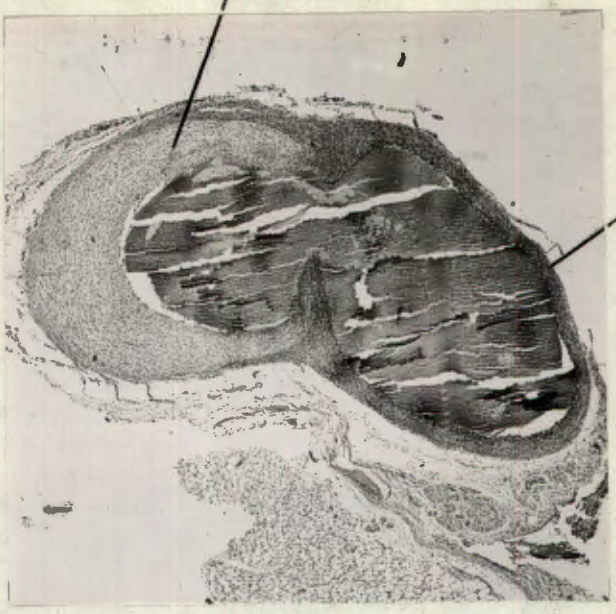
In addition, the following observations have been made regarding the cellular structure of the ductus arteriosus. The adventitia is thin, and possesses no unusual characteristics. The intima is several layers thick and internal elastic lamina is ill-developed. It is the media particularly which shows interesting features. It possesses two layers - an outer, consisting of circular muscle fibres, and an inner which shows several layers of large polygonal cells with a faintly staining vacuolated protoplasm and nuclei containing very little chromatin -

resembling epitheloid cells. These cells are obviously modified smooth muscle cells. Furthermore, the elastic tissue so prominent in other vessels of that size, particularly of the pulmonary artery and the aorta, at that site, is very scanty (Fig.33). The above description tallies with that of the arterio-venous anastomoses, as first described by Sucquet (1865) and Hoyer (1877) and later by Grosser (1903) and others. These These are also characterised by the absence of elastic tissue and by the presence of an inner layer of epitheloid cells as described above. These arterio-venous anastomoses are seen in the central parts of the web of certain birds (ostrich, duck, etc.) and in mammals, in the wings of the chiroptera, matrix of the hoof of ungulates, etc., and in the tips and nailbed of the fingers and palmar surfaces of the hands and feet in man.

The similarity in structure of the ductus arteriosus to the arterio-venous anastomoses, may imply a similarity of function. The latter can remain closed for a considerable time after initial contraction, by virtue of the fact that the epitheloid cells possess the property of imbibing fluid, and by so doing, can occlude the lumen.

The subsequent changes in the ductus arteriosus are mainly those of a disintegration of the intimal epitheloid cells, probably due to ischaemia, and the eventual replacement of the ductus by a singularly acellular fibrous tissue. These changes will be best appreciated by looking at the microphotographs and citation.

Fig. 26



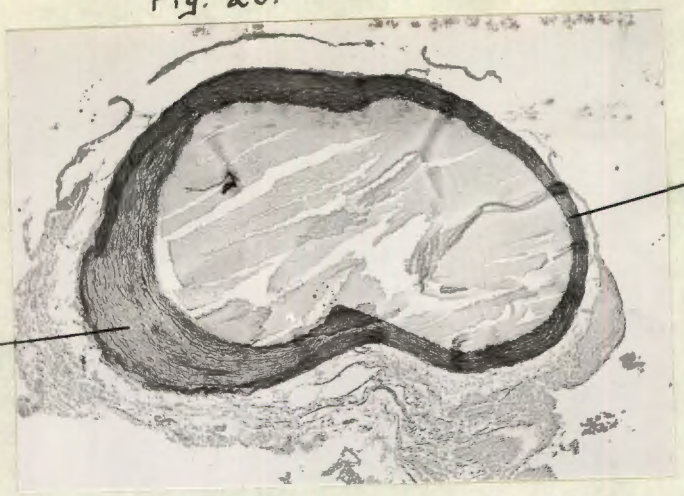

Harts Elastica. 30 X.


Fig. 27

Two sections showing the ductus coming off the pulmonary artery.
In top section note the folds between the ductus and the pulmonary artery.
In lower section the pulmonary trunk has given off a branch.

Haematoxylin and Eosin. 30 X.
Full term guinea pig.
Still-born foetus.

Fig. 28.



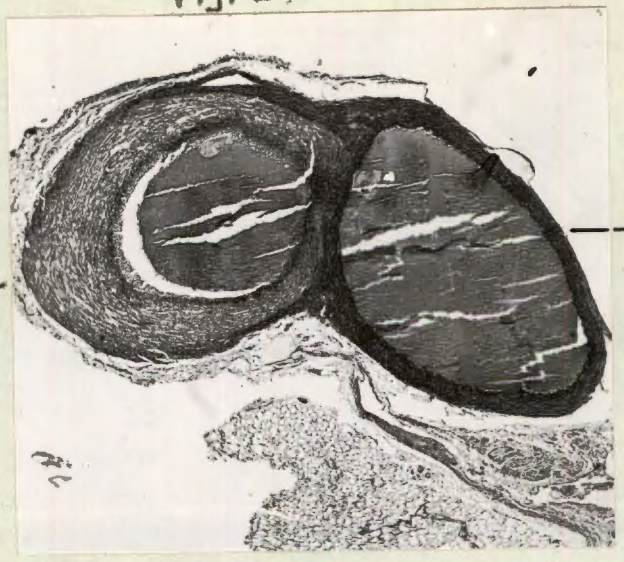

Ductus a stage further in process of coming off. Note the diminution in elastic tissue in ductus as compared with the pulmonary artery. Elastic tissue seen only in periphery of media.

Fig. 29.


Ductus has just come off pulmonary artery.

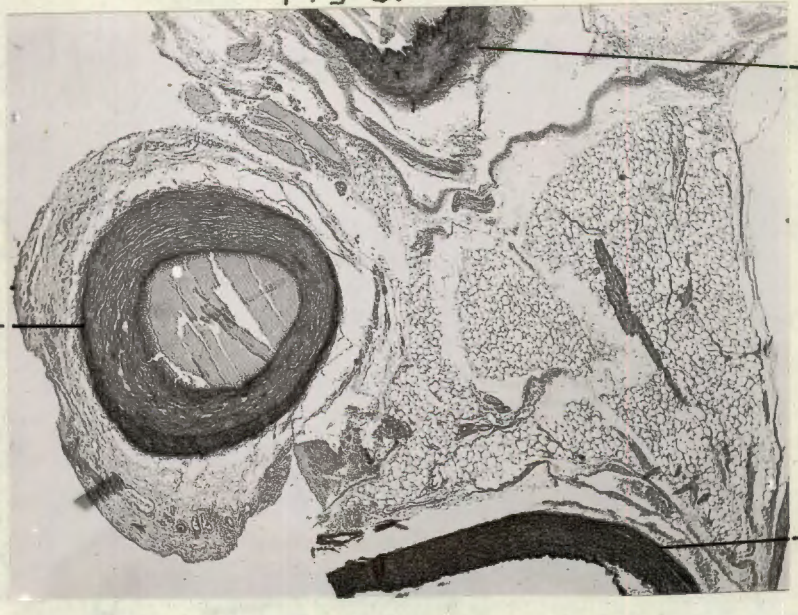
Harts Elastica. 30 X.

Fig. 30




Ductus has come off pulmonary artery. Note relative thickness of wall of ductus as compared with pulmonary artery. Note also difference in elastic tissue.

Fig. 31



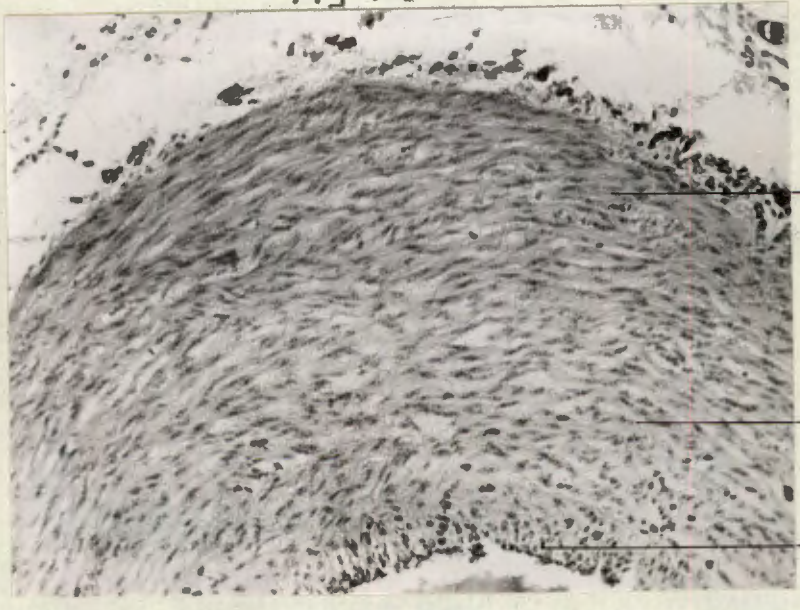

Section from ductus arteriosus in full term, still-born guinea pig. Compare pulmonary artery and aorta.

Harts Elastica. 30 X.

Fig. 32.


Guinea pig foetus 2 hours old. Note the lumen of the ductus is partially closed. This section is taken from near the pulmonary end of the ductus ~~Harts Elastica.~~ 30 X.

Fig. 33.




High power (225 X) H. and E.
Showing outer layer of media well defined
Smooth muscle cells
Inner layer of media contains polygonal,
vacuolated epitheloid cells.
Intima several layers thick.

Fig. 34.

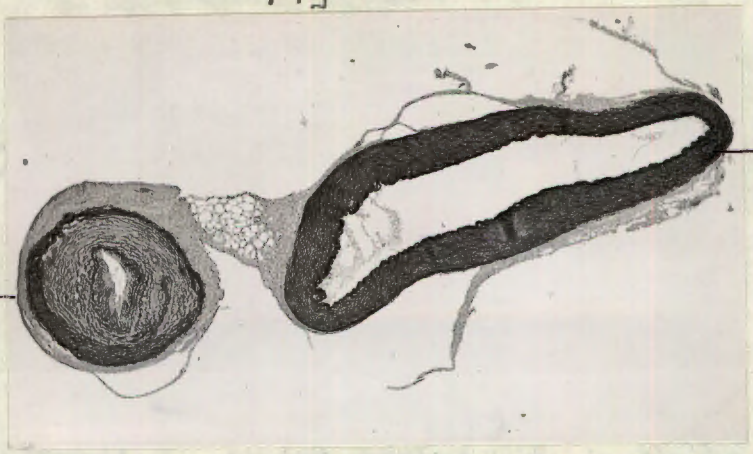
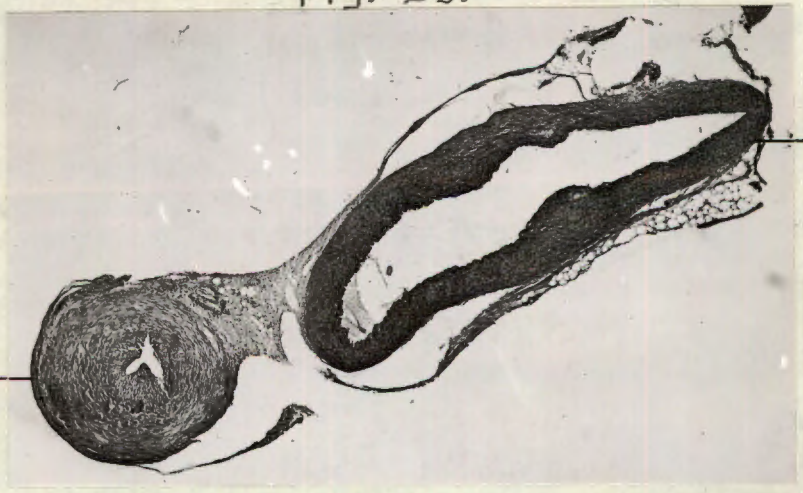


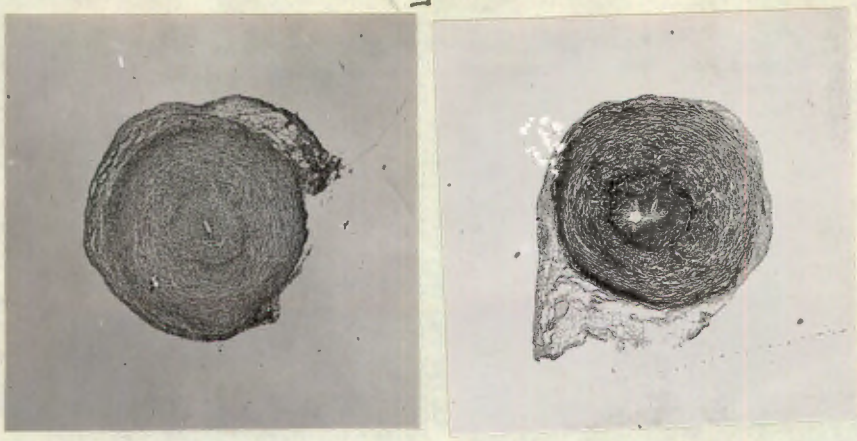

Fig. 35.




Two sections taken from a day-old guinea pig. The upper nearer the end of the ductus shows more patency than the lower which is taken from the central portion of the ductus. There is no disintegration of cells.
N.B. ALL the photographs were taken with the same magnification for comparison of size of ducti at all stages.

Harts Elastica. 30 X.

Fig. 36.



Ductus arteriosus in guinea pig
3 days
Pyknosis of cells setting in

He. and E.
30 X.

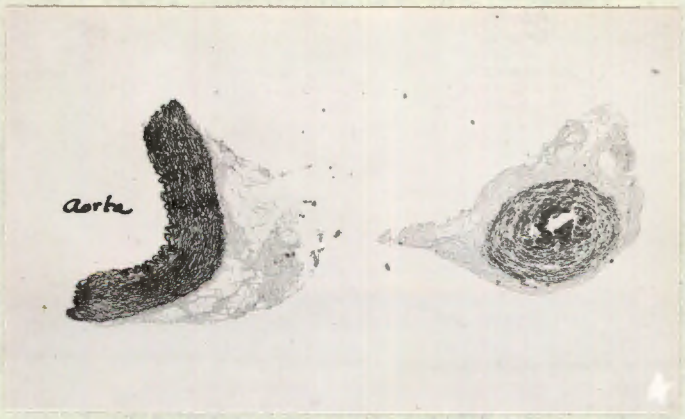
Harts Elastica.
30 X.

Fig. 37.

Ductus arteriosus - guinea pig - at 6 days.
Left hand picture taken near the end - shows lumen filled with white thrombus

Right hand picture taken from centre of ductus - complete occlusion.

Fig 38.




Ductus Arteriosus - guinea pig - 13 days.

Note size in comparison with wall of aorta.

Elastica stain. 30 X.

Fig. 39.

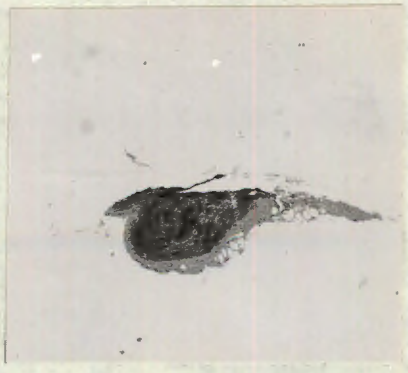


Fig. 39.

Ductus Arteriosus at 21 days - complete fibrosis.

H. and E. 30 X.

Elastica.

30 X.

## SUMMARY.

(1) A review of the literature of the surgery of the patent ductus arteriosus has been given.

(2) Eleven patients with patent ductus have been investigated.

(3) The "blowing test", which it is hoped will prove of value in the diagnosis, has been described for the first time.

(4) Plethysmographic studies have (as far as is known) been done on patients with patent ductus arteriosus for the first time.

(5) The problem of the post-natal closure is discussed.

(6) A preliminary report of experimental studies on this aspect is presented.

(7) Histological studies, too, are described.

## ASPECTS RECOMMENDED FOR FURTHER STUDY.

(1) Histological investigation of the arterioles of the lungs to observe any changes suggesting a compensatory response to the increased blood pressure and volume in the pulmonary vessels.

(2) Further investigation of the "blowing test".

(3) Further plethysmographic studies.

(4) Investigation of the changes in the haemodynamics of the great vessels and heart that follow the inflation of the lungs.

(5) Study of the effect on the haemodynamics of the great vessels of alteration of the anatomical relations as produced in models.

(6) Tomokymographic studies are suggested with a view to visualizing the ductus.

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