THE DIAGNOSTIC VALUE OF AUSCULTATION AND PHONOCARDIOGRAPHY IN PULMONARY STENOSIS AND FALLOT'S TETRALOGY

THEIR USE IN DIFFERENTIAL DIAGNOSIS, ASSESSMENT OF SEVERITY, PREDICTION OF THE POST-OPERATIVE RESULT AND PHYSIOLOGICAL STUDIES

THESIS

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By

LOUIS VOGELPOEL

M.B., Ch.B. (Cape Town), M.R.C.P. (Lond.)

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To

MY WIFE

and

My Mother, Mr. R.P. Cain, Mr. and Mrs. F. Gardner.

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This work could never have been accomplished without the valuable help and cooperation from my colleagues in the Cardiac Clinic, Dr. V. Schrire, Dr. M. Mellen, Dr. A Swanepoel, Prof. R.H. Goetz and Dr. G. Sutin. To their unstinting help I owe deep gratitude. I wish to pay special tribute to Dr. V. Schrire who has been intimately associated with this work since its inception. His enthusiasm and boundless energy have been a constant stimulus. Special thanks are due to Dr. Maurice Mellen for obtaining multichannel recording apparatus, technical assistance and for his association and cooperation.

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".....This discovery, indeed, is almost of that kind which I call Serendipity, a very expressive word, which, as I have nothing better to tell you, I shall endeavour to explain to you: you will understand it better by the derivation than by the definition. I once read a silly fairytale, called The Three Princes of Serendip: as their Highnesses travelled, they were always making discoveries, by accidents and sagacity, of things they were not in quest of: for instance, one of them discovered that a mule blind of the right eye had travelled the same road lately, because the grass was eaten only on the left side, where it was worse than on the right - now do you understand Serendipity? One of the most remarkable instances of this accidental sagacity, (for you must observe that no discovery of a thing you are looking for, comes under this description,) was of my Lord Shaftsbury....."

- LETTER CCLI, Jan.28, 1754.

Quotation from "LETTERS OF HORACE WALPOLE, Earl of Oxford, to SIR HORACE MANN". VOL.lll. London: Richard Bentley, 1833.

SERENDIPITY 1754. Coined by Horace Walpole upon the title of the fairy-tale "The Three Princes of Serendip", the heroes of which ' were always making discoveries, by accidents and sagacity, of things they were not in quest of.' The faculty of making happy, unexpected discoveries by accident.

- Oxford English Dictionary.

INTRODUCTION

Interest in the diagnosis of pulmonary stenosis and Fallot's tetralogy was first stimulated by two provocative findings. I found that there was a striking difference in the length of the systolic murmur, whereas no important difference in the systolic murmur had been previously reported, and that splitting of the second sound occurred in Fallot's tetralogy, yet it was standard teaching that the second sound was always single in this condition. These observations called for an intensive study since the differentiation of Fallot's tetralogy from pulmonary stenosis with intact ventricular septum was an important and frequently difficult diagnostic challenge. It was shown that in severe cases of both conditions the difference in murmur length was so striking that the diagnosis could be settled by simple bedside auscultation. This seemed to be an important contribution since elaborate investigations were usually necessary to establish the diagnosis. The original observations, first made in 1953, were reported in collaboration with Dr. V. Schrire in 1955. The work has expanded since then and publication deliberately delayed because several projects required time for completion. The chief delay was in obtaining proof of the thesis by studying the effects of surgery on the murmur and heart sounds. Cardiac surgery was in its infancy at Groote Schuur Hospital at the outset of this study; however, rapid strides have since been made providing a valuable opportunity to observe the effect of different operative procedures in both conditions. The delay has been worthwhile for many other reasons. With the development of the Cardiac Clinic, excellent multichannel recording apparatus and

technical assistance were obtained enabling physiological studies originally planned in 1953 to be satisfactorily performed. These have not only added support to the thesis but have led to better understanding of the mechanism of heart murmurs and sounds and, more important, to valuable diagnostic tests which clinch the diagnosis in the difficult case.

The background to the original observation may be worth describing since its discovery was the outcome of a mistake. In 1952, after a valuable period of training at the National Heart Hospital, London, I joined Dr. V. Schrire and Dr. M. Mellen in the Cardiac Clinic, Groote Schuur Hospital and was anxious to develop a phonocardiographic service. I soon made a serious blunder in confidently diagnosing a patent ductus arteriosus in a patient who had a loud, prolonged, late systolic murmur extending beyond the aortic second sound into diastole thereby resembling a continuous murmur. However, cardiac catheterisation revealed pulmonary stenosis with intact ventricular septum and no patent ductus. I had not appreciated that the murmur of pulmonary stenosis is much more prolonged than aortic stenosis and that it may extend well beyond the aortic second sound into left ventricular diastole thus resembling a continuous murmur. Leatham had clearly shown that murmur of pulmonary stenosis may be longer than the midsystolic murmur of aortic stenosis, and attributed this to delay in right ventricular systole. He also showed that pulmonary stenosis caused wide splitting of the second sound from delayed closure of the pulmonary valve. It therefore seemed reasonable to postulate that increasingly severe pulmonary stenosis should cause progressive lengthening of the murmur and greater width of splitting. However, within the same week, I examined a severe case of Fallot's tetralogy expecting to find a very prolonged murmur since severe pulmonary stenosis was obviously present. To my surprise, the murmur, although loud, was short. It had an early systolic crescendo, followed by a rapid diminuendo and ended before the loud aortic second sound. Why then this paradox in two patients both of whom had severe pulmonary stenosis? Clearly the major difference between them was an intact ventricular septum in the first and a large septal defect in the second. The importance of a large septal defect in modifying the dynamic response to pulmonary stenosis had been known for several years. Could it be that the murmur, too, reflected the fundamentally different haemodynamic situation in the two conditions?

The hypothesis put forward to explain the difference in murmur length was as follows. In pulmonary stenosis with intact ventricular septum, the right ventricle can only discharge its blood through the stenosed orifice. Thus, when the stenosis is severe, the duration of right ventricular systole greatly exceeds that of the left; hence the late, prolonged, systolic murmur extending beyond the aortic second sound but ending before a very delayed soft pulmonary second sound. By contrast, in the tetralogy, the right ventricle is able to discharge its contents into two competing orifices, namely, the stenosed outflow tract offering a high resistance, and the aortic, a lower (systemic) resistance. Due to the safety valve provided by the large septal defect, the right ventricular pressure can never

significantly exceed the systemic since the resistance to ejection into the aorta is much less than into the pulmonary artery. This presumably would account for the shorter murmur found in the tetralogy and suggested that the murmur should become shorter, earlier and softer, the severer the stenosis.

This hypothesis stimulated a series of projects, each of which yielded new facts of considerable diagnostic and physiological value. For this reason, the title selected for this study had to be more general than first planned.

The Structure and Sequence of the Thesis

The original observation first had to be investigated in order to establish its validity. This is described in the first chapter, which is a reprint of the paper published in 1955 in collaboration with Dr. V. Schrire. Here, the basic hypothesis was elaborated in some detail, while attention was drawn to the occurrence and significance of splitting of the second sound in Fallot's tetralogy as well as the significance of aortic and pulmonary ejection sounds in pulmonary stenosis. It was clearly shown that the diagnosis could be settled by auscultation in severe (cyanosed) cases of pulmonary stenosis. The murmur in the tetralogy, being short, ended before or at the aortic second sound, whereas in severe pulmonary stenosis, it extended well beyond and engulfed this sound.

The next investigation was a comprehensive study of the two conditions in order to assess the merits of various methods used in the diagnosis. This paper, which was published in 1957 in collaboration with Drs. V. Schrire, M. Nellen and R.H. Goetz, emphasised the value of the new auscultatory signs and illustrated how closely the two conditions resembled each other. It was not surprising that the syndrome of pulmonary stenosis with reversed interatrial shunt,

(the so-called Fallot's "trilogy") had escaped full recognition until the era of cardiac catheterisation and cardiac surgery. In this paper, the practical importance of correct anatomical diagnosis was described, and this still holds for the new surgical techniques which have developed since this work was published.

It soon became apparent that milder cases of each condition could not be so easily distinguished by auscultation. This observation again was the outcome of a mistake. I made a confident diagnosis of pulmonary stenosis with intact ventricular septum in an acyanotic patient who presented a loud, long murmur which almost buried the aortic second sound but stopped before a delayed, soft, audible pulmonary component. Such a murmur seemed far too long for Fallot's tetralogy and splitting of the second sound appeared to exclude it. Yet, over the years, Dr. V. Schrire had seriously considered mild tetralogy on the grounds of a Sabot shaped heart and a previous history of squatting. Cardiac catheterisation was inconclusive but angiocardiography proved Fallot's tetralogy. It seemed, then, that mild Fallot's tetralogy could result in a prolonged murmur as well as splitting of the second sound. One was already familiar with the possibility of splitting of the second sound in Fallot's tetralogy since this had been described in the first paper. Also, attention had been drawn to the marked lengthening of the murmur and emergence of wide splitting in a severe tetralogy rendered mild by a successful valvotomy. It thus seemed that mild tetralogy would be associated with a long, loud murmur and even splitting of the second sound. Such a behavior was clearly the opposite to that anticipated in cases with an intact ventricular septum. Here the murmur should shorten and soften the milder the stenosis. This, then, was an interesting new concept to be investigated, namely, the opposite behavior of the murmur with varying degrees of severity of each condition. Also, the idea of mild acyanotic Fallot's tetralogy, masquerading as pulmonary stenosis with intact ventricular septum. These ideas stimulated the further work and led to a better insight into the diagnostic features and mechanisms of the auscultatory signs in pulmonary stenosis.

The next project was to test the idea that murmur length is directly related to severity of stenosis when the septum is intact, but inversely related in the tetralogy. A new method of measuring murmur length first had to be devised. The length of murmur thus measured was correlated with the severity of the stenosis, as determined by the right ventricular pressure in the case of intact ventricular septum and a clinical method of assessment in the tetralogy. In a large series of cases it was shown that increasingly severe stenosis induced progressive lengthening of the murmur and delay in pulmonary

valve closure when the septum was intact whereas in Fallot's tetralogy the opposite effect was obtained, the murmur becoming shorter, earlier and softer. In both conditions reliable criteria were defined, enabling accurate prediction of the severity of stenosis from bedside auscultation.

The thesis at this stage could be more simply stated. In Fallot's tetralogy, where severe stenosis is combined with a large septal defect, the length and intensity of the systolic murmur is determined both by the severity of the stenosis and the systemic resistance. For a constant systemic resistance, and hence constant right ventricular pressure, the severer the stenosis the less the volume rate of blood ejected through the stenosis. Conversely, for a constant degree of stenosis, an increase in systemic resistance should increase right ventricular pressure and both pulmonary blood flow and murmur, while a decrease in systemic resistance should produce the opposite adverse effect. When the ventricular septum is intact, however, murmur length and intensity is determined by the severity of the stenosis and not by the systemic resistance.

The next project was designed to test the validity of these suppositions by studying the effect of a valvotomy or infundibular resection on the murmur length in both conditions. By creating a mild stenosis the murmur should shorten when the septum is intact, but lengthen in the tetralogy. This was shown to be the case. Furthermore, the Blalock-Taussig operation for the tetralogy which is capable of a functional result as good as obtainable by the direct operation, failed to cause any lengthening of the murmur because the stenosis was not relieved by the procedure. By using the criteria defined, auscultation proved an excellent method of predicting the surgical result.

The final investigation was to study the effect of sudden manipulation of the systemic resistance in the two conditions. Amyl nitrite was selected to reduce the resistance and phenylephrine to increase it. Decreased systemic resistance shortened and softened the murmur of Fallot's tetralogy by reducing right ventricular pressure and pulmonary blood flow but intensified the murmur when

the septum was intact due to the rise in righ ventricular pressure caused by the increased venous return after amyl nitrite. Conversely, increased systemic resistance lengthened and intensified the murmur in Fallot's tetralogy by increasing right ventricular pressure and pulmonary blood flow, but had no effect on the murmur when the septum was intact. These studies, in addition to clinching the thesis, led to the development of new important diagnostic tests, especially valuable in differentiating mild or acyanotic Fallot's tetralogy from moderately severe pulmonary stenosis with intact ventricular septum.

Other Observations.

During the course of this study several additional original contributions are believed to have been made.

1. It has long been assumed that the murmur in Fallot't tetralogy is produced by turbulant ejection of blood through the stenosis, while the septal defect (VSD) is silent. That this assumption is correct can be shown by data arising from this thesis. Marked unidirectional flow from one ventricle to the other as found in small VSD without pulmonary stenosis does not occur in the tetralogy since the ventricular pressures are equal and the overriding aorta provides a common exit. The degree of right to left shunt even in severe tetralogy is never sufficiently large to cause a VSD regurgitant murmur. Clearly, in mild cases with slight bi-directional shunting, there is even less flow and in acyanotic cases with up to 2 litres/min. left-to-right shunt it is doubtful whether the loud murmur is due to VSD flow. The absence of a panasystolic murmur in other conditions associated with large ventricular septal defect and equal pressures (Eisenmenger's complex, truncus and pseudotruncus arteriosus) supports this view. However, proof that the VSD is silent is obtainable by the following observations. The murmur became softer, shorter and earlier the severer the stenosis and the greater the right-to-left shunt. Had the murmur been attributable to the VSD, it should have increased in length and intensity with the increasing right-to-left shunt. Conversely, the milder the stenosis the longer and louder the murmur despite less right-to-left shunt. This was well demonstrated by the Brock operation, which relieves only the stenosis. Here the murmur became loud and panasystolic with great diminution of the right-to-left shunt. Finally, manipulation of the systemic resistance caused pronounced changes in murmur length and intensity despite maintained equalisation of ventricular pressures. When the systemic resistance dropped, the murmur softened and shortened despite increased right-to-left shunt; conversely, increased resistance decreased the shunt but intensified the murmur. These observations all prove that the murmur length and loudness is a function of the volume rate of Blood ejected through the stenosis and that the septal defect is silent.

2. Hitherto, no reliable method of assessing pulmonary blood flow in the tetralogy was available. However, it was shown that the murmur length and loudness reflects this very accurately and has thrown considerable light on the mechanism of cyanotic attacks in the tetralogy, confirming the concept of functional infundibular spasm of the infundibulum of the right ventricle.

3. Splitting of the second sound in Fallot's tetralogy has been found to be surprisingly common in mild cases and a sensitive indication of the pulmonary arterial pressure.

4. Since appreciating that mild cases of Fallot's tetralogy present features indistinguishable from moderately severe pulmonary stenosis with intact septum, increasing numbers of mild tetralogies have been discovered by the routine use of amyl nitrite and phenylephrine tests. In fact, amyl nitrite has become an obligatory test in the acyanotic patient with a loud prolonged systolic murmur, with an audible, soft, delayed, pulmonary component, for there may be no other way of diagnosing this problem at the bedside.

5. The significance of the aortic ejection in Fallot's tetralogy and the pulmonary ejection sound in pulmonary stenosis and its absence in infundibular stenosis has been analysed.

6. Exceptionally wide splitting was encountered both in pulmonary stenosis and infundibular stenosis. In the former it was attributable to excessive post-stenotic dilatation, suggesting a new factor in determining pulmonary valve closure time. In infundibular stenosis the delay was thought to be due to delayed emptying of the infundibular chamber distal to the stenosis.

7. Serial sound tracings after valvotomy for pulmonary stenosis with intact ventricular septum can determine whether or not spontaneous regression of secondary infundibular stenosis is taking place.

The thesis has convinced me that the study of heart sounds and murmurs is capable of conveying unique information of great diagnostic and physiological value. It has already thrown much light on other conditions and the future for phonocardiography as a research, diagnostic and teaching tool is bright.

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CHAPTER 1

THE ROLE OF AUSCULTATION IN THE DIFFERENTIATION OF FALLOT'S TETRALOGY FROM SEVERE PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM AND RIGHT-TO-LEFT INTERATRIAL SHUNT

FOREWORD

This chapter, which is presented as a reprint, should be regarded as the preliminary communication to the thesis. Several original observations are reported, the chief being that the length of the systolic murmur in severe pulmonary stenosis differs strikingly from that of Fallot's tetralogy. This was attributed to the gross alteration in the volume rate of pulmonary blood flow caused by the presence of a large ventricular septal defect in Fallot's tetralogy. The chapters that follow confirm and extend this basic thesis.

Other important, original observations are reported, namely, the presence, probable significance and mechanism of splitting of the second sound in Fallot's tetralogy; the presence, probable significance and mechanism of the aortic ejection sound in the tetralogy and pulmonary ejection sound in pulmonary stenosis; the beneficial effect of high systemic resistance (coarctation of the aorta) in increasing pulmonary blood flow and murmur in the tetralogy. The subsequent chapters add much more information about these findings.

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The Role of Auscultation in the Differentiation of Fallot's Tetralogy from Severe Pulmonary Stenosis with Intact Ventricular Septum and Right-to-Left Interatrial Shunt

By LOUIS VOGELPOEL, M.B., M.R.C.P. AND VELVA SCHRIRE, M.B., PH.D., M.R.C.P.

A clinical and phonocardiographic study has been made of the murmurs and heart sounds in the differentiation of Fallot's tetralogy from severe pulmonary stenosis with intact septum and right-to-left interatrial shunt. A striking difference in the behaviour of the systolic murmur was found in the two conditions and this affords a new, simple bedside method of diagnosis. Important differences in the behaviour of the heart sounds were also found, but these are usually more difficult to evaluate clinically and may require special study.

THE value of auscultation in the diagnosis of congenital heart disease has not been sufficiently appreciated. This paper is concerned with the importance of auscultation in the differential diagnosis between Fallot's tetralogy and severe pulmonary stenosis with intact ventricular septum and reversed interatrial shunt. Accurate diagnosis is of great importance. The Blalock-Taussig operation is contraindicated for severe pulmonary stenosis with reversed interatrial shunt, whereas it has proved to be an excellent operation for Fallot's tetralogy.[1-5] The diagnosis can generally be made with a reasonable degree of accuracy from consideration of the clinical, radiological and electrocardiographic findings. However, it is often necessary to confirm the diagnosis by means of cardiac catheterisation and angiocardiography. Even with all available methods, certain difficulties arise as discussed elsewhere.[6]

Any additional, clinical differentiating sign is therefore of value and it is the purpose of this communication to present new physical signs, which will enable accurate diagnosis to be made by careful bedside auscultation. Furthermore, certain clinical and phonocardiographic observations made during the study will be presented.

From the Cardiac Clinic, Department of Medicine, University of Cape Town and Groote Schuur Hospital. This study was supported in part by a grant from the Dr. C. L. Herman Staff Research Fund, University of Cape Town.

CLINICAL MATERIAL AND METHODS

All cases accepted for this study presented the common diagnostic problem of pulmonary or infundibular stenosis associated with central cyanosis. This combination usually resolves itself into the diagnosis of Fallot's tetralogy and severe pulmonary stenosis with reversed interatrial shunt. Pulmonary stenosis with rare associations such as transposition of the great vessels, single ventricle and tricuspid atresia were excluded from this study.

Eighteen cases of Fallot's tetralogy and six cases of severe pulmonary stenosis with intact ventricular septum form the basis of this study. All cases had central cyanosis. Cases were accepted only if cardiac catheterisation, selective angiocardiography, intravenous angiocardiography or necropsy proved (a) whether severe pulmonary valvular or infundibular stenosis was present and, (b) whether the ventricular septum was intact or not. If the right-to-left shunt took place in the ventricle through a ventricular septal defect and over-riding aorta, then Fallot's tetralogy was considered proven. If it was established that the ventricular septum was intact Fallot's tetralogy could be excluded. In the latter case a reversed interatrial shunt was assumed to be present though often difficult to prove.[2,8] A complete analysis of the findings in each case is presented elsewhere.[6] Necropsy confirmation of the diagnosis was obtained in seven cases.

In addition to full clinical examination, special attention was devoted to auscultation. All cases of pulmonary or infundibular stenosis had a systolic murmur (grade 2 to 5[7]) usually maximal in the second left intercostal space but occasionally in the third and fourth left spaces. Special care was taken

at the site of maximal intensity of the murmur to determine whether the murmur was loudest in early, mid or late systole. Even more important, the relation of the end of the murmur to the second sound was observed. The presence or absence of splitting of the second sound was noted. Lastly the first heart sound and diastole were studied for any abnormality.

The Sanborn Stetho-Cardiette was used to obtain phonocardiograms in each case. Logarithmic (high frequency) sound tracings, which give an accurate graphic representation of human hearing[8-10] were recorded synchronously with a suitable electrocardiographic lead, carotid or jugular pulse tracing. The sound recordings were taken in succession from the mitral area (MA), fourth left intercostal space just to the left of the sternum (4LS), the third left space (3LS), pulmonary area (PA) and aortic area (AA). The amplification chosen was purely qualitative, designed to give the best record for a particular purpose. Thus to record a very soft sound greater amplification was used. The carotid and jugular tracings were obtained by placing a crystal microphone directly on the neck, thus avoiding delay from air conduction.

The components of split first and split second sounds were identified by determining their respective relationship to the onset and nadir of the dicrotic notch of a synchronously recorded right carotid pulse tracing. Tracings taken at high speed (75 mm. per second) were essential for accurate study. Since the dicrotic notch is produced by aortic valve closure, it can be used to identify the components of a widely split second sound [11-13] (figs. 4, 6 to 8). Thus the onset of the component due to aortic valve closure, precedes the nadir of the notch by a short interval (average 0.03 second), due to the delay in pulse wave transmission from the aortic valve to the carotid artery. It was assumed that the component occurring after the dicrotic notch could only be due to pulmonary valve closure. In very wide splitting of the second heart sound as encountered in severe pulmonary stenosis, the soft pulmonary component may be mistaken for a third heart sound. The relation of this sound to the summit of the "v" wave in the jugular phlebogram was used to exclude a third heart sound arising from the right ventricle (figs. 4 and 6). The fact that the soft sound just preceded the "v" wave indicated that it was produced just before opening of the tricuspid valve, at the time of pulmonary valve closure. The occurrence of this sound only in the pulmonary area and third left space is in keeping with a soft pulmonary second sound and unlike a third sound arising in the left ventricle, which is best heard at the apex or just internal to it.

Synchronous carotid tracings gave a time relation between the first sound, added early systolic sounds and the opening of the aortic valve (figs. 4, 10 and 11).[11-13] Delay in pulse wave transmission from aortic valve to carotid artery was assumed to be given by the time interval from the onset of aortic component of the second sound to the nadir of the dicrotic notch. This interval averaged, as in a previous study,[12] 0.03 second.

Results

Auscultatory and phonocardiographic findings are shown in tables 1 and 2 and figures 1 and 2.

Discussion

The Second Heart Sound

The second sound is produced by closure of the aortic and pulmonary valves and asynchronous closure of these valves results in splitting of the second sound. Splitting in the pulmonary area is an almost invariable finding in healthy children and young adults. The degree of splitting is greatly influenced by respiration; splitting is widest at the end of inspiration and narrows or disappears during expiration. By means of synchronous phonocardiograms from the mitral, aortic and pulmonary areas, Leatham and Towers[14] showed that the pulmonary valve normally closes after the aortic valve. This had also been shown by Wolferth and Margolies in their studies of bundle branch block, using aortic kymograms and carotid artery tracings.[11] Splitting is best heard in the second and third left intercostal spaces but not in the mitral and aortic areas because the normal pulmonary component is not usually conducted to these areas.[15, 10] Increase in the width of splitting on inspiration is due to delay of the pulmonary component. The delayed closure of the pulmonary valve induced by inspiration has been attributed not only to the fall in pulmonary artery diastolic pressure, but also to prolongation of right ventricular systole from increased filling.[10]

It has become important during auscultation to note both the degree of splitting and the intensity of the two components of the second sound in the pulmonary area. Splitting may be normal (grade 1 and 2) or abnormally wide (grade 3 and 4).[16] A well known example of abnormal splitting is that often found in right bundle branch block presumably due to delayed activation of the right ventricle. Comparison of the intensity of each component also provides important information. Thus in pulmonary hypertension the pulmonary element is accentuated and is audible over a wide area even as far as the apex.

We have paid special attention to the presence or absence of splitting, and to the degree of reduction of intensity of the pulmonary component in cases of pure pulmonary stenosis of differing severity and in cases of Fallot's tetralogy. Pulmonary valvular stenosis and infundibular stenosis, unlike aortic stenosis,

TABLE 1.—*Auscultatory Findings in Six Patients with Severe Pulmonary Stenosis with Intact Ventricular Septum and Right-to-Left Interatrial Shunt*

No.	Case, age, sex	Central cyanosis (1–4)	Disability (1–4)	Auscultation								Phonocardiogram	Site of stenosis	Proof
				Systolic murmur (at site of max. intensity)			2nd sound (at site of max. intensity of SM.)		1st sound	Atrial sound	Diast. murmur			
				Site of max. intensity	Grade (1–6)	Relation to 2nd sound	Single or split	Intensity						
1	E. B., 49, F	2	3	PA	4	Long SM. Stops before soft P_2. A_2 not heard.	Single	Very soft	Loud and click-like on exp. only. Max. in PA.	Loud on insp.	0	A_2 buried in prolonged SM which stops before soft P_2. Width of split about 0.13 sec. Loud first sound on expir.; loud auric. sound on inspir.	Valvular	Necropsy
2	S. J., 9, F	1	1	4LS	5	Long SM. A_2 & P_2 inaudible.	0	0	N	0	0	A_2 buried in prolonged SM. No P_2 recorded. Normal A_2 at MA & AA.	Valvular	Cath. Angio. Valvotomy
3	J. F., 36, F	3	2	PA	4	Long SM. Stops before soft P_2. A_2 not heard.	Single	Very soft	N	Loud on insp.	Presystolic (Max. in PA)	A_2 buried in prolonged SM, which stops before soft P_2. Width of splitting about 0.14 sec. Loud auric. sound and presyst. murmur	Valvular	Cath. Sel. angio (RV).
4	N. S., 22, F	3	2	3LS	3	Long SM. A_2 & P_2 inaudible.	0	0	N	0	0	PCG taken after valvotomy. Prolonged SM extends beyond A_2 but does not obscure it. No P_2.	Valvular	Cath. Angio. Valvotomy
5	P. P., 42, M	1	2	PA	4	Long SM. Stops before soft P_2. A_2 just audible.	Split (Very wide.)	A_2 N P_2 very soft	Loud and click-like on exp. only. Max. 3LS.	Loud on insp.	0	A_2 buried by prolonged SM, which stops before soft P_2. Width of split ca. 0.11 sec. Loud first sound on exp., loud auric. sound on insp.	Valvular	Cath. Angio.
6	S. D., 10, M	1	1	PA	5	Long SM. A_2 & P_2 inaudible.	0	0	Loud and sharp.	0	0	A_2 buried by prolonged SM which stops before soft P_2. Width of split ca. 0.11 sec.	Valvular	Cath. Sel. angio (RV.)

A_2 = Aortic component of second sound. P_2 = pulmonary component of second sound. Sel. angio (RV.) = selective angiocardiogram from right ventricle.

result in a fall in pressure distal to the obstruction and in consequence the second or pulmonary component of the second sound becomes soft or inaudible depending upon the degree of stenosis. Furthermore, the low pulmonary diastolic pressure and probable prolongation of the right ventricular systole results in delayed closure of the pulmonary valve so that *wide splitting* of the second sound is heard or recorded provided the pulmonary component is loud enough.

The Second Sound in Severe Pulmonary Stenosis with Closed Ventricular Septum. It is easier to understand the findings in severe pulmonary stenosis if one first considers the changes that occur in mild pulmonary stenosis. In most cases of mild pulmonary stenosis, as defined by Abrahams and Wood,[16] we heard and recorded a normal to widely split second sound with a normal to soft pulmonary component (fig. 3). The pulmonary systolic murmur in all cases filled systole extending up to the first or aortic component of the split second sound. Even in cases of moderate pulmonary stenosis it was often possible to hear wide splitting of the second sound but the pulmonary component was always abnormally soft, thus confirming the previous observations of Leatham.[10] An exaggeration of these findings might be anticipated in severe pulmonary valvular stenosis.

In *severe* pulmonary stenosis clinical analysis of the altered second sound is difficult. In three of the 6 cases the harsh prolonged pulmonary systolic murmur stopped before an extremely soft sound, but in the remaining three no pulmonary component could be heard. In one case only (case 5, P. P.) was very wide splitting (grade 4) appreciated by the ear. In this case the aortic component was not completely obscured by the murmur. The phonocardiogram with synchronous carotid and jugular tracings were essential in analysing these changes. In each case the systolic murmur in the pulmonary area was so prolonged that it had extended beyond the first or aortic component of a widely split second sound (figs. 4 and 8). In fact the aortic sound was completely buried in the murmur in all except one case. The buried sound could be identified by the dicrotic notch of the carotid tracing and also by sound tracings taken at the apex or fourth left space where a normal aortic sound was less obscured by the systolic murmur (fig. 4). The systolic murmur ended before a very soft pulmonary second sound which was recorded in four out of six cases, thus proving that *very wide* splitting was in fact present in severe pulmonary stenosis. In the remaining two cases the second sound was presumably so soft that even considerable amplification failed to reveal its presence.

Thus in severe pulmonary stenosis with intact septum, although the phonocardiogram demonstrates very wide splitting of the second sound and may therefore be useful as a special test, clinical auscultation at the site of maximal intensity merely reveals a harsh prolonged systolic murmur which may be followed by a very soft pulmonary second sound. However, auscultation in the mitral area and fourth left space where the murmur is less intense reveals an aortic second sound of normal intensity.

The Second Sound in Fallot's Tetralogy. In Fallot's tetralogy, where the severity of the stenosis is of an order comparable to severe pulmonary stenosis with intact septum, a similar alteration of the second sound might be anticipated. This is, in fact, not the case. In Fallot's tetralogy the second sound is often abnormally loud and thus usually palpable (table 2). This may be due to the fact that the aortic valve is brought closer to the anterior chest wall by the dextroposition of the aortic root. Furthermore, the systolic murmur finishes or diminishes markedly before the aortic second sound (vide infra) thereby contributing to the striking clarity of the second sound in Fallot's tetralogy. Phonocardiograms confirmed these clinical findings in all cases (figs. 2 and 5). Comparison of figure 4 with figure 5 shows how the aortic second sound is obscured by the prolonged systolic murmur in severe pulmonary stenosis with intact septum whereas in Fallot's tetralogy the loud aortic second sound stands well to the right of a shorter pulmonary systolic murmur.

The problem of the pulmonary second sound in Fallot's tetralogy is of considerable academic

TABLE 2.—*Auscultatory Findings in 18 Patients with Fallot's Tetralogy*

No.	Case, age, sex	Central cyanosis (1–4)	Disability (1–4)	Auscultation								Phonocardiogram	Site of stenosis	Proof
				Systolic murmur (at site of max. intensity)			2nd sound (at site of max. intensity of SM.)		1st sound	Atrial sound	Diast. murmur			
				Site of max. intensity	Grade (1–6)	Relation to 2nd sound	Single or split	Intensity						
7	H. J., 16, F	3	2	PA	3	Short SM. Stops before A_2.	Single	Loud (palpable)	N	0	0	SM max. before midsystole. Stops before loud A_2. No P_2.	Infundib.	Necropsy
8	W. K., 9, F	3	3	PA	4	Short SM. Stops well before A_2.	Single	Loud (palpable)	N	0	0	SM max. by midsystole. Stops well before loud A_2. Very soft P_2. Width of split 0.09 sec.	Valvular	Cath. Angio.
9	E. W., 19, M	3	1	PA	3	SM stops before A_2.	Single	Loud (palpable)	N	0	0	SM stops just before loud A_2. No P_2.	Infundib.	Necropsy
10	C. G., 8, M	1	3	PA	5	SM stops well before A_2.	Single (pre-op) Split (post-op)	Loud (palpable) P_2 v. soft post-op.	N	0	0	SM max. by midsystole. Stops before loud A_2. No P_2. Post-Op: Soft P_2. Width of split 0.08 sec.	Infundib.	Cath. Sel. Angio. (RV) Blalock-Taussig op.
11	R. P., 27, F	2	1	3LS	4	SM stops before A_2.	Single	Loud (palpable)	N	0	0	SM max. before midsystole. Stops just before loud A_2. No P_2.	Infundib.	Cath. Angio.
12	E. K. 10, M	2 (Preop 3)	3 (Preop 4)	3LS	2	Short SM. Stops well before A_2.	Single	Loud (palpable)	Aortic early systolic sound at all areas.	0	0	Short SM. Stops long before loud A_2. No P_2. Split 1st sound plus aortic early systolic sound.	Infundib. (Severe)	Cath. Blalock-Taussig op.
13	V. B., 5, M	4	4	3LS	2	Very short early SM. Stops long before A_2.	Single	Loud (palpable)	Aortic early systolic sound at all areas.	0	0	Very short early SM. Loud A_2. No P_2. Split 1st sound plus aortic early systolic sound.	Infundib. (Extreme)	Necropsy
14	L. E., 29, F	2	2	4LS	4	SM stops before A_2.	Single	Loud (palpable)	N	0	0	SM max. by midsystole. Stops before loud A_2. No P_2.	Infundib.	Cath. Angio. Blalock-Taussig op.

15	L. K., 6, M	4	4	3LS	2	Short SM stops well before A_2.	Single	Loud	Aortic early systolic sound loud at all areas.	0	0	Short SM after aortic early systolic sound. Stops before loud A_2. No P_2.	Infundib. plus Valvular (extreme)	Necropsy
16	C. S., 14, M	3	2	4LS	5	SM stops before A_2.	Single	Loud (palpable)	N	0	0	SM max. in midsystole. Stops just before A_2. No P_2.	Infundib. plus Valvular	Cath. Sel. Angio (RV)
17	S. P., 17, M	2	1	PA	4	SM stops just before A_2.	Split	A_2 loud P_2 soft	Loud	0	0	SM max. in midsystole. Stops at loud A_2. P_2 recorded. Width of split 0.08 sec.	Valvular	Cath.
18	A. H., 5, M	1	3	PA	4	SM stops well before A_2.	Single	Loud (palpable)	N	0	0	SM max. before midsystole. Ends before loud A_2. No P_2.	Infundib.	Cath.
19	N. J., 18, F	4	3	PA	4	SM stops well before A_2.	Single	Loud (palpable)	N	0	0	SM max. before midsystole. Ends well before A_2. No P_2.	Infundib.	Angio.
20	R. B., 12, M	2	1	3LS	4	SM stops before A_2.	Single	Loud (palpable)	N	0	0	SM max. by midsystole. Stops before loud A_2. No P_2.	Infundib. plus Valvular	Cath. Sel. Angio (RV).
21	L. K., 5, M	1	1	3LS	5	SM longer than usual but stops before A_2.	Single	Loud	N	0	0	SM Max. in midsystole. Stops just before loud A_2. Very soft P_2. Width of split 0.08 sec.	Infundib. plus Valvular	Cath. Angio.
22	R. M., 7, F	4	3	3LS	1	SM very short and early.	Single	Loud (palpable)	Aortic early systolic sound at all areas.	0	0	Very short early SM. Stops before midsystole. Aortic early systolic sound.	Valvular (extreme)	Necropsy
23	J. V., 35, F	1	1	PA	4	SM stops before A_2.	Single	Loud (palpable)	Loud	0	0	SM max. by midsystole. Stops just before loud A_2. No P_2.	Infundib.	Cath. Sel. Angio (RV).
24	M. F., 7, F	4	3	PA	4	SM stops well before A_2.	Single	Loud (palpable)	N	0	0	SM max. before midsystole. Stops well before loud A_2. No P_2. Variable mid-systolic click.	Infundib. (severe)	Necropsy

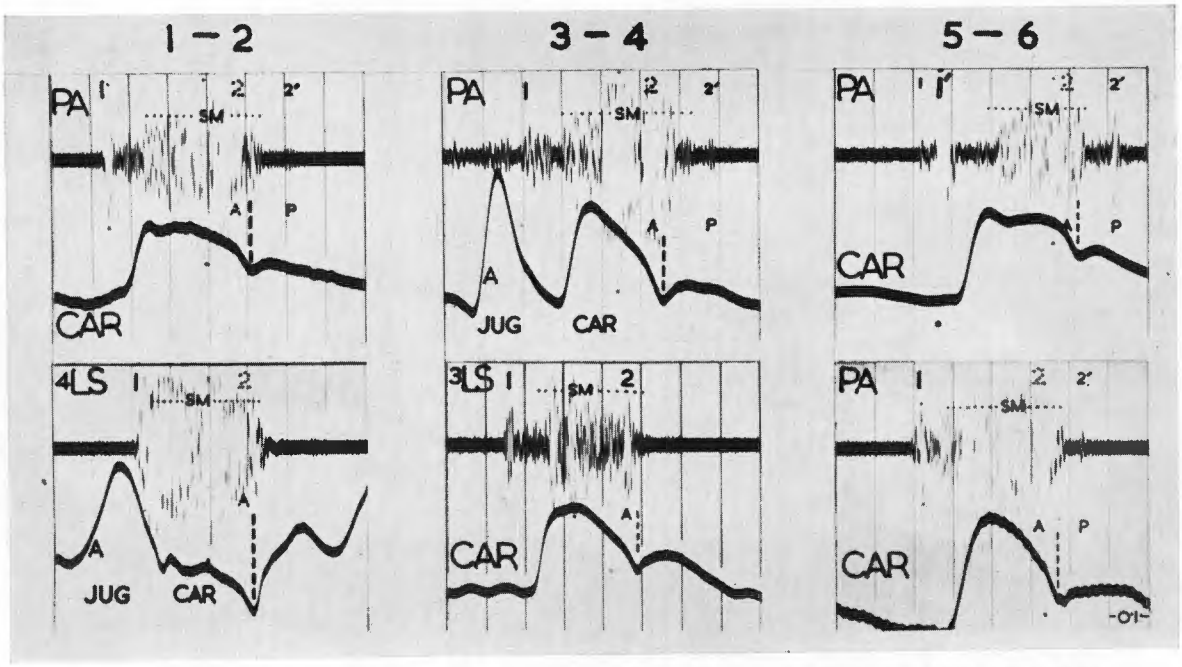

FIG. 1. *Six cases of Severe Pulmonary Stenosis with Intact Ventricular Septum and Right-to-Left Interatrial Shunt.* In all the phonocardiograms were taken at the site of maximal intensity of the murmurs. In each case the systolic murmur (SM) is intense and so prolonged that it extends beyond and drowns the normal aortic component (A) of the very widely split second sound (2,2′). It stops before the delayed diminutive pulmonary component (P) when recorded. With the exception of case 4, which was recorded after a partially successful pulmonary valvotomy, the approximate position of the buried aortic component is indicated by the dicrotic notch of the synchronously recorded carotid pulse. Black dots have been used to indicate the limits of the sound vibrations in this and subsequent figures.

interest. It is generally stated that a pure single second sound occurs in Fallot's tetralogy. While this is usually true our observations prove that in some cases the pulmonary second sound follows the aortic second sound and we believe that splitting of the second sound in Fallot's tetralogy would be elicited more often were it not for the fact that the pulmonary valve closure is so quiet. In one remarkable case (case 17, S. P.) of proven Fallot's tetralogy, wide splitting of the second heart sound was easily detected clinically (fig. 6) and gave rise to considerable diagnostic difficulties. The unusually high pulmonary artery pressure found in this case seemed the best explanation of the audible pulmonary second sound. In case 10 (C. G.) careful auscultation two months after a successful Blalock-Taussig operation revealed definite splitting of the second heart sound whereas prior to operation only a single second sound was heard and recorded (fig. 7). The appearance of the soft pulmonary second sound after the operation suggested that the pulmonary artery pressure had risen above a critical level necessary for production of audible valve closure. In two further cases (case 8, W. K., and case 21, L. K.) a definite diminutive pulmonary second sound was recorded but not heard. This evidence suggests that the usual single second sound in Fallot's tetralogy is not due to synchronous closure of the aortic and pulmonary valves. It is, in fact, due to aortic valve closure alone, which is followed by pulmonary valve closure, presumably inaudible because of the low pulmonary diastolic pressure.

Although the series is small, the width of splitting in Fallot's tetralogy appears to be considerably less than that in severe pulmonary stenosis with intact septum (figs. 4, 6, 7 and 8). In both conditions there is a low pulmonary diastolic pressure which is an

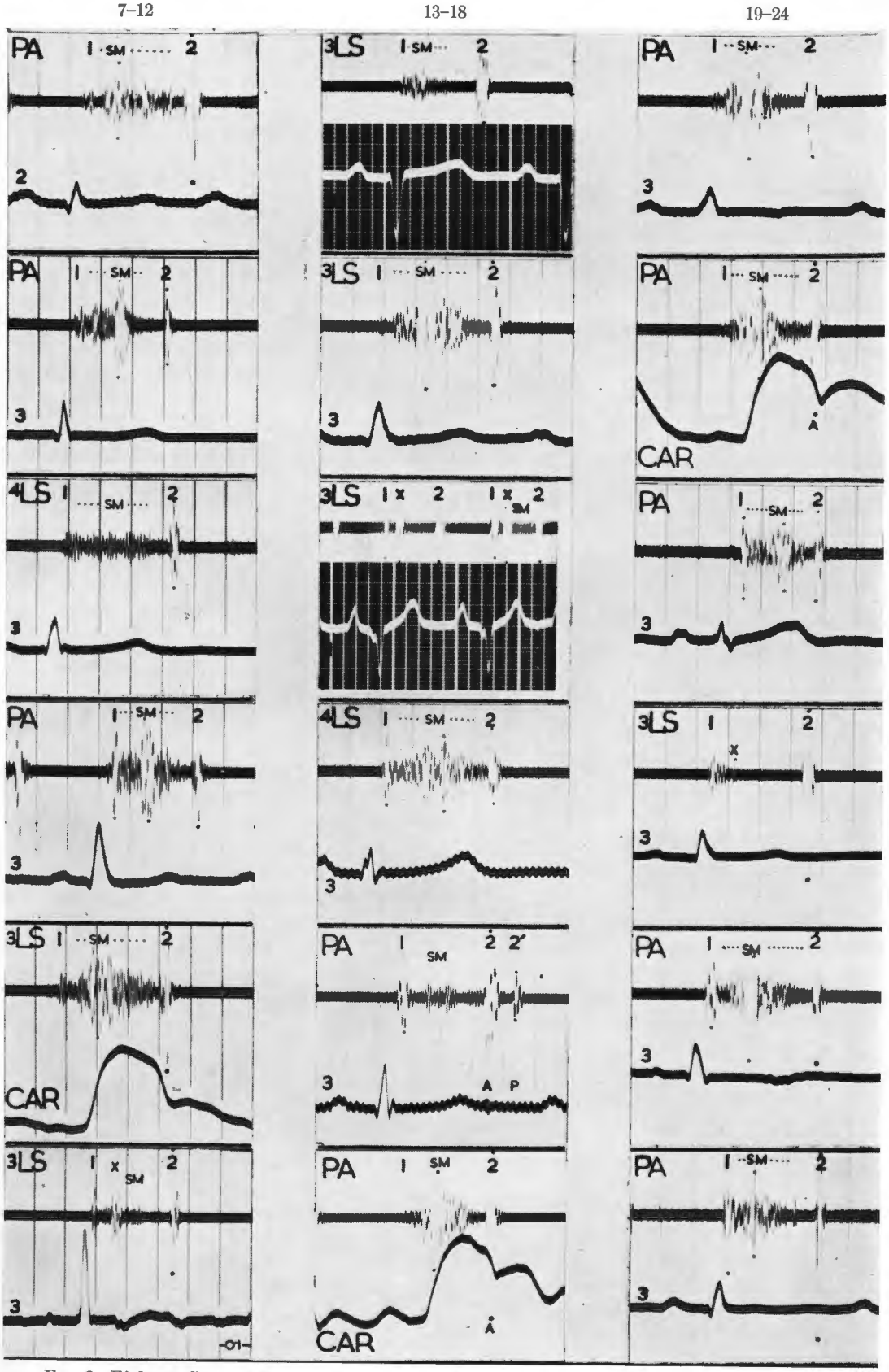

FIG. 2. *Eighteen Cases of Fallot's Tetralogy.* In all cases the phonocardiograms were taken at the site of maximal intensity of the murmur. In each case the murmur commences soon after the first sound, reaches maximal intensity by midsystole, and then diminishes markedly, usually ending before the single, loud aortic component of the second sound which is not in any way obscured by the murmur. In the four most severe cases (cases 12, 13, 15 and 22) the systolic murmur was soft, early and short.

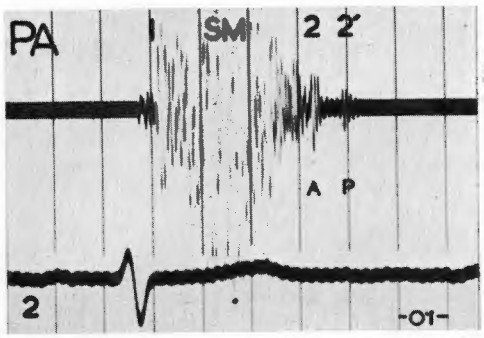

FIG. 3. Synchronous phonocardiogram (PCG) at the pulmonary area (PA) and lead II (75 mm./sec.), from a case of *mild* pulmonary valve stenosis with intact septum (RVP 30/0; PAP 10/4 mm. Hg). The loud systolic murmur (SM) fills systole, extending up to, but not obscuring, the first or aortic component (A) of the well split second sound. The second or pulmonary component (P) is moderately reduced in intensity.

important common factor in the production of the split sound. It is suggested that the greater delay of the pulmonary component in severe pulmonary stenosis with intact septum is due to the additional factor of prolongation of right ventricular systole (vide infra).

The Systolic Murmur

In all cases studied a systolic murmur was present. The murmur was usually harsh and loud (grade 3 to 5[7]) in which case its intensity was of no help in differentiating the two conditions. However, in four cases of Fallot's tetralogy (cases 12, 13, 15 and 22), all severe, the systolic murmur was soft (grade 1 or 2). On this basis alone Fallot's tetralogy was favored as in all cases of severe pulmonary stenosis with intact ventricular septum the murmur was loud.* The site of maximal intensity, however, was of no real help in the differential diagnosis. Where the stenosis was valvular in both conditions, the murmur was maximal at the second and third left intercostal spaces (with the exception of case 2, S. J.). In infundibular stenosis the murmur was as often maximal in the second as in third and fourth intercostal spaces. A murmur maximal in the fourth space favored infundibular stenosis and hence Fallot's tetralogy because infundibular stenosis occurs so much more commonly in this condition. However, in one case of valvular stenosis with intact ventricular septum (S. J.), the murmur was maximal in the fourth intercostal space.

Previous studies of the systolic murmur have failed to reveal any characteristic distinguishing feature.[4, 10, 16-25] We agree that the loudness and the site of maximal intensity of the murmur is usually of no real help in the differential diagnosis of Fallot's tetralogy from severe pulmonary stenosis with intact septum. However, we have found that there is a striking difference in the two murmurs, if attention is directed to the duration of the systolic murmur in relation to the second sound and to the position in systole of maximal intensity. Our findings have led us to believe that an accurate diagnosis can be made by careful bedside auscultation.

The Systolic Murmur in Severe Pulmonary Stenosis with Intact Ventricular Septum. Auscultation *at the site of maximal intensity* of the murmur reveals a prolonged systolic murmur. The aortic component of the second sound is rarely heard, being drowned by the crescendo of the murmur (figs. 1, 4, 8). The murmur stops before the delayed diminutive pulmonary component which may occasionally be heard by very careful auscultation in the pulmonary area. In the mitral area where the systolic murmur is much less intense, the aortic second sound, of normal intensity, is not drowned and is therefore usually clearly audible (fig. 4).

The Systolic Murmur in Fallot's Tetralogy. In Fallot's tetralogy the behaviour of the pulmonary systolic murmur is quite different. However loud or soft, the systolic murmur *at the site of maximal intensity*, is much less prolonged than in severe pulmonary stenosis with intact ventricular septum. It commences soon after the first sound, reaches maximal intensity by mid-systole and then diminishes markedly, usually ending before the single loud aortic component of the second sound (figs. 2, 5, 6, 7). The phonocardiogram may record small rapidly diminishing vibrations right up to the second sound, but these are

*We have since encountered one case of unusually severe pulmonary stenosis in heart failure in whom the systolic murmur was grade 2 only.

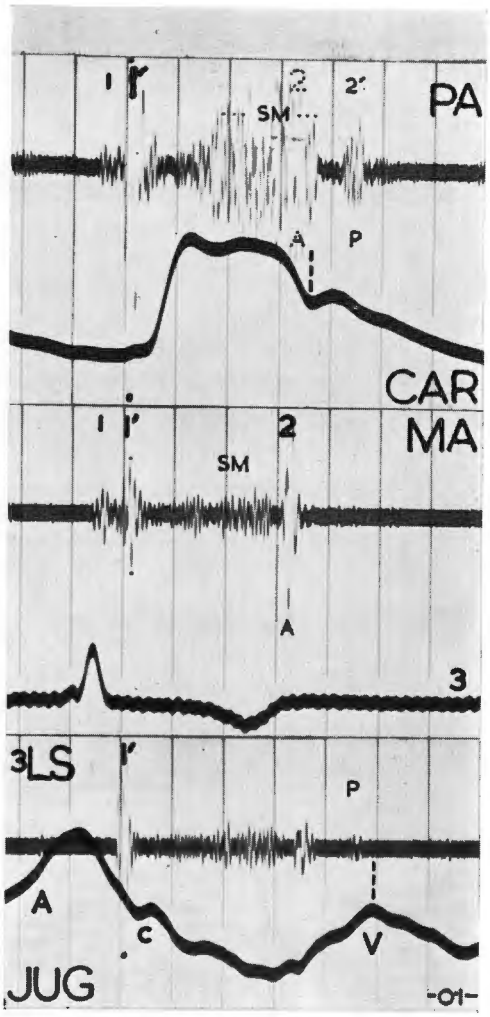

FIG. 4. *Case 5 (P. P.) Severe Pulmonary Stenosis with Intact Septum.* The systolic murmur at the site of maximal intensity (PA) is so prolonged that it extends beyond the first or aortic component (A) of the very widely split second sound (2,2′). The aortic sound is, in fact, completely buried in the murmur. The buried sound can be identified by the dicrotic notch of the carotid tracing (CAR) and by the PCG taken at the mitral area (MA) where the normal aortic sound (A) is not obscured by the systolic murmur. The systolic murmur ends before the soft pulmonary component (P). The latter is identified by the fact that it just precedes the "V" wave of the jugular venous tracing (JUG) indicating that it is produced just before opening of the tricuspid valve, at the time of pulmonary valve closure. The tracing also records the extremely intense "second component" (1′) of the first sound maximal in the PA commencing 0.01 second before the onset of ejection into the aorta (a delay of 0.03 second in pulse wave transmission from the aortic valve to the carotid artery has been assumed). As the heart rate was identical, the tracings as mounted, here and elsewhere, are virtually synchronous.

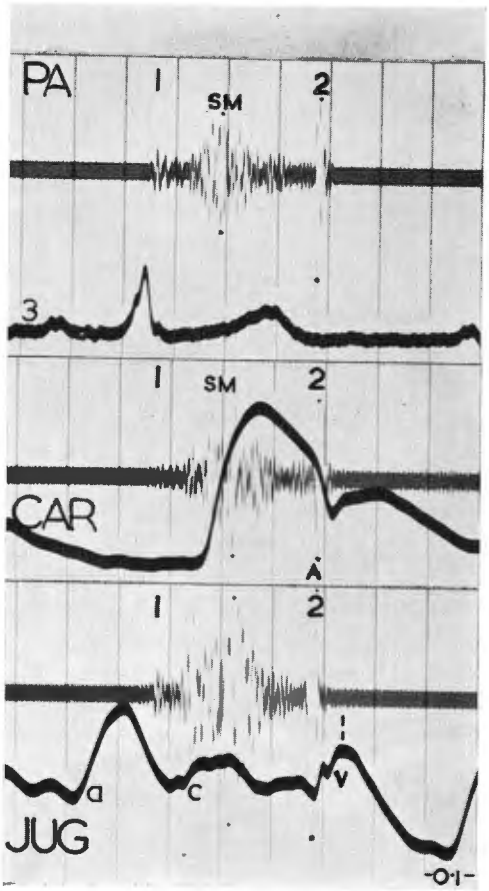

FIG. 5. *Case 20 (R. B.). Fallot's Tetralogy.* The systolic murmur at the site of maximal intensity (PA) commences soon after the first sound (1), reaches maximal intensity by mid-systole and diminishes markedly ending before the loud aortic component of the single second sound (A), which is identified by the dicrotic notch of the carotid tracing. Pulmonary valve closure is not recorded but it must occur before the summit of the "V" wave (i.e. within 0.08 second after the onset of the aortic second sound).

not detected by the ear, the murmur appearing to end well before the loud second sound.

As far as we are aware this difference in the behavior of the pulmonary systolic murmur in the two conditions has not been hitherto described.

COMMENT

The striking difference in the duration of the systolic murmur can probably be related

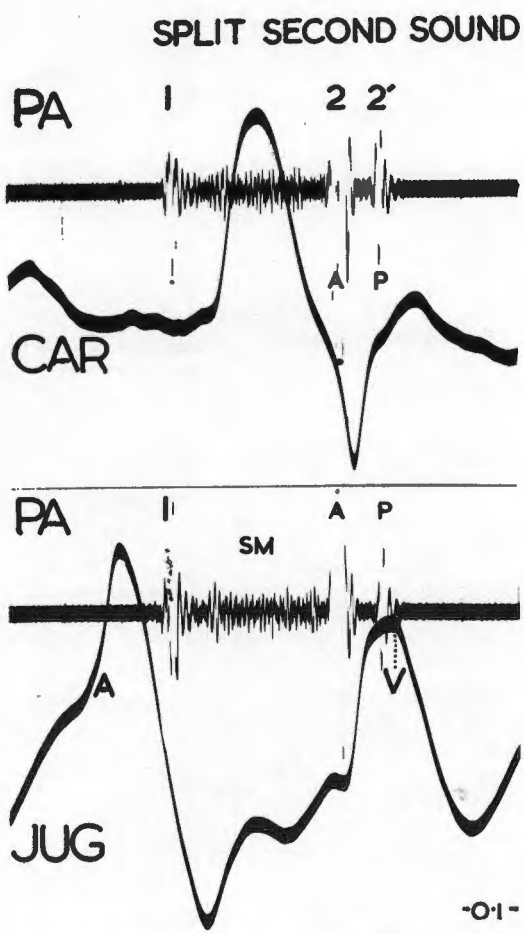

FIG. 6. *Case 17 (S. P.) Fallot's Tetralogy.* The systolic murmur commences soon after the first sound and ends before the loud aortic component (A) of the second sound which is identified by the dicrotic notch of the carotid tracing. The unusually loud pulmonary component (P) is identified by the fact that it just precedes the "V" wave of the jugular venous tracing. The width of splitting measures 0.08 second as compared with 0.11 second in figure 4 and ca. 0.14 second in figure 8.

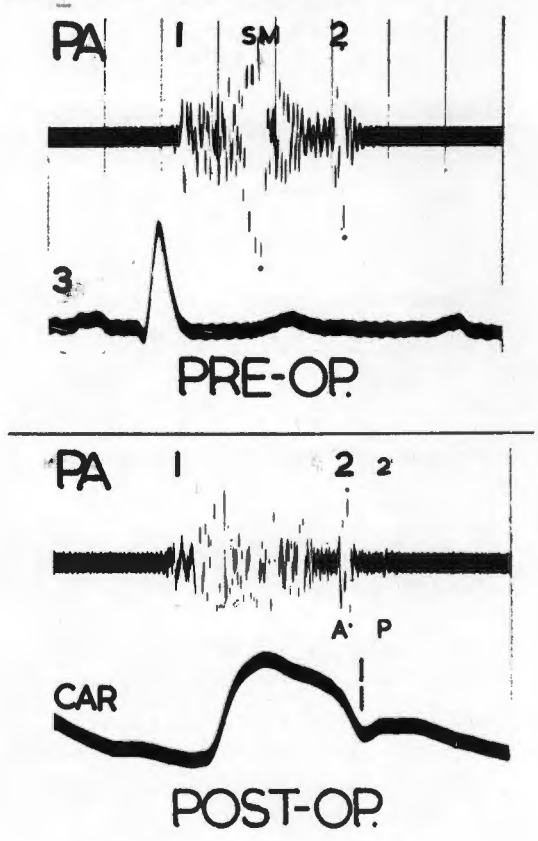

FIG. 7. *Case 10 (C. G.) Fallot's Tetralogy.* (a) The systolic murmur reaches maximal intensity by mid-systole and diminishes markedly before the loud aortic component of the single second sound. (b) Two months after a Blalock-Taussig operation the pulmonary component (P) of the second sound became just audible giving rise to splitting of the second sound (2,2'), measuring 0.08 second.

to the fundamentally different dynamics of the two conditions.

In severe pulmonary stenosis with intact ventricular septum the right ventricle alone has to develop great pressure to effect adequate blood flow across the stenotic valve. Thus the systolic pressure in the right ventricle often exceeds the aortic and left ventricular systolic pressures, especially after effort.[25-28, 16, 40, 6] The giant "a" wave in the venous pulse is indicative of the right atrial hypertrophy which augments filling of the right ventricle and assists it in generating such high pressures.[30, 16, 40] A considerable difference in the amplitude and duration of the pressure curves in the right and left ventricles must occur. We have shown that the second sound is widely split due to marked delay of the very soft pulmonary component. The delayed closure of the pulmonary valve is due not only to the low pulmonary diastolic pressure, but also to prolongation of the ejection phase of right ventricular systole as compared with that of the left ventricle. Flow will continue across the stenotic pulmonary valve as long as a pressure gradient exists between the right

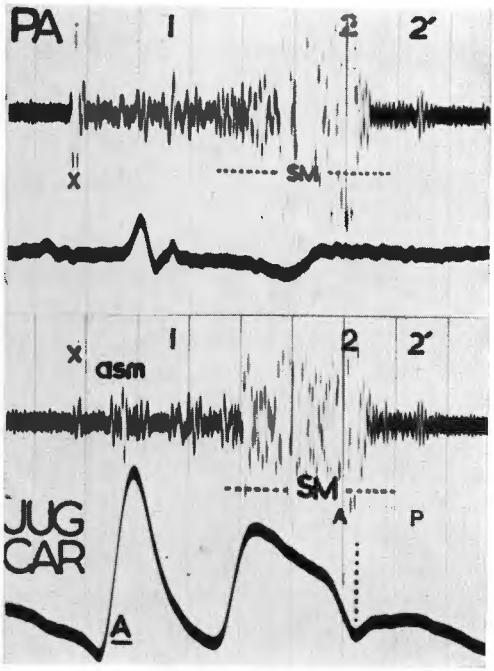

FIG. 8. *Case 3 (J. F.) Severe Pulmonary Stenosis with Intact Septum.* The prolonged systolic murmur reaches a late crescendo completely obscuring the aortic component (A) of the second sound, as identified by the dicrotic notch of the carotid tracing. It ends before the soft pulmonary component (P) of the very widely split (ca. 0.14 second) second sound (2,2'). The loud atrial sound (X) is followed by a murmur (asm). This presystolic murmur occurs after the onset of right atrial contraction which is unusually powerful as revealed by the giant "a" wave (A).

ventricle and the pulmonary artery. Thus when the aortic valve closes at the end of the normal or reduced left ventricular systole active flow still continues across the pulmonary valve. Since the intensity of the systolic murmur is probably proportional to the speed and volume of flow, other factors such as degree of stenosis and viscosity being equal, it is not surprising to find the pulmonary systolic murmur continuing beyond the aortic second sound (diagram I).

In Fallot's tetralogy, unlike severe pulmonary stenosis with intact ventricular septum, the ventricular septal defect and the over-riding aorta both act as a safety valve to the right ventricle; no matter how severe the pulmonary or infundibular stenosis, the right ventricular systolic pressure can never significantly exceed that in the aorta and left

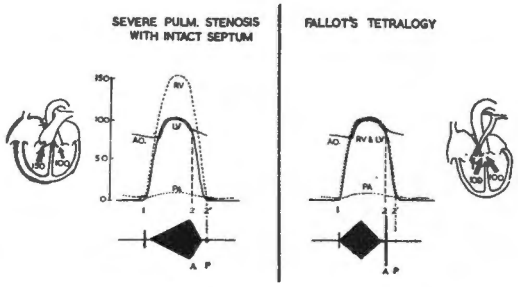

Diagram I: The diagram attempts to explain the dynamic basis for the striking difference in the duration of the systolic murmur in relation to the aortic second sound (2, A) and greater width of splitting in severe pulmonary stenosis with intact ventricular septum. See text for details.

ventricle.[16, 25, 27-29] Thus clinical evidence of right ventricular and right atrial hypertrophy is much less. This is shown by the absence of a giant "a" wave in the venous pulse, the slight lift over the right ventricle and the absence of marked right ventricular enlargement radiologically. In Fallot's tetralogy the right and left ventricles virtually function as a single ventricle from which blood is discharged into two competing orifices, namely the aortic with normal systemic peripheral resistance* and a stenotic pulmonary valve or infundibulum with a much higher resistance. The ventricular pressure curve in both ventricles is conditioned by the lesser resistance offered by the aorta and hence adaptation to the severe pulmonary stenosis is much less effective than in pulmonary stenosis with an intact septum. Thus effective systole cannot be more prolonged in the right ventricle than the left because by the time the aortic valves close the ventricles have virtually discharged their contents. This is well illustrated by angiocardiography which reveals rapid discharge of diodone from the right ventricle into the aorta in Fallot's tetralogy contrasting sharply with the delayed emptying of the right ventricle seen in severe pulmonary stenosis with intact septum.[31, 32, 26, 41] Maximal flow across the stenotic valve or chamber occurs early in systole at the time of

* This has not been measured by us but the absence of hypertension in our cases of Fallot's tetralogy at least indicates a normal systemic peripheral resistance.

maximal flow into the aorta; during the phase of reduced ejection from the ventricles into the aorta, flow into the pulmonary artery is likewise reduced. By the time the aortic valve closes flow into the pulmonary artery has virtually ceased being entirely dependent on the rapidly diminishing pressure gradient between the right ventricle and pulmonary artery and the little available residual blood.

It is therefore not surprising that the pulmonary systolic murmur* in Fallot's tetralogy attains maximal loudness by mid-systole and then diminishes rapidly, usually ending before the aortic second sound. Variation in the intensity and duration of the murmur does, however, occur. In our four most disabled patients (cases 12, 13, 15 and 22, in three of whom extreme stenosis was proven at necropsy) the murmur was soft and short reaching a crescendo well before midsystole and ending long before the aortic second sound (figs. 2, 12 and 10). A short murmur thus appears to indicate severe stenosis. This inference is not unreasonable for the severer the stenosis the less the flow across the pulmonary valve. Unlike pulmonary stenosis with intact septum, the systemic peripheral resistance and not the pulmonary stenosis determines the level of the right ventricular systolic pressure. This is grossly inadequate in extreme pulmonary stenosis and thus flow sufficient to produce a murmur is limited to the early ejection phase of the right ventricle. In milder cases of Fallot's tetralogy the murmur appears to be longer (fig. 12) but we have not yet encountered any case in which the murmur obscured the second sound.†

*We are in agreement with the generally held view that the ventricular septal defect plays little or no part in the production of the systolic murmur in Fallot's tetralogy. Marked unidirectional flow from one ventricle to the other as found in ventricular septal defect with normal aortic root and normal pulmonary vascular resistance does not occur in Fallot's tetralogy because the pressures in both ventricles are of the same order and the overriding aorta provides a common exit. Moreover, in other conditions associated with a ventricular septal defect and similar ventricular dynamics (Eisenmenger's complex, truncus and pseudotruncus arteriosus), there is often no systolic murmur (fig. 11), and, if present, the murmur is short and does not resemble Roger's murmur.

Auscultatory Observations of Lesser Diagnostic Value

Diastolic Murmurs. No case had pulmonary or aortic incompetence. In one case of severe pulmonary stenosis with intact ventricular septum (case 3, J. F.), a presystolic murmur was well heard in the second, third and fourth intercostal spaces, being loudest in the pulmonary area. It was not heard at the apex. The murmur was preceded by a loud atrial sound also best heard at the pulmonary area (fig. 8). The murmur occurred after the onset of right atrial contraction which was unusually powerful as revealed by the giant "a" wave (fig. 8). Cardiac catheterisation showed a right atrial systolic pressure of considerable magnitude transmitted into the left atrial and pulmonary veins as reported elsewhere.[6] Abrahams and Wood[16] have encountered in severe pulmonary stenosis a similar presystolic murmur which they attributed to flow across a patent foramen ovale shown at necropsy. In our case flow across the pulmonary valve produced by the powerful right atrial contraction may be an alternative explanation.

The Atrial Sound. In three cases of severe pulmonary stenosis with intact ventricular septum (cases 1, 3 and 5), a singularly loud

† Unusual prolongation of the systolic murmur in Fallot's tetralogy may occasionally occur. The second sound, however, is still not obscured by the murmur. In our only case of proven Fallot's tetralogy where this occurred, coarctation of the aorta was also present, causing a systemic blood pressure of 170/80 mm. Hg. It is probable that the unusually high right ventricular systolic pressure conditioned by the high aortic resistance permitted vigorous flow to continue through the stenosed pulmonary valve for a longer duration than the usual case of Fallot's tetralogy. This is supported by the fact that the patient's cyanosis had disappeared clinically during observation over several years, and his effort tolerance had increased. Furthermore, the pulmonary artery pressure was unusually high and the second sound was widely split with a very soft but audible pulmonary component. Being complicated by coarctation the case has not been included in this series but is discussed elsewhere.[6]

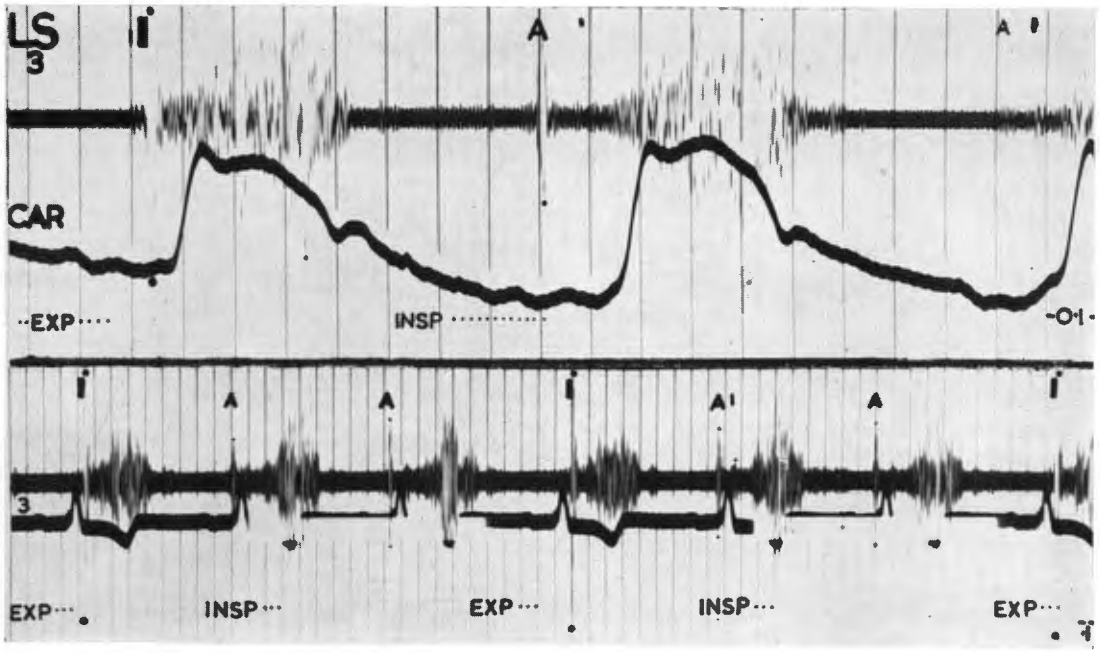

FIG. 9. *Case 1 (E. B.). Severe Pulmonary Stenosis with Intact Septum.* (a) Synchronous phonocardiogram at 3 LS and carotid tracing at 75 mm./sec. (b) synchronous phonocardiogram at 3 LS and lead III at 25 mm./sec.

An extremely loud *first* sound appears suddenly during expiration only to disappear completely during inspiration (INSP.). It occurs just after the *first* sound and before the onset of the carotid pulse. The marked effect of respiration on the atrial (A) is recorded, being loud during inspiration and absent during expiration. The characteristic systolic murmur of pulmonary stenosis with intact septum is also shown.

auricular sound was heard and recorded in the second, third and fourth intercostal spaces but not at the apex (figs. 8 and 9). The intensity was markedly influenced by the phase of respiration, being loud during inspiration and soft during expiration (fig. 9). This sound was attributed to vibrations occurring in the right ventricle or pulmonary valve produced by the powerful atrial systolic filling wave.

In no case of Fallot's tetralogy was an atrial sound heard. This is in keeping with the concept already discussed that the right ventricle and right auricle in Fallot's tetralogy are under far less stress than in severe pulmonary stenosis with intact ventricular septum. It is concluded that an audible atrial sound favours the diagnosis of severe pulmonary stenosis with intact septum.

The First Heart Sound. Several points of interest emerged from the study of the first sound which require further investigation and may prove to be of additional diagnostic value.

In Fallot's tetralogy the first sound was usually normal, being either single or closely split. In four cases it was apparently "widely split". The second component, however, was not attributed to the second component of a physiologically split first sound but to an aortic early systolic sound[12] because of the wide transmission to all areas including the aortic area and the marked degree of splitting. Furthermore, the phonocardiogram proved the separate identity of this added sound by showing normal splitting of the first sound preceding the aortic sound (fig. 10). Moreover, this sound occurred about 0.04 second after ejection into the aorta, a delay of 0.03 second in pulse wave transmission from aortic valve to carotid artery being assumed. The aorta is dextroposed and nearer the chest wall than normal. It is dilated and receives a greater

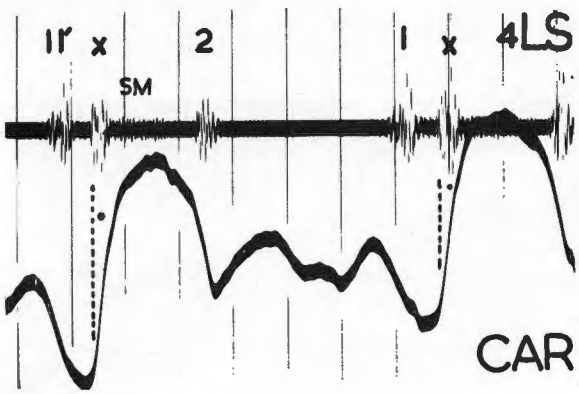

FIG. 10. *The Aortic Early Systolic Sound in Severe Fallot's Tetralogy. (Case 12, E. K.)* There is normal splitting of the first sound (1,1′) followed by a loud aortic early systolic sound (X). This sound occurred about 0.04 second after the onset of rise of pressure in the aorta (a delay of 0.03 second in pulse wave transmission from aortic valve to the carotid artery has been assumed). The added ejection sound was transmitted widely to all areas including the aortic area. The characteristic systolic murmur of Fallot's tetralogy although soft is also shown.

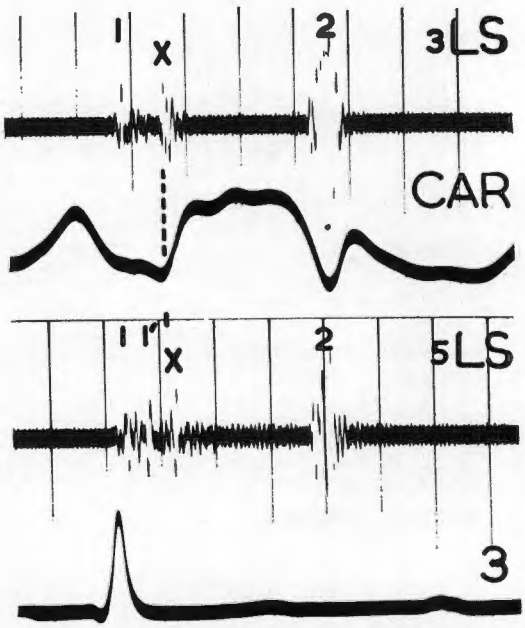

FIG. 11. *The Aortic Early Systolic Sound in Pulmonary Atresia.* There is normal splitting of the first sound (1,1′) at 5 LS followed by a loud early systolic sound (X). This sound occurred about 0.03 second after the onset of ejection into the aorta. As this case had pulmonary atresia the ejection sound could only be "aortic". It had the same features as the ejection sound (X) shown in figure 10.

volume of blood than normal, being the main exit of blood from both ventricles. These factors may be responsible for this audible ejection sound. The presence of this sound appears to be an indication of the severity of the lesion. The more severe the pulmonary stenosis the greater the volume of blood ejected into the aorta, and hence the larger the aorta. This combination favours the production of an audible ejection sound. This sound was only present in our four most disabled cases (cases 12, 13, 15 and 22). Furthermore, in two cases of pulmonary atresia, where the output of both ventricles was discharged into a single dilated "pseudotruncus arteriosus", a striking aortic systolic sound was heard (fig. 11). Although the aortic early systolic sound has been described in a variety of conditions affecting the aorta and aortic valves,[33, 34, 12] its occurrence in Fallot's tetralogy is much less well known[35, 36] and in pulmonary atresia it has not been described before.

In severe pulmonary stenosis with intact septum the first sound was usually normal. However, in two cases of this series a remarkable abnormality with striking respiratory variation was found (figs. 4 and 9). An extremely loud, palpable, click-like first sound would suddenly appear during expiration only to disappear completely during inspiration. It occurred just after the first sound, giving the impression of close splitting. Phonocardiograms showed that this sound was present only in expiration and was synchronous with the second component of a closely split first sound occurring before the onset of the carotid pulse (figs. 4 and 9). Clinically, it was quite unlike the second component of a normally split first sound both in intensity and in that it was maximal at the pulmonary area and not the mitral area or fourth intercostal space.[12] This was confirmed in one of the two cases (case 1, E. B.) when the heart was palpated at operation and the sound appeared to originate in region of the pulmonary valve. It thus appears to be related to the phase of ejection from the right ventricle and not to auriculoventricular valve closure. Because of the great shortening of the isometric contraction phase

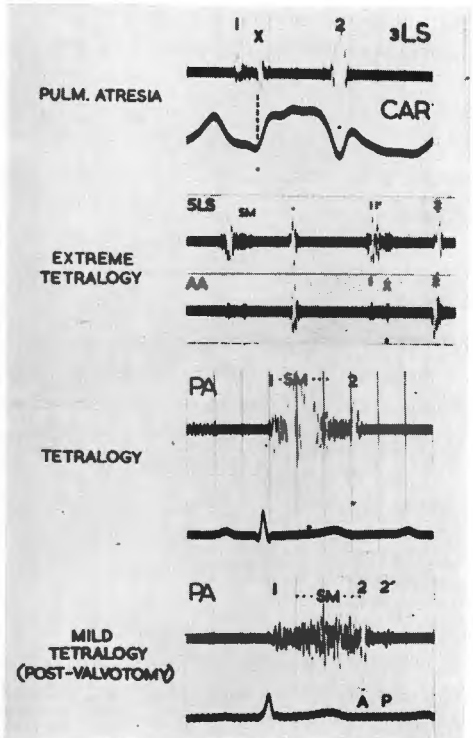

FIG. 12. *The Duration of the Systolic Murmur in Relation to the Severity of Fallot's Tetralogy.* In pulmonary atresia there is usually no systolic murmur. In Fallot's tetralogy with extreme stenosis the murmur is short, soft and confined to early systole. In both these conditions an aortic early systolic sound (X) is usually heard. In the majority of cases of the tetralogy the systolic murmur is loud, reaches its crescendo by midsystole and diminishes rapidly before the loud aortic second sound. In mild cases of the tetralogy the murmur appears to be of longer duration, as shown in the tracing taken six months after a successful valvotomy. The murmur extends up to the aortic second sound (A) but does not obscure it. The pulmonary second sound (P) has become audible, producing wide splitting (0.09 second), indicating Fallot's tetralogy with mild stenosis. (The pulmonary valvotomy has presumably produced a rise in the pulmonary diastolic pressure.)

of the right ventricle, due to the very low pulmonary diastolic pressure, this ejection sound may be almost superimposed on the tricuspid component of the first heart sound. Like the pulmonary early systolic sound in dilatation of the pulmonary artery,[12] this sound is also related to the phase of early ejection from the right ventricle into the pulmonary artery. The mode of production, however, is possibly different. Audible vibrations may be set up by the sudden tautening of the stenotic pulmonary valve bulging into the pulmonary artery at the moment of ejection into the pulmonary artery. This sign is not confined to severe pulmonary stenosis but has also been encountered in moderate and mild stenosis. It was first described by Petit[37] in 1902 and by several workers since.[33, 38, 12, 39] We have not encountered this sign in Fallot's tetralogy.

SUMMARY

1. The differentiation of Fallot's tetralogy from severe pulmonary stenosis with intact ventricular septum and reversed interatrial shunt is important because the surgical treatment is different. While the diagnosis can generally be made on clinical grounds alone, it is usually necessary to confirm the diagnosis by special investigations.

2. A clinical and phonocardiographic study of the heart sounds and murmurs has been made in six cases of severe pulmonary stenosis with intact septum and in 18 cases of Fallot's tetralogy.

3. A striking difference in the behaviour of the systolic murmur *at the site of maximal intensity* was found in the two conditions, if attention was directed to the duration of the systolic murmur in relation to the second heart sound and to the position in systole of its maximal intensity. In Fallot's tetralogy the systolic murmur, however soft or loud, starts soon after the first sound, reaches maximal intensity by mid-systole and then diminishes markedly, usually ending before the single loud, often palpable, aortic component of the second sound. By contrast, in severe pulmonary stenosis with intact ventricular septum, the systolic murmur is so prolonged, that it extends beyond and drowns the normal aortic component of the very widely split second sound. It stops before the delayed, diminutive pulmonary component which may or may not be audible.

4. This significant difference in the systolic murmur so clearly shown by phonocardiography is readily appreciated by the ear and affords a new simple bedside method of diagnosis.

5. Phonocardiographic studies revealed

further points of interest. In severe pulmonary stenosis with intact septum the second heart sound is very widely split due to a diminutive pulmonary second sound being widely separated from the normal aortic component. In Fallot's tetralogy the second sound is usually single because the loud aortic sound is followed by an inaudible pulmonary sound. However, if the pulmonary artery pressure is sufficiently high, this delayed pulmonary second sound becomes recordable and even audible. The mechanism underlying these findings is fully discussed.

6. A presystolic murmur loudest in the left parasternal region was heard in a case of severe pulmonary stenosis with intact ventricular septum and reversed interauricular shunt. It was attributed to flow through the atrial septum or the stenosed pulmonary valve during atrial systole.

7. A loud atrial sound was heard in three cases of severe pulmonary stenosis with intact septum but not in Fallot's tetralogy.

8. In four severe cases of Fallot's tetralogy in whom the murmur was not intense, an early systolic sound was heard which caused "wide splitting" of the first sound. In two cases of severe pulmonary stenosis with intact ventricular septum close splitting of the first sound was heard with an intense clicking second component. The mechanism underlying these findings is discussed.

SUMMARIO IN INTERLINGUA

1. Le differentiation de tetralogia de Fallot ab sever stenosis pulmonar con intacte septo ventricular e revertite derivation interatrial es importante proque le tractamento chirurgic differe in le duo casos. Ben que le diagnose es generalmente facibile super le base de datos clinic, il es usualmente necessari verificar le diagnose per investigationes special.

2. Esseva executate un studio clinic e phonocardiographic del sonos e murmures cardiac in sex casos de sever stenosis pulmonar con intacte septo e in dece-octo casos de tetralogia de Fallot.

3. Esseva trovate un frappante differentia inter le duo conditiones in le murmure systolic *al sito de intensitate maximal*. Iste differentia esseva manifeste in le relation inter le duration del murmure systolic e le secunde sono cardiac e in le puncto del systole ubi le murmure attingeva su intensitate maximal. In casos de tetralogia de Fallot le murmure systolic—sin reguardo a si illo es forte o basse—comencia tosto post le prime sono; illo attinge su intensitate maximal in mediesystole; e tunc illo diminue marcatemente e se termina usualmente ante le unic e forte e frequentemente palpabile componente aortic del secunde sono. Per contrasto con isto, in casos de sever stenosis pulmonar con intacte septo ventricular, le murmure systolic es si prolongate que illo ultrapassa e inunda le normal componente aortic del secunde sono que alora es nettemente dividite. Illo se termina ante le retardate e minime componente pulmonar que a vices es audibile e a vices non.

4. Iste significative differentia in le murmure systolic, que se demonstra si clarmente per medios phonocardiographic, es facilemente perceptibile per le aure e representa un nove e simple methodo de diagnose clinic.

5. Studios phonocardiographic revelava altere punctos de interesse. In casos de sever stenosis pulmonar con intacte septo, le secunde sono es dividite a longe intervallo in consequentia del facto que un minime secunde sono pulmonar es nettemente separate ab le normal componente aortic. In tetralogia de Fallot le secunde sono es generalmente non-dividite proque le forte sono aortic es sequite per un inaudibile sono pulmonar. Nonobstante, si le pression pulmonoarterial es sufficientemente alte, le retardate secunde sono pulmonar deveni registrabile e mesmo audibile. Le mechanismo al base de iste constatationes es discutite.

6. Un murmure presystolic que habeva su intensitate maximal in le region sinistro-parasternal esseva audite in un caso de sever stenosis pulmonar con intacte septo ventricular e revertite derivation interauricular. Illo esseva attribuite a un fluxo a transverso le septo auricular o a un stenosis del valvula pulmonar durante le systole auricular.

7. Un forte sono auricular esseva audite in tres casos de sever stenosis pulmonar con intacte septo sed non in tetralogia de Fallot.

8. In quatro sever casos de tetralogia de Fallot le murmure non esseva intense, sed il se audiva un prompte sono systolic que causava un division a grande intervallo del prime sono. In duo casos de sever stenosis pulmonar con intacte septo ventricular, un division a breve intervallo esseva audite in le prime sono. Le secunde componente representava un intense clic. Le mechanismo al base de iste constatationes es discutite.

Addendum

Since this paper was submitted we have encountered three further cases of severe pulmonary stenosis with intact ventricular septum and right-to-left interatrial shunt and eight cases of Fallot's tetralogy. In each case a correct diagnosis was made from auscultation alone. Furthermore, in Fallot's tetralogy it was usually possible to assess whether the stenosis was extreme, average or mild by paying careful attention to the auscultatory features discussed above (fig. 12). These cases are discussed elsewhere.[6]

Acknowledgments

We are deeply grateful to our colleagues of the Vascular Investigation Unit, Professor R. H. Goetz, head of the unit, and Dr. Maurice Nellen. Without their cooperation conclusive proof of the diagnosis in every case could not have been established. We should like to thank Professor J. F. Brock for his encouragement and interest. We also thank Professor J. F. Brock, Professor F. Forman, Dr. L. Mirvish and Dr. M. Nellen for permission to study cases under their care, and Dr. N. H. G. Cloete, the Superintendent of Groote Schuur Hospital. We are particularly indebted to Dr. L. Mirvish for making the Sanborn Stetho-Cardiette available to the Cardiac Clinic.

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ADDENDUM

This work has been abundantly confirmed by a study of a greater series of cases in Chapters III and IV. Comparison of Fig. 2 in Chapter III with Fig. 3 in Chapter IV and Fig. 5 in Chapter IV, shows at a glance that murmur length in relation to the aortic second sound in Fallot's tetralogy differs greatly from severe (cyanotic) cases of stenosis with intact ventricular septum. These figures show, however, that the murmur configuration and width of splitting in mild tetralogy may be indistinguishable from moderately severe pulmonary stenosis. Differentiation of this diagnostic problem is readily made by amyl nitrite as discussed in Chapter VI.

The role of infundibular contraction in the mechanism of the shorter murmur of Fallot's tetralogy is fully discussed in Chapter IV, as well as the incidence and mechanism of wide splitting of the second sound in the tetralogy.

The role of the systemic resistance in determining volume rate of blood flow through the stenosis, and hence murmur, in Fallot's tetralogy, is described in Chapters VI and VII.

CHAPTER II

THE DIFFERENTIATION OF THE TETRALOGY OF FALLOT FROM SEVERE PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM AND RIGHT-TO-LEFT INTERATRIAL SHUNT

FOREWORD

This chapter, which is presented as a reprint, evaluates the merit of various diagnostic methods in differentiating Fallot's tetralogy from pulmonary stenosis, thereby emphasising the importance of auscultation and phonocardiography. It also shows the method of proof of the diagnosis which has been applied to the larger series of cases studied in Chapters III and IV. Since this publication, diagnosis has been aided by better recording apparatus, greater technical assistance and the development of open-heart surgery, but the basic principles described here still apply. However, the amyl nitrite and phenylephrine tests (Chapters VI and VII) were developed subsequent to this study and now occupy an important place in the diagnosis.

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THE DIFFERENTIATION OF THE TETRALOGY OF FALLOT FROM SEVERE PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM AND RIGHT-TO-LEFT INTERATRIAL SHUNT[1]

LOUIS VOGELPOEL, M.B., M.R.C.P., VELVA SCHRIRE, M.Sc., PH.D., M.B., M.R.C.P., MAURICE NELLEN, M.D., M.R.C.P., AND ROBERT H. GOETZ, M.B., CH.B., M.D.

Pulmonary stenosis was one of the first congenital anomalies described (1), and this malformation has continued to receive particular attention throughout the years (2). However, it is only since the development of cardiac catheterization, angiocardiography, and cardiac surgery that a better understanding of the syndromes associated with pulmonary stenosis have emerged. Fundamentally, the syndromes associated with pulmonary stenosis are dependent on the state of the ventricular septum and the aortic root (3). When there is a defect in the ventricular septum and the aorta arises partly from the right ventricle the entity is that of the tetralogy of Fallot. On the other hand, when the septum is intact and the aortic root normal, the condition is known as pulmonary stenosis with intact ventricular septum.

Abrahams and Wood (3) in their excellent study of pulmonary stenosis with intact ventricular septum have emphasized the importance of the severity of the stenosis in determining the clinical picture and prognosis. When the stenosis is mild or moderate as is commonly found, there is little or no disability and no cyanosis. An associated foramen ovale will remain functionless and even if the auricular septum is defective the left-to-right shunt will not be reversed. When the stenosis is severe the disability is much greater and central cyanosis may develop. The latter is dependent on the condition of the atrial septum and the relative pressures in both atria. If this septum is intact and the foramen ovale sealed, central cyanosis will not develop. However, if there is a patent foramen ovale or an atrial septal defect a right-to-left interatrial shunt may develop giving rise to central cyanosis (4). This will only occur if the stenosis is of such severity that the right atrial pressure exceeds the left.

It is well recognized that the syndrome of severe pulmonary stenosis with intact ventricular septum and right-to-left interatrial shunt[2] can be readily confused clinically with the tetralogy of Fallot (3, 5, 6, 7, 4, 1). Although it occurs less frequently than the tetralogy, the importance of correct diagnosis is imperative because the surgical treatment is different. A systemic-pulmonary arterial anastomosis is contraindicated in this condition, whereas it has proved to be a very useful procedure in the tetralogy of Fallot (6, 8–11), and as yet less hazardous than a pulmonary valvotomy or an infundibular resection.

[1] From the Cardiac Clinic, Department of Medicine, University of Cape Town, and Groote Schuur Hospital and the Department of Surgical Research, University of Cape Town. This study was supported in part by a grant from the Dr. C. L. Herman Staff Research Fund, University of Cape Town, and grants received from the Council for Scientific and Industrial Research and the Fourcade Bequest, University of Cape Town.

[2] Hereafter to be referred to as severe pulmonary stenosis with intact ventricular septum.

This paper is concerned solely with an evaluation of the diagnostic criteria used in the differentiation of these two conditions.

MATERIAL AND METHODS

All patients accepted for this study presented the common diagnostic problem of pulmonary valve or infundibular stenosis associated with central cyanosis. Only those patients in whom the diagnosis was established beyond doubt have been subjected to a complete analysis (see tables). Patients were accepted only if cardiac catheterization, selective angiocardiography, intravenous angiocardiography, or necropsy proved (a) severe pulmonary valvular or infundibular stenosis and (b) whether the ventricular septum was intact or not. If the right-to-left shunt took place through a ventricular septal defect and overriding aorta, the tetralogy of Fallot was considered proved. If it was established that the ventricular septum was intact, then the tetralogy of Fallot could be excluded. In the latter case, a reversed interatrial shunt was assumed to be present although it was often difficult to prove. There were 14 cases of severe pulmonary stenosis with intact ventricular septum and 48 cases of tetralogy.

All patients were examined and assessed personally by the authors. A full clinical examination with special emphasis directed to the points analyzed in the tables was performed in every case. Disability, central cyanosis, clubbing and all other findings except systolic murmurs were graded 0 to 4 and the 4 positive grades represented slight, moderate, considerable, and gross throughout (12).

Since we have become aware of the value of auscultation and phonocardiography in the diagnosis, special attention has been paid to this method of examination. Cases 3 to 7 of severe pulmonary stenosis with intact ventricular septum and cases 24 to 41 of the tetralogy of Fallot have been published elsewhere (13). Both in these and in subsequent cases particular care has been taken at the site of maximal intensity of the murmur to determine whether the murmur was loudest in early, mid, or late systole. Even more important, the relation of the end of the murmur to the second sound was observed. The intensity of the murmur was graded 1 to 6 as described by Levine (14). The presence or absence of the splitting of the second sound was noted. Lastly, the first heart sound and diastole were studied for any abnormality. A Sanborn Stetho-Cardiette, modified by one of the authors (L. V.) was used to obtain phonocardiograms to confirm the auscultatory findings as described elsewhere (13).

The internal jugular venous pulsations received special study in all cases, and in the majority, jugular venous tracings were used to confirm the clinical findings. With the patient suitably postured and relaxed the venous waves were timed against the opposite carotid artery. Particular attention was paid to the size of the atrial or "a" wave (table 1). An approximate but not an absolute estimate of the size of the "a" wave was obtained by measuring the height of the summit of this wave above the preceding "y" descent. Considerable increase in the size of the "a" wave occurs during inspiration. The maximum "a" wave reached during quiet inspiration was estimated. The "a" wave is a pulsation of

short duration, normally no greater in amplitude than the "v" wave. When right atrial hypertrophy occurs the "a" wave becomes dominant or even giant depending on the degree of right atrial hypertrophy. The term dominant "a" wave is used for a pulsation greater than normal but less than 5 cm in height. The term giant "a" wave is used for a pulsation over 5 cm in magnitude. When present the giant "a" wave is a most striking pulsation, and because of its rapid sharp action may readily be mistaken for overactive carotid pulsation. Moreover, it may move the lobe of the ear and is both palpable and audible. The crucial finding is that this wave is presystolic—thereby excluding carotid pulsation, the systolic venous pulsation of tricuspid incompetence, and "Cannon A" waves (15).

Attention was also paid to the presence or absence of a lift (grade 0–4) over the right ventricle on palpation of the third and fourth left interspaces to the left of the sternum. Palpability of the heart sounds was noted as well as the presence of any abnormal pulsations. The site, situation, and character of the apex beat was also studied.

Electrocardiograms were taken routinely. The standard limb leads, unipolar extremity, and unipolar precordial leads were used in every case. These were analyzed as shown in the tables.

Standard teleradiograms in the postero-anterior and the two oblique projections were taken. In addition each case was personally screened. The findings were analyzed as shown in the tables.

Cardiac catheterization was performed by the usual technique described by Cournand *et al.* (16). Pressures were measured by means of the saline manometer in the 10 earlier cases studied and by the strain gage electromanometer in 34 cases. Synchronous pressure and phonocardiographic recordings were obtained by using a 6-channel recorder constructed by one of the authors (R. H. G.). The oxygen content of blood samples was analyzed by the Haldane method and more recently with a Kipp oximeter. In each case an attempt was made to prove pulmonary valvular or infundibular stenosis by withdrawing the catheter tip slowly from the main pulmonary artery to the lower region of the right ventricle under fluoroscopic guidance. The pressure pulses were recorded continuously during the withdrawal. By this means valvular stenosis, or infundibular stenosis, or both together, could often be proved and the site of the stenosis located (fig. 9). An attempt was always made to enter the aorta from the right ventricle (fig. 12) and the left auricle from the right atrium. Pressures were taken routinely from all heart chambers and vessels entered by the catheter. Whenever possible, the systemic blood pressure was measured sphygmomanometrically while pressure recordings from the ventricle or aorta were made. Exercise was performed by flexing and extending the legs against manual resistance.

Selective angiocardiograms were performed in 4 cases of severe pulmonary stenosis with intact ventricular septum and 16 cases of the tetralogy at the end of the cardiac catheterization before withdrawal of the catheter from the heart. Ten to 15 cc of 70 per cent diodone were injected as fast as possible through

TABLE 1

Number	Case	Age	Race and Sex	Central Cyanosis		Clubbing (1–4)	Disability (1–4)	Squatting	"A" Wave	R. V. Lift (1–4)	Heart Size (N–++)	Thrill	Systolic Murmur		Diagnosis on Auscultation and PCG	ECG					Radiology							
				Age of onset	Degree (1–4)								Maximal site	Grade (1–6)		P 2 mm	P-R sec.	Conduction	T inversion	Severity of R.V.H.	Oligemia	Pulmonary arc (1–4)	Sabot	Infundib. chamber	Size of R.V. (1–4)	R. A. (1–4)	Position of aorta	C. T. Ratio
Severe pulmonary stenosis with intact ventricular septum																												
		yr.																										
1	D. S.	25	E.* F.†	Birth	2	2	4	0	Giant	2	N‡	+	2LS§	4		3	0.22	N	V1–2	3	+	1	0	0	2	2	N	
2	A. H.	8	E. M.¶	6	2	2	3	+	Dom.‖	3	+	+	2LS	4	P. S.	4	0.15	N	V1–4	4	+	2	0	0	3	2	N	60
3	E. B.	49	E. F.	10	2	1	2	0	Dom.	3	+	+	2LS	4	P. S.	1.5	0.20	Inc. RBBB	V1	2	+	2	0	0	2	2	N	58
4	S. J.	9	E. F.	2 mo.	1	1	1	+	Dom.	2	N	+	4LS	5	P. S.	2.5	0.16	Inc. RBBB	V1–2	3	+	2	0	0	2	2	N	54
5	J. F.	36	E. F.	6	3	1	3	0	Giant	2	N	+	2LS	4	P. S.	3.2	0.22	N	V1–4	4	+	2	0	0	2	1	N	47
6	N. S.	22	E. F.	5–10	3	2	2	0	N	0	N	+	3LS	3	P. S.	2.5	0.16	Inc. RBBB	V1	2	+	N	0	0	1	N	N	46
7	P. P.	42	C.[a] M.	40	1	3	2	0	Dom.	1	N	+	2LS	4	P. S.	2	0.20	N	V1–7	4	+	4	0	0	2	2	N	54
8	M. M.	5½	E. F.	4½	1	0	4	0	Giant	2	++	0	2LS	2	P. S.	4	0.15	N	V1–4	4	+	0	0	0	4	3	N	70
9	E. E.	10	E. F.	1	2	2	3	+	Giant	2	N	+	2LS	4	P. S.	4	0.14	N	V1–7	4	+	2	0	0	2	1	N	53
10	S. M.	17	B.[b] F.	Birth	2	2	4	+	Hidden by corrigan	0	+	+	3LS	5	P. S. and AI[e]	1.5	0.18	N	V1	3	+	2	0	0	2	1	N	53
11	J. C.	21	E. F.	18	1	0	2	0	Dom.	0	N	+	2LS	5	P. S. and PI[d]	1	0.16	N	V1	2	+	1	0	0	1	N	N	50
12	B. Y.	11	E. F.	10	1	0	1	0	Dom.	0	N	+	2LS	6	P. S.	1	0.12	N	0	2	+	3	0	0	1	N	N	43
13	J. D.	32	E. F.		1	0	1	0	N	1	+	+	2LS	4	P. S.				V1–4		+		0	0			N	
14	D. A.	5½	C. F.	Birth	3	2	3	+	N	1	N	+	2LS	4	F. T.	1.2	0.14	N	0	1	+	2	0	0	2	2	N	48
Tetralogy of Fallot																												
15	J. B.	6	E. M.	6 mo.	3	3	3	+	N		N	+	3LS	4		1.5	0.13	N	V1	1	+	N	0	0	N	N	N	46
16	A. H.	9	E. F.	1½	3	3	3	+	N	0	N	0	2LS	3		4.5	0.13	N	V1–2	2	+	D	+	0	1	N	N	
17	J. G.	10	C. M.	2	3	3	3	0	N	0	N		2LS	2		3	0.16	N	V1	1	+	0	+	0	1	N	R[e]	50
18	J. S.	8	E. M.	Birth	3	3	2			1	+		2LS								+	D	+	0	1	N	N	45
19	G. Z.	19	E. M.	Birth	3	4	2	+		1	N	+	3LS	4							+	N	0	0	N	1	N	49
20	J. P.	10	C. M.	3	3	3	3	+	N	1	N	+	2LS	4		3	0.16	N	V1	2	0	N	0	0	1	N	N	50
21	E. O.	11	E. F.	2	1	1	2	+	N	0	N	+	3LS	4		0.5	0.12	N	0	2	+	1	0	+	N	N	N	47
22	R. M.	9	E. M.	Birth	2	2	3	+	Dom.	1	N	0	4LS	3		3.5	0.16	N	V1	2	+	N	+	0	1	N	N	50

23	S. D.	10	E. M.	6 n o.	1	1	1	+	Dom.	1	N	+	2LS	5	P.S., later F. T.	1.2	0.14	N	0	2	+	0	+	0	2	N	N	52
24	M. J.	16	C. F.	Birth	3	3	2	+	N	2	N	+	2LS	3	F. T.	4	0.13	N	V1	2	2	N	0	+	1	1	N	50
25	W. K.	9	C. F.	Birth	3	3	3	+	N	1	N	+	2LS	4	F. T.	2	0.15	N	V1-4	2	+	1	0	0	1	1	N	48
26	E. W.	19	C. M.	Inf.[f]	3	3	1	+	Dom.	1	N	+	2LS	3	F. T.	1	0.16	Inc. RBBB	0	2	+	N	0	+	1	N	N	50
27	C. G.	8	E. M.	Inf.	1	2	3	+	N	1	N	+	2LS	5	F. T.	2	0.12	N	0	2	+	N	0	+	1	1	N	50
28	R. P.	27	C. F.	Inf.	2	3	2	+	N	N	N	+	3LS	4	F. T.	1	0.18	N	0	1	+	N	0	+	N	N	N	46
29	E. K.	10	E. M.	1	2	2	3	+	N	1	N	+	3LS	2	F. T.	2	0.14	N	V1	2	+	N	0	0	1	N	R	50
30	V. B.	5	C. M.	1½	4	4	4	+	? Dom.	1	N	0	3LS	2	F. T.		0.13	N		2	+	N	0	0	1	N	N	53
31	L. E.	29	E. F.	Birth	2	3	2	0	N	0	N	+	4LS	4	F. T.	2	0.20	N	V1-3	2	+	N	0	+	1	N	N	50
32	L. K.	6	E. F.	Birth	4	4	4					0	3LS	2	F. T.	3.5	0.16	N	V1	2	+	0	0	0	1	N	N	50
33	C. S.	14	E. M.	Birth	3	3	2	+	N	1	N	+	4LS	5	F. T.	2.5	0.14	N	V1	2	+	N	0	+	1	N	N	40
34	S. P.	17	C. M.	?	2	3	1	0	Dom.	1	N	+	2LS	4	F. T.	3.5	0.15	N	V1	1	+	N	0	0	1	N	N	49
35	A. H.	5	E. M.	Inf.	0	1	3	+	N	1	N	+	2LS	4	F. T.	1.5	0.18	Inc. RBBB	V1	2	+	0	+	+	1	N	N	45
36	N. J.	18	C. F.	Inf.	4	4	3	+	N	1	N	+	2LS	4	F. T.	4	0.18	N	V1-3	3	+	0	+	0	1	N	N	52
37	R. B.	12	C. M.	Inf.	2	3	1	+	N	1	N	+	3LS	4	F. T.	2	0.16	N	0	2	+	N	0	+	1	N	N	48
38	L. K.	5	E. M.	Inf.	1	2	1	+	N	1	N	+	3LS	5	F. T.	1	0.16	N	V1-2	1	+	2	0	0	1	N	N	46
39	R. M.	7	C. F.	1 mo.	4	4	3	0	N	0	N	0	3LS	1	F. T.	2	0.18	N	V1	2	+	0	+	0	2	2	N	60
40	J. V.	35	E. F.	Inf.	1	1	1	0	? Dom.	1	N	+	2LS	4	F. T.	2	0.15	N	V1-7	2	0	N	0	+	1	N	N	43
41	M. F.	7	E. F.	Inf.	4	4	3	+	N	1	N	+	2LS	4	F. T.	3	0.13	N	V1-3	3	+	0	0	0	1	1	N	54
42	M. S.	33	C. M.	Inf.	2	3	1	+	? Dom.	0	N	+	3LS	4	F. T.	2	0.19	N	V1-4	2	+	0	+	0	2	N	R	53
43	A. W.	18	C. M.	Child	1	2	1	0	Dom.	1	+	+	3LS	4	F. T. + coarct.	1	0.14	N	V1-4	1	+	D	0	0	1	1	N	54
44	E. C.	10	E. M.	1¼	2	3	2	+	N	0	N	+	3LS	4	F. T.	2.5	0.16	N	V1	2	+	D	+	+	1	N	N	50
45	G. R.	2¾	E. M.	Birth	3	2	4	0	N	0	N	+	3LS	3	F. T.	2	0.16	N	V1	2	+	D	+	0	1	N	N	
46	A. W.	10	E. M.	9 mo.	1	1	2	+	N	0	N	+	3LS	4	F. T.	1.5	0.17	N	0	1	0	1	0	+	1	N	N	46
47	J. T.	7	E. M.	4	3	3	3	+	N	0	N	+	3LS	4	F. T.	3	0.16	N	0	1	+	N	0	0	N	N	N	43
48	G. S.	9	E. M.	2	4	4	4	+	N	0	N	0		0	Pulm. atresia	4	0.14	N	V1-2	2	+	0	+	0	1	1	N	46
49	M. P.	8	C. F.	Birth	4	4	3	+	Dom.	1	N	0	2LS	2	F. T.	3	0.16	N	V1	1	+	0	+	0	1	N	N	54
50	N. N.	18	E. M.	6 mo.	2	3	2	+	N	0	N	+	3LS	4	F. T.	2	0.16	N	V1-2	2	+	N	+	0	1	N	N	48
51	T. R.	5	E. M.	6 mo.	1	1	1	0	N	1	N	+	3LS	4	F. T.	2	0.16	N	0	1	+	0	+	+	1	N	N	52
52	E. S.	12	E. F.	?	1	0	1	0	N	0	N	+	3LS	3	F. T.	1.5	0.16	N	V1	2	0	1	0	+	N	N	N	47
53	M. M.	8	C. F.	?	2	2	2	+	N	0	N	+	3LS	4	F. T.	2	0.16	N	V1	1	+	2	0	+	1	N	R	49

TABLE 1 (*Continued*)

Number	Case	Age	Race and Sex	Central Cyanosis: Age of onset	Central Cyanosis: Degree (1–4)	Clubbing (1–4)	Disability (1–4)	Squatting	"A" Wave	R. V. Lift (1–4)	Heart Size (N–++)	Thrill	Systolic Murmur: Maximal site	Systolic Murmur: Grade (1–6)	Diagnosis on Auscultation and PCG	ECG: P2 mm	ECG: P-R sec.	ECG: Conduction	ECG: T inversion	ECG: Severity of R.V.H.	Radiology: Oligemia	Radiology: Pulmonary arc (1–4)	Radiology: Sabot	Radiology: Infundib. chamber	Radiology: Size of R. V. (1–4)	Radiology: R. A. (1–4)	Radiology: Position of aorta	Radiology: C. T. Ratio
	Tetralogy of Fallot (*Continued*)																											
		yr.																										
54	A. M.	9	C. M.	Birth	2	1	1	+	N	0	N	+	2LS	4	F. T.	2	0.13	N	0	1	0	N	0	0	N	N	R	
55	R. N.	12	E. M.	?	1	0	1	+	N	0	N	+	3LS	4	F. T.	3	0.14	N	V1	2	0	N	0	+	N	N	R	44
56	JvZ	3½	E. M.	Birth	2	2	?	0	N	0	+	+	3LS	4	F. T.	0.5	0.10	N	V1	1	+	1	0	0	2	2	N	62
57	V. D.	16	E. F.	2	1	0	1	0	Dom.	0	N	+	2LS	4	Ausc. ? PCG. F. T.	2	0.16	N	V1	2	0	N	0	0	1	1	N	48
58	A. S.	3½	E. M.	Birth	2	1	2	+	N	0	N	+	3LS	4	F. T.	1.8	0.12	N	V1	2	+	1	0	0	1	N	N	48
59	R. M.	14	E. M.	Birth	1	1	2	+				+	2LS	4	F. T.	1	0.20	RBBB	V1–3	3	0		+					
60	M. D.	3	A. F.	4 mo.	3	3	4	0	N	1	N	0	2LS	1	F. T.	2.2	0.12	N	0	1	+	0	+	0	2	1	N	60
61	J. S.	6	E. M.	1¼	2	2	1	+	N	1	N	+	2LS	3	F. T.	1.5	0.12	N	V1–2	2	+	0	0	0	1	N	N	49
62	E. R.	20	E. F.	3 mo.	3	2	1	0	N	0	N	0	2LS	3	F. T.	1	0.16	N	V1–4	3	+	2	+	0	2	N	N	56

* E = European.
† F = Female.
‡ N = Normal.
§ LS = Left interspace.
¶ = Male.
‖ Dom. = Dominant.
[a] C = Cape colored.
[b] B = Bantu.
[c] AI = Aortic incompetence.
[d] PI = Pulmonary incompetence.
[e] R = Right-sided aorta.
[f] Inf. = Infancy.

the catheter with the tip placed in the body of the right ventricle. A single exposure was made at the end of the injection. The size of the catheter usually determined the speed of the injection. The time of onset of the systemic effects of the diodone after injection of the dye was also noted. It was occasionally necessary to repeat the injection.

Intravenous angiocardiography was performed in 32 cases. Diodone was injected through a polythene tube inserted through a median basilic vein into the subclavian or innominate vein or higher, or through the saphenous vein into the inferior vena cava. The angiocardiographic technique has been described elsewhere (17). Exposures were made at one-second intervals in the left oblique and antero-posterior projections. The findings are analyzed in the tables.

Necropsy proof of the diagnosis was obtained in 4 cases of severe pulmonary stenosis with intact ventricular septum and in 12 cases of the tetralogy.

RESULTS

The clinical electrocardiographic and radiologic findings in each case are shown in table 1. The results of catheterizations, selective angiocardiography and intravenous angiocardiography are shown in table 2.

DISCUSSION

The fundamental difference in the dynamics of the two conditions form the basis of all the differentiating features (13). In the tetralogy of Fallot although the degree of pulmonary or infundibular stenosis is always severe (18), the presence of a ventricular septal defect and an overriding aorta act as a safety valve to the right ventricle. In fact, the right ventricular systolic pressure never significantly can exceed that in the left ventricle and aorta (3–5, 19, 20). In consequence the right ventricle is seldom under severe stress and heart failure is rare. By contrast, in pulmonary stenosis with intact ventricular septum there is no such limiting factor to the height of the right ventricular systolic pressure and consequently when the pulmonary stenosis is severe the right ventricle has to generate great pressure to maintain circulation (3–5, 19, 21, 22). This also results in marked right atrial stress which causes the right atrial pressure to exceed the left atrial pressure and thus cause central cyanosis from a right-to-left interatrial shunt.

SYMPTOMS AND SIGNS

Comparison of the findings summarized in table 1 reveals that in general the onset of central cyanosis occurs earlier in the tetralogy of Fallot than in severe pulmonary stenosis with intact ventricular septum. Thus in 44 cases in whom the age of onset of cyanosis was known, cyanosis was present in all by the age of 5 years. In severe pulmonary stenosis with intact ventricular septum only 6 out of 14 had developed cyanosis before 5 years. In fact, in one case of severe pulmonary stenosis with intact ventricular septum cyanosis developed at the age of 40 years. It would appear that the development of cyanosis in infancy is common to both conditions and therefore of no differential value. However, delayed

TABLE 2

No.	Catheter								Angiocardiography						Selective Angiocard from R.V.		Site of Stenosis	Ultimate Proof
	P. A. pressure	Infundib. R.V.P.	Low R.V.P.	B.P. cuff	Aorta	"A" wave R.A.	L. A. entered	L. V. entered	Simultaneous filling of P.A. and aorta	Early L. A. & L. V. filling (L.O. view)	Size of M.P.A.	Site of stenosis	Aorta: Size (N-++++)	Aorta: Abnormality	Aorta filled	Site of stenosis		
Severe pulmonary stenosis with intact ventricular septum																		
1				130/75			Yes		Yes	Yes	2		N	0			V	Necropsy P.S. and A.S.D.
2				105/75					Yes	Yes	3	V	N	0			V	Surgery
3	10			135/80			Yes										V	Necropsy P.S. and P.F.O.
4	10/2	150/0	150/0	120/80		9									No	V	V	Valvotomy now A.S.D.
5	7/0	155/16	155/16	115/85		13									No		V	
6	7/2	150/2	150/2	110/80		7	3	90/2	Yes	Yes		?V					V	Valvotomy
7	13/5	67/10	67/10	120/90		8			No	No	4	?V	N	0	No		V	
8				115/80		16											V	Necropsy P.S. and P.F.O.
9									Yes	Yes	2	?V	N	0			V	
10	9/4	15/1	104/8	125/65		8			No	No	N	?	0	0			I	
11	20/10	225/5	225/5	120/80		10									No		V	Valvotomy
12	22/10		200/15	120/60		5											V	Valvotomy. Sel. angio from R.A. shunt in atria
13	5		155/5			6		85/0									V	Valvotomy
14	16/4		90/6	100/65		3			Yes	Yes	2		N	0	No		V	Necropsy. Valv. and infund. sten. Hypoplastic R.V. Large P.F.O.
Tetralogy of Fallot																		
15	9(M*)		48(M)						Yes	No	N		+	0			I	Surgery
16									Yes	No	D†	I	+	0			I	
17	6(M)	40(M)	40(M)	100/?							D	V	++	R†			V	Necropsy P.S. No. L.P.A.
18									Yes	No	No L.P.A. D	?V	++	0				Necropsy
19	3(M)		44(M)	135/100													I	
20				100/80	60/30				Yes	Slight	N	I					I & V	Necropsy infund. and valv.
21	3	18/−2	74/0		66/45	2									Yes	I	I & V	
22				115/?100					Yes	Slight	D	?V	+	High				Necropsy
23	13/5	85/5	105/9	90/60		3			Yes	No	N		+	L			?V	
24	9/3	11/5	110/9	120/75	100/70	2			Yes	No	D	I	+	0			I	Necropsy infund.

25	13/2	90/8	90/8	90/70		2			Yes	No	D		+	High	Faint	V	V	Valvotomy
26		42/6	130/0	125/85		3									Yes	0	I	Necropsy infund.
27	10/6	18/3	113/4	100/70		2									No	0	I & V	Surgery
28			42(M)	115/85					Yes	No	N	I	+	0			I	
29	11/6	12/3	125/10	110/70	125/78	2											I	Surgery
30									Yes	No	D	I	+	Yes			I	Necropsy infund.
31	16/6	32/0	120/8	125/80					Yes	No	D	I	+	0			I & V	Surgery
32	9/3		50/12	60/2		2									Yes		I & V	Necropsy infund. and valv.
33	13/5	18/3	112/3	100/80	103/65	3	13/3								Yes	I	I	Surgery
34	15/4	105/0	105/0		100/75	2											V	
35	12/?	25/?	60/?		60/?												I & V	
36																	I	Necropsy infund.
37	19/9	45/−6	100/6	90/75	90/57	4									Yes		I & V	
38	10/3	25/1	105/4	100/60		3			Yes	No	N	?	N	0	No	I	I & V	
39			114/9	120/80		5			Yes	No	D	I	++	0	Yes		V	Necropsy valv. P.F.O.
40	14/2	14/0	150/0	135/85		2									Yes	I	I	
41									Yes	Yes	D		+	0				Necropsy infund. + A.S.D.
42	5(M)	37(M)	37(M)	100/80					Yes	Yes	D	?	+	R			?V	
43	21/11	160/2	L.A. 170/80 R.A. 98/95			11			Yes	No	N		+	Coarct			V	
44	4(M)	13/0	80/−5	96/50					Yes	No	N	I	+	0			I	Surgery
45																	I	Surgery; aorta entered from R.V.
46				105/70	Entered		Yes	Yes	Yes	No	N	I	N	0			I	Surgery
47	6	100/0	100/0		100/80				Yes	No	2	V	+	High			V	Surgery
48		140/0		95/?		4			Yes	No	D	?	+++					Surgery
49									Yes	Slight	D	?I	+++	0			V	Surgery
50	3/2	18/1	110/0	105/?		5									Yes	I	I & V	Necropsy infund. and valv.
51																	I	Surgery; aorta entered from R.V.
52	15/5	115/4	115/4	110/90		8			Yes	No	N		N	0	No	0	V	
53	14/10	95/3	95/3	90/65		2			Yes	No	N	V	N	R	No	0	V	
54	25/7	90/0	90/0	90/60		3									Yes		V	
55	25/4	25/0	118/0	105/80		4									Yes	I	I	
56									Yes	No	N	?I	N	0			?I	
57	15/8	113/5	113/5	104/80		5			Yes	No	I	?	N	0			V	
58									Yes	No	I	?I	N	0			?I	
59	10/5	80/0	90–100/0	100/65													V	Valvotomy
60									Yes				++	0			V	Valvotomy (extreme tetralogy)
61									Yes	No	N	I	N	0			I	
62									Yes	No	2	V	++	0			V	Valvotomy

* M = Mean pressure.
† D = Diminished.
‡ R = Right-sided aorta.

onset of cyanosis favors severe pulmonary stenosis with intact ventricular septum, although the occasional case of the tetralogy may also show delayed cyanosis. Our findings are in agreement with most reported studies (3, 22–24), although this has not been a universal finding (25).

The intensity of cyanosis at rest was on the whole greater in the tetralogy of Fallot than in severe pulmonary stenosis with intact ventricular septum. Similar findings have been reported by others (22). However, in an individual case the intensity of the cyanosis is of no help, for in the tetralogy there may be no cyanosis at rest (case 35), while in severe pulmonary stenosis with intact ventricular septum the cyanosis may be severe (case 5). Spontaneous fluctuations in the intensity of the cyanosis occurred in both groups and was of no help in the diagnosis.

Cyanotic attacks associated with loss of consciousness occurred infrequently and were present in both conditions.

There was a history of squatting in the majority of cases of the tetralogy of Fallot (70 per cent), whereas 36 per cent of the cases of severe pulmonary stenosis with intact ventricular septum adopted this posture. The relative infrequency of squatting in severe pulmonary stenosis with intact ventricular septum has been reported by others. Thus Abrahams and Wood (3) found squatting in only 1 of their 8 cases of severe pulmonary stenosis with intact ventricular septum and Campbell (22) in 6 of his 31 cases. However, in de Balsac's (26) series squatting occurred in as many as 30 per cent of cases. Although squatting is less frequent in severe pulmonary stenosis with intact ventricular septum it would appear that in the individual case the presence or absence of squatting is of little value in the differential diagnosis.

Severe angina pectoris was a striking symptom in 2 of our cases of severe pulmonary stenosis with intact ventricular septum and in 1 of them (case 1), in which diffuse fibrosis of right ventricle was found at necropsy, the pain was incapacitating. Pain with some of the features of angina pectoris was noted in 1 of Abrahams and Wood's (3) cases. It was found in only 1 of our cases of the tetralogy of Fallot.

Dyspnea on effort was graded according to Campbell and his co-workers (27, 28). Dyspnea of varying severity was noted in all cases, and its severity was no help in the diagnosis. Although it has been stated that the patient is more dyspneic than cyanosed in severe pulmonary stenosis with intact ventricular septum, we have found this combination in both conditions. However, severe cyanosis with mild dyspnea was found only in the tetralogy.

Clubbing of the fingers and toes was present in the majority of cases usually proportionate to the degree of cyanosis.

General appearance. Abrahams and Wood (3) have claimed that a moon facies is associated with severe pulmonary stenosis with intact ventricular septum but not with the tetralogy of Fallot. This has not been our experience, which has been more in accord with that of Campbell (22). Two of our cases of severe pulmonary stenosis with intact ventricular septum were thin and under-developed, but the majority were of normal build without any particular fullness of face.

The majority of cases of the tetralogy of Fallot were small and under-developed. Our series is unusual in the relatively large number of 10 mild adult cases of the tetralogy with reasonably normal development. In 1 severe case of the tetralogy of Fallot the face was moon-shaped.

Other associated abnormalities such as long, tapering fingers, high arched palate, and pigeon chest, were of no help in the differential diagnosis.

The extremities in the tetralogy tended to be warmer and the veins fuller, whereas in severe pulmonary stenosis with intact ventricular septum the extremities were often cool and peripheral cyanosis appeared to be superimposed on central cyanosis.

No differential feature emerged from examination of the pulse in either volume or rhythm. Also no difference was found in the blood pressure and in both conditions it was often difficult to obtain an accurate diastolic pressure.

Jugular venous pulse. Although Laubry and Pezzi (29), as long ago as 1913, drew attention to the presence of an exaggerated "a" or auricular wave in the jugular venous pulse in 5 cases of congenital heart disease, the paramount importance of this sign has only recently emerged. Abrahams and Wood (3) found a correlation between the severity of the pulmonary stenosis with intact ventricular septum, and the size of the "a" wave. An "a" wave of around 5 mm Hg was found in moderate cases with a right ventricular systolic pressure of 51 to 100 mm Hg, whereas a giant "a" wave of about 10 mm Hg was associated with ventricular pressures between 125 to 175 mm Hg. In their 7 cases of severe pulmonary stenosis with intact ventricular septum and reversed interatrial shunt, "typical giant 'a' waves were seen in every case." Great diagnostic importance was attached to the presence of a giant "a" wave as it was never observed in the tetralogy of Fallot. Of our 14 cases of severe pulmonary stenosis with intact ventricular septum, the "a" wave was dominant[3] in 6 and giant in 4. In the remainder it was thought to be normal. This correlated with the catheter finding of an "a" wave of 3 to 9 mm Hg in the cases showing a dominant "a" wave which is not giant by Abrahams and Wood's criteria, whereas in 2 of the 3 cases with a giant "a" wave which was measured with an electromanometer it was 13 and 16 mm Hg respectively. In 1 case the "a" wave was not visible because of anatomic reasons (short neck); in another an arterial Corrigan pulse of coincidental aortic incompetence obscured the "a" wave of 8 mm Hg measured in the right auricle; but in 1 case an "a" wave of 6 mm Hg was missed. In only 1 case was the "a" wave normal (case 14).

In the tetralogy of Fallot, on the other hand, a dominant "a" wave was occasionally encountered but a giant "a" wave was never found. This was confirmed by cardiac catheterization which did not reveal an "a" wave exceeding 5 mm Hg except in 3 unusual cases (cases 43, 52, and 57).

Thus the presence of a giant "a" wave is a most valuable sign in the differential diagnosis. Its presence excludes the tetralogy of Fallot. If this wave is dominant only, although favoring severe pulmonary stenosis with intact ventricular septum, it is not diagnostic. On the other hand, as recognition of the "a" wave

[3] Refer to material and methods.

is not always easy, and may for anatomic reasons be impossible (22), the absence of a visible dominant "a" wave does not exclude severe pulmonary stenosis with intact ventricular septum.

Palpation of the chest. In the tetralogy of Fallot the position of the apex beat was almost always within normal limits, which is in keeping with general experience (28, 30). In all except 3 of our cases of severe pulmonary stenosis with intact ventricular septum the findings were similar, but it is well known that this condition is capable of causing much greater cardiac enlargement than the tetralogy of Fallot (6, 22). In neither series was a thrusting localized left ventricular impulse felt. The apex beat was usually difficult to localize, and instead, a tapping sensation produced by palpable first sound was found. However, palpation of the right ventricle in the third and fourth left spaces between sternum and midclavicular line was of some help. Thus the lift was never marked in the tetralogy, whereas in most cases of severe pulmonary stenosis with intact ventricular septum an abnormal sustained lift was present despite the normal size of the heart.

Pulsation in the second left space was never present in severe pulmonary stenosis with intact ventricular septum nor was it felt in all but 2 cases of the tetralogy of Fallot. In these 2 cases (cases 24 and 39), the pulsation, although suggesting pulmonary hypertension (Eisenmenger's complex), was attributed to an anteroposed aorta and the diagnosis later confirmed by necropsy. In no case of severe pulmonary stenosis with intact ventricular septum was the second sound palpable; however, this was a striking feature in most cases of the tetralogy. This finding has been commented on before and attributed by Vogelpoel and Schrire (13) to loud aortic valve closure presumably due to anteroposition of the aorta. We believe that the palpability of the second sound is of some value in the differential diagnosis.

A systolic thrill was present in all but 1 of the cases of severe pulmonary stenosis with intact ventricular septum being associated with a loud systolic murmur. In the tetralogy a short systolic thrill was often felt between the palpable first and second sounds, but in the severe cases it was usually absent.

Auscultation. Our findings are in full agreement with numerous pervious studies (3, 5–7, 18, 23, 25, 31–35) in failing to show any difference in the systolic murmur of the two conditions if attention is limited to the intensity of the murmur and the site of its maximal intensity. Thus the murmur was usually harsh and loud (grade 3 to 5), in which case its intensity was of no help in differentiating the two conditions. However, in 7 cases of the tetralogy of Fallot (cases 17, 29, 30, 32, 39, 49, and 60), all severe, the systolic murmur was soft (grade 1 to 2) and in 1 extremely severe case (case 48) the murmur was absent. A soft systolic murmur, therefore, appeared to favor the tetralogy as in all but 1 case of severe pulmonary stenosis with intact ventricular septum the murmur was loud. In this 1 case (case 8) a loud murmur had been noted in infancy but when examined preterminally the murmur had become much reduced in intensity. As the site of maximal intensity of the murmur in both conditions varied between the second and fourth spaces (table 1), it provided no real help in differential

diagnosis. Moreover, there was no strict correlation between the site of the stenosis and the site of maximal intensity of the murmur.

However, we have recently become aware of a striking difference in the murmur and our findings in cases 3 to 7 of severe pulmonary stenosis with intact ventricular septum, and cases 24 to 41 of the tetralogy of Fallot (table 1) have been published elsewhere (13). Since this publication, we have encountered 8 further cases of severe pulmonary stenosis with intact ventricular septum (cases 2, 8–14) and 21 cases of the tetralogy (cases 42 to 62), which have shown the same diagnostic features. Thus in the tetralogy of Fallot a short systolic murmur is heard between loud first and second sounds, whereas in severe pulmonary stenosis with intact ventricular septum, the murmur is more prolonged and is not followed by a loud second sound. This difference in the behavior of the systolic murmur is readily appreciated if, at the site of maximal intensity of the murmur, attention is directed to the duration of the systolic murmur in relation to the second sound and to the position in systole of its maximal intensity. In the tetralogy of Fallot the murmur commences soon after the first sound, reaches maximal intensity by midsystole and usually ends before the single loud, often palpable, aortic component of the second sound (figs. 1 and 8). By contrast, in several pulmonary stenosis with intact ventricular septum, the murmur is so

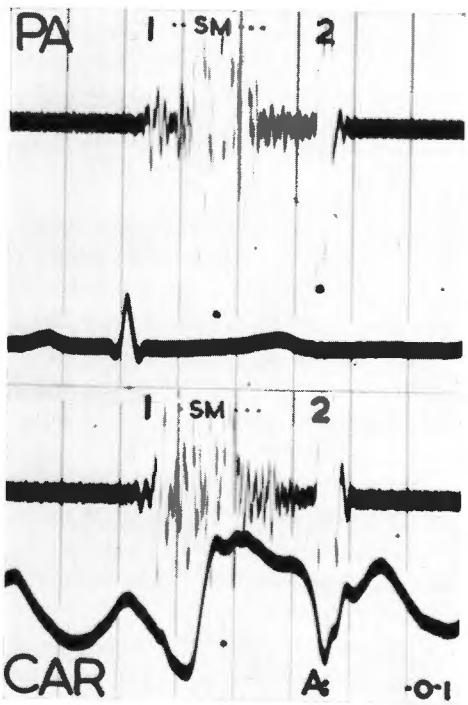

FIG. 1. The tetralogy of Fallot. The systolic murmur, *SM*, at the site of maximal intensity, begins shortly after the first sound, *1*, reaches its crescendo by midsystole and stops before the loud aortic component, *A*, of the second heart sound, *2*. The pulmonary component is inaudible and thus the second sound is single (case 25).

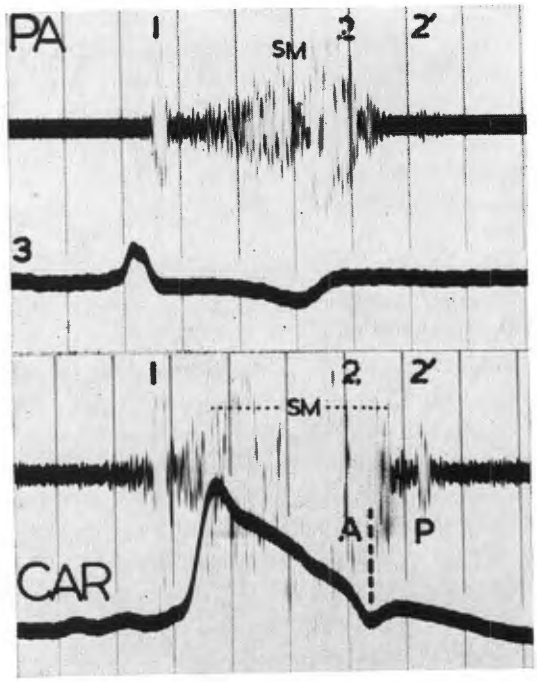

FIG. 2. Severe pulmonary stenosis with intact ventricular septum. The systolic murmur, *SM*, at the site of maximal intensity, has its crescendo in late systole and is so prolonged that it obscures the aortic component, *A*, of the very widely split second sound, 2 and 2'. It stops before the diminutive pulmonary component, *P*. The dicrotic notch of the carotid tracing has been used to identify the position of the buried aortic component of the second sound (case 3).

prolonged that it extends beyond and obscures the aortic component of the very widely split second sound. It stops before the delayed diminutive pulmonary component which may or may not be audible (figs. 2 and 11).

In the tetralogy of Fallot the second sound was single in all but 4 of our 48 cases. This we have attributed to the fact that the pulmonary component is inaudible with the low pulmonary artery pressures commonly found in this condition. When the pulmonary artery pressure approximates the normal level, as in the exceptional mild case and after successful operation, the pulmonary component may become just audible giving rise to wide splitting of the second sound. The second sound, although shown to be produced by the aortic valve closure alone, is particularly loud because of several factors such as anteroposition of the aortic root bringing the aortic valves closer to the chest wall, the increased size of the aorta together with the decreased size of the main pulmonary artery, and the fact that the murmur ends before and does not obscure it.

In severe pulmonary stenosis with intact ventricular septum, on the other hand, we and others have shown that the second sound is very widely split (13, 31). At the site of maximal intensity of the murmur, the aortic component is usually obscured in the late crescendo of the murmur. The pulmonary compo-

nent which follows the murmur is always markedly diminished and usually inaudible. Thus, auscultation at the site of maximal intensity of the murmur merely reveals a harsh prolonged systolic murmur which may or may not be followed by a very soft pulmonary second sound. However, auscultation in the mitral area and fourth left space, where the murmur is less intense, reveals an aortic second sound of normal intensity.

In 6 cases of severe tetralogy of Fallot an early systolic sound giving rise to "wide splitting of the first sound" was heard. This has been shown to be due to an audible ejection sound arising in the aorta (13). It was not heard in severe pulmonary stenosis with intact ventricular septum. However, in 2 cases of the latter, close splitting of the first sound was heard with an intense clicking second component. This sound was maximal in the second and third left spaces, and varied strikingly with respiration, being intense during expiration and absent during inspiration. The significance and mechanism of these findings have been discussed elsewhere (13, 36).

In our view auscultation plays the most important role in the differential diagnosis of the two conditions. Furthermore, the intensity of the systolic murmur may reflect the severity of the tetralogy of Fallot. Thus a short soft murmur with an aortic early systolic sound suggests extreme severity whereas a relatively long systolic murmur with a recordable or even audible pulmonary component of the second sound suggests a mild case (13).

Phonocardiography with synchronous electrocardiograms and jugular and carotid tracings have been of great value in both the diagnosis and better appreciation of the auscultatory findings in the two conditions. In 2 cases of the tetralogy (case 23 and 54) an unusually long murmur gave rise to difficulty in the auscultatory diagnosis. The phonocardiogram, however, was conclusive in case 54, showing that the murmur did not obscure the aortic sound nor did it extend beyond it. In case 23 both auscultation and phonocardiography favored severe pulmonary stenosis with intact ventricular septum. However, with deterioration in his condition, the murmur became clearly shorter and diagnostic of tetralogy which was confirmed by angiocardiography. As could be predicted from the length of the murmur, both were unusually mild cases of the tetralogy.

In only 1 case of severe pulmonary stenosis with intact ventricular septum (case 14) was the murmur unusually short. This was attributed to the absence of prolongation of the right ventricular systole probably associated with the small hypoplastic right ventricule which was a most unusual finding at necropsy.

RADIOLOGIC FEATURES

In the tetralogy of Fallot a classic radiologic appearance has been generally recognized. In the postero-anterior projection, the heart is usually normal in size but owing to the hypoplasia of the outflow tract of right ventricle there is a marked concavity of the left border. This, together with the lifting up of the apex, constitutes the sabot shaped heart (fig. 3 *A*, *B*, *C*). The vascular pedicle is made up almost entirely of the anteroposed aorta and is narrow (30). In the left anterior oblique view the forward projection of the right ventricle brings it

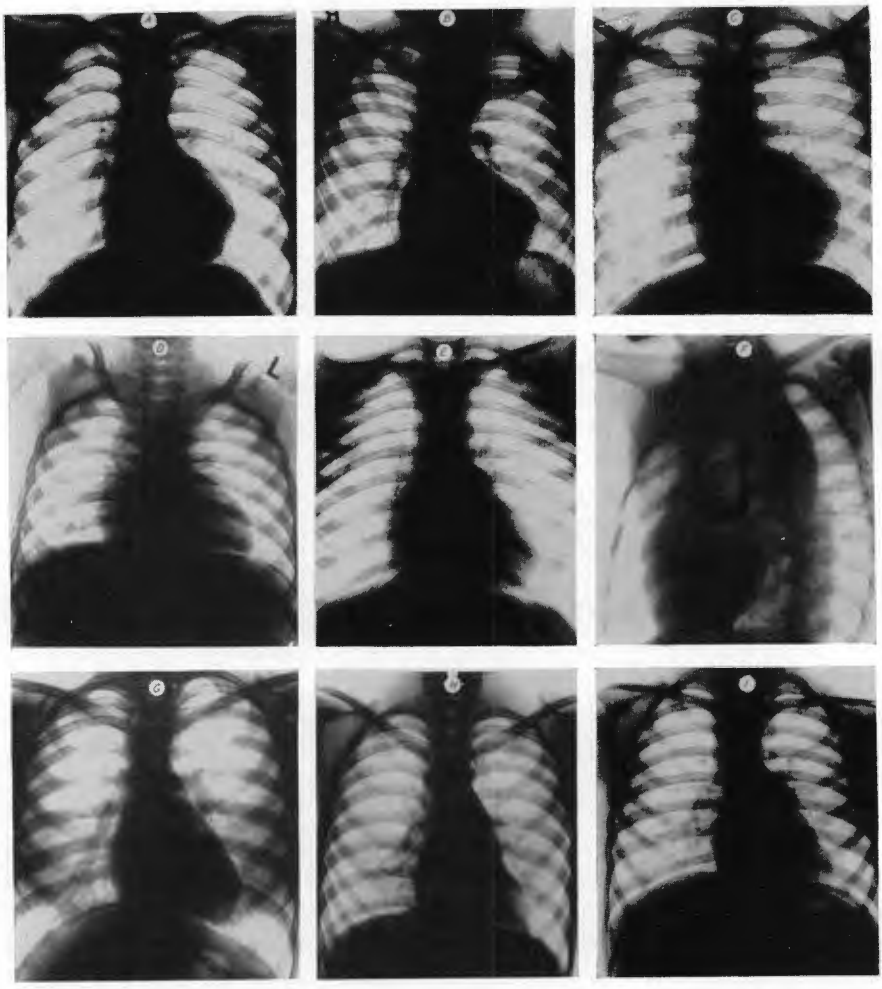

FIG. 3. The cardiac silhouette in the tetralogy of Fallot. *A–C* show the typical sabot shaped heart. In *B* the aortic arch is unusually high. In *C* and *H* the arch is right sided. *D* shows the large aorta with diminutive pulmonary arteries and bronchial collateral vessels. The infundibular chamber is shown in *E*. In *F* an unusually enlarged aorta is seen. A virtually normal silhouette with normal pulmonary arteries is shown in *G*. The unusual poststenotic dilatation in *H* and *I* makes the silhouette indistinguishable from pulmonary stenosis with intact ventricular septum (*A* to *I* represent cases 50, 22, 42, 41, 44, 34, 52, 53, 38 respectively).

closer to the chest wall. The aorta, being anteroposed, is closer to the anterior chest wall than normal (fig. 3 *F*). The aortic window is abnormally clear. In the right anterior oblique view the left atrium is not enlarged and there is absence of prominence of the outflow tract of the right ventricle. The hilar shadows are small and the lung fields abnormally clear.

In severe pulmonary stenosis with intact ventricular septum, on the other hand, the heart is often enlarged in the postero-anterior projection (22). Because

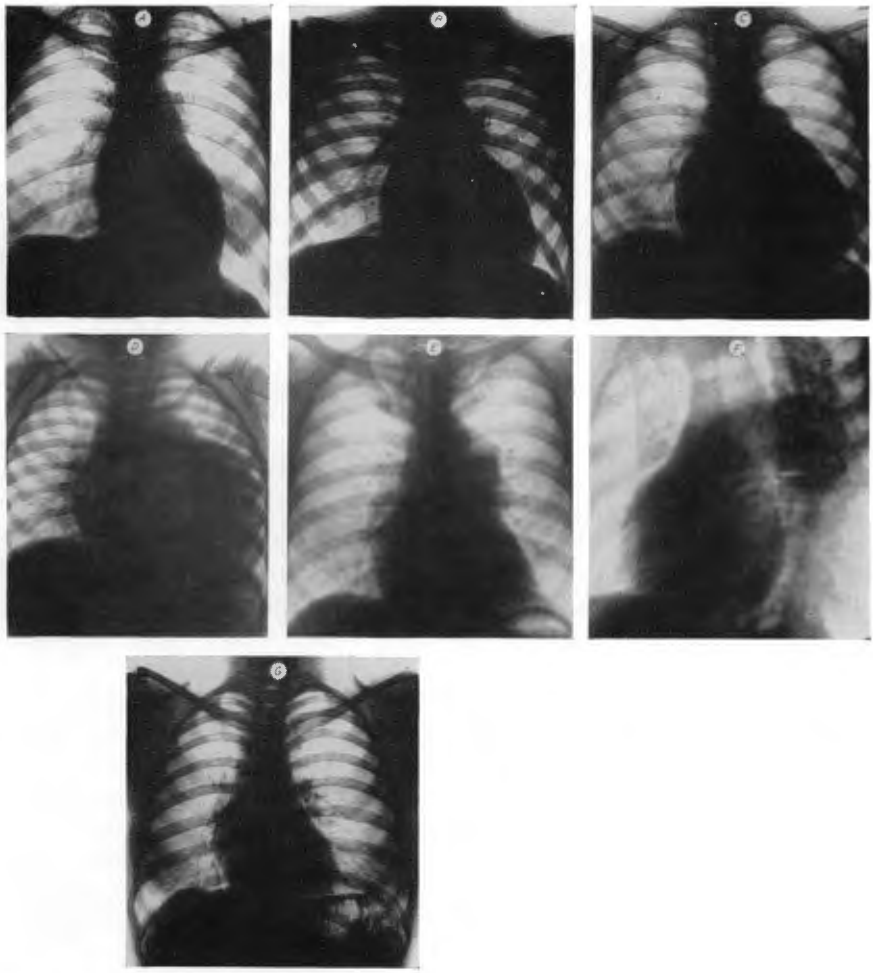

FIG. 4. The cardiac silhouette in severe pulmonary stenosis with intact ventricular septum. *A–D* show the range in size from slight to extreme right heart enlargement. The usual poststenotic dilatation of the main and left pulmonary arteries and the normal or small aorta are shown in *A–C*. In *E* and *F* the dilatation is aneurysmal whereas in *D* the enlarged cardiac shadow obscures the pulmonary arc. In *G* the cardiac silhouette is almost normal apart from slight right atrial enlargement. (*A–G* represent cases 5, 2, 4, 8, 7, 7, and 6 respectively).

of the poststenotic dilatation which affects chiefly the main and left pulmonary arteries, there is a marked convexity on the left cardiac border. The right ventricle is markedly hypertrophied and the apex is not lifted up from the diaphragm (fig. 4 *A* to *E*). The right atrium is often enlarged and the amplitude of pulsation in the right atrium and ventricle is abnormally forceful. The vascular pedicle is prominent due to the poststenotic dilatation of the pulmonary artery and a normally placed aortic root (fig. 4 *C* and *E*). In the left anterior oblique projection the marked hypertrophy of the right ventricle is particularly well seen.

The left ventricle is often displaced posteriorly so that it overlaps the spine and may be mistaken for left ventricular enlargement. The aortic window is often obscured by the large left pulmonary artery (fig. 4 *F*). In the right anterior oblique projection there is prominence of the outflow tract of the right ventricle. The hilar shadows are enlarged, especially the left, but do not show pulsation. The lung fields are abnormally clear.

When the classic radiologic appearance is present the diagnosis may be made with ease. However, a significantly large number of either group do not show these features.

Less than half of our cases of the tetralogy (18 of 48 cases) had the characteristic sabot shaped heart. This is in agreement with Baker *et al.* (28). Most had a more normal shaped heart with a straight left border (fig. 3 *G*) and in some the apex was slightly lifted (table 1). In 10 cases a prominence below the pulmonary artery was present and shown to be due to an infundibular chamber (fig. 3 *E*). In 3 cases the heart was moderately enlarged (fig. 3 *D*), and in 1 (case 56), considerably enlarged (CTR 62). In 15 cases the left pulmonary artery was smaller than normal but in the remainder this vessel was normal in size and in 4 was more prominent than normal, and in 3 there was marked poststenotic dilatation (fig. 3 *H* and *I*). The latter case could readily be confused with severe pulmonary stenosis with intact ventricular septum. In all except 8 cases there was oligemia.

In severe pulmonary stenosis with intact ventricular septum, 8 of 13 cases had an increased cardiothoracic ratio. The cardiac silhouette was typical in 10 cases. In 1 case the silhouette was almost normal (fig. 4 *G*).

The aorta in the tetralogy of Fallot is often prominent (11 cases) and in young children may be quite a striking feature (fig. 3 *D* and *F*). An unusual elongation and prominence of the knuckle was present in 4 cases (fig. 3 *B*). Six of the 48 cases showed a right-sided aorta (fig. 3 *C* and *H* and fig. 15 *C*). On the other hand, in severe pulmonary stenosis with intact ventricular septum, the aorta was never unduly prominent and was usually overshadowed by the poststenotic dilatation of the pulmonary artery (fig. 4 *C* and *E*). A right-sided aortic arch is extremely rare in severe pulmonary stenosis with intact ventricular septum and to our knowledge has been reported only twice (22, 41).

Radiology, therefore, is important enabling the diagnosis to be made with reasonable certainty in a large number of cases. Thus the sabot-shaped heart excludes severe pulmonary stenosis with intact ventricular septum with rare exceptions; conversely obvious poststenotic dilatation and cardiac enlargement strongly favor the latter diagnosis. A heart of normal shape and size occurs in both conditions but more commonly in the tetralogy. A right-sided aorta strongly favors the tetralogy (22).

THE ELECTROCARDIOGRAM

Right axis deviation and right ventricular hypertrophy were found in all our cases of the tetralogy and severe pulmonary stenosis with intact ventricular septum. It is generally held that the pattern of marked right ventricular hypertrophy with deep T inversion and S-T depression extending across the chest to

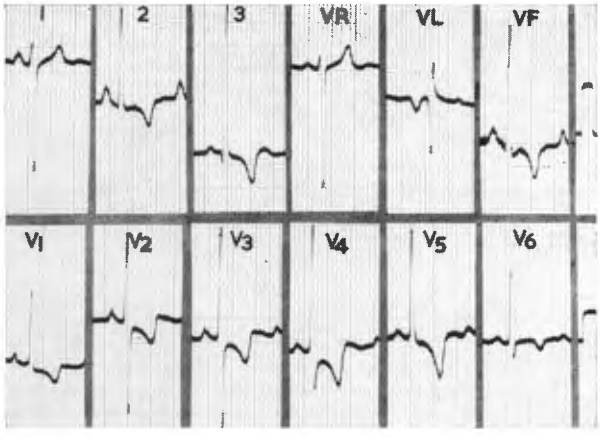

FIG. 5. The pattern of extreme right ventricular hypertrophy often encountered in severe pulmonary stenosis with intact ventricular septum. Right atrial hypertrophy is also shown (case 9).

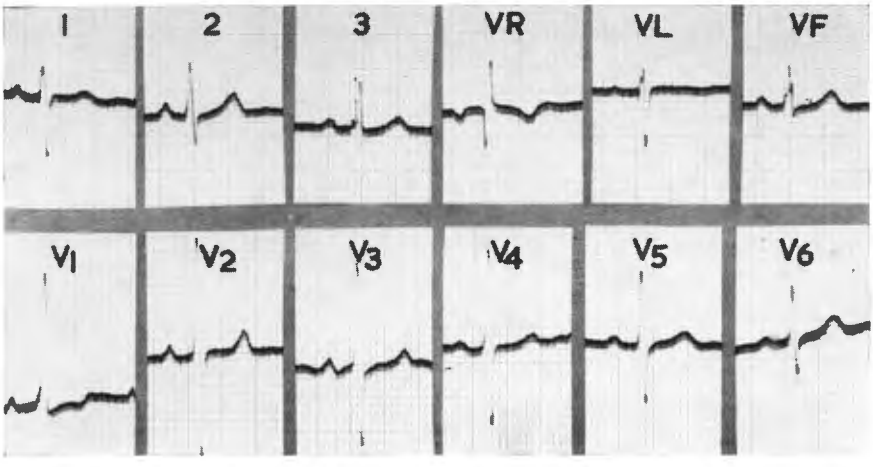

FIG. 6. The pattern of moderate right ventricular hypertrophy usually seen in the tetralogy of Fallot (case 52).

V4 with tall R waves occurs only in severe pulmonary stenosis with intact ventricular septum (37) (6 of 14 cases; fig. 5). In 5 cases of the tetralogy T-wave inversion was present from V1 to 4, but there was not S-T depression and the T waves were not deeply inverted. In the majority of cases of the tetralogy (31), T-wave inversion did not extend beyond V1 (fig. 6) but this finding also occurred in 5 of the 14 cases of severe pulmonary stenosis with intact ventricular septum. Whereas there appears to be some correlation between the severity of the pattern of the right ventricular hypertrophy and the severity of the stenosis in cases with intact ventricular septum (22), no such correlation exists in the tetralogy of Fallot. Thus in an extreme case of the tetralogy (case 49) right axis deviation alone was present (fig. 7).

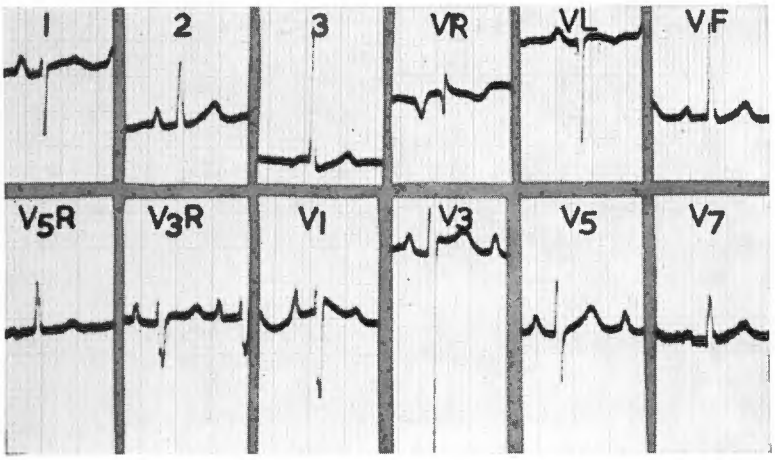

FIG. 7. Right axis deviation only in a case of extreme tetralogy (case 49) illustrating the lack of correlation between the severity of right ventricular hypertrophy and the severity of the stenosis. The right auricular hypertrophy is well shown.

Incomplete right bundle-branch block was found in 3 cases of severe pulmonary stenosis with intact ventricular septum and 2 cases of the tetralogy, but in no case was complete right bundle-branch block encountered. The presence of right bundle-branch block has been considered to favor strongly severe pulmonary stenosis with intact ventricular septum (7). Tall P waves denoting right atrial hypertrophy were encountered sufficiently commonly in both conditions to be of no real value in differential diagnosis (figs. 5 and 7). The P-R interval was prolonged in 2 cases of severe pulmonary stenosis with intact ventricular septum, but was of normal duration in all cases of the tetralogy.

Thus, as a rule, the electrocardiogram is of no special value in the differential diagnosis. However, the presence of marked right ventricular hypertrophy and stress favors severe pulmonary stenosis with intact ventricular septum.

SPECIAL INVESTIGATIONS

Special investigations are required to establish the diagnosis and to provide information required by the surgeon.

Wherever possible, cardiac catheterization has been the initial investigation. If the diagnosis was established during this procedure (*vide infra*) angiocardiography was no longer required for diagnostic purposes and was usually omitted. If the aorta was not entered from the right ventricle, a selective angiocardiogram from the right ventricle was usually performed. By this means full intravenous angiocardiography could sometimes be avoided. This is important because if the essential information can be obtained at one investigation, the patient is saved another procedure which in itself is not without danger.

CARDIAC CATHETERIZATION

Site of stenosis. Twelve of the 14 cases of severe pulmonary stenosis with intact ventricular septum were catheterized. In 9 the pulmonary artery was entered

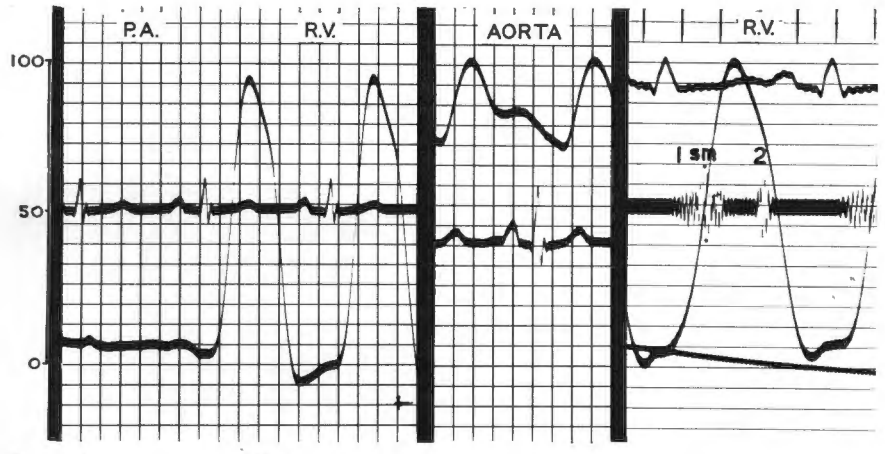

FIG. 8. The tetralogy of Fallot. A pulmonary artery pressure of 6 with a right ventricular pressure of 100/0 mm Hg proves pulmonary valve stenosis. The aorta was entered from the right ventricle. The murmur is loudest in early systole and ends well before the aortic second sound in contrast to the prolonged murmur shown in fig. 11 (case 47).

and severe stenosis proved in each case (fig. 8). In 2 cases (S. M., case 10, and D. A., case 14) infundibular stenosis was present as well; in 1 of these the infundibular stenosis was missed during catheterization but was found at operation and necropsy.

Thirty-two of our cases of the tetralogy of Fallot were catheterized. In 28 the pulmonary artery was entered and stenosis demonstrated. However, it is not always easy to locate the site of the stenosis accurately. In 24 of these where electromanometric tracings were obtained, the stenosis appeared to be valvular in 9 (fig. 8), infundibular in 6, and in the remaining 9 valvular and infundibular stenosis was present, infundibular stenosis usually predominating (fig. 9).

Thus in agreement with most workers, if catheterization proves an infundibular stenosis the diagnosis is usually the tetralogy of Fallot, whereas if it is valvular, no such inference can be made. In all cases the pulmonary and infundibular stenosis was of a severe order, but there was no significant difference in the level of the pulmonary arterial pressures.

Catheterization of the aorta from the right ventricle. If the catheter tip can be advanced into the aorta from the right ventricle (fig. 12), the ventricular septum can not be intact and hence severe pulmonary stenosis with intact ventricular septum is conclusively excluded. Unfortunately, it is not always easy to do this in the tetralogy, for the aorta was entered in 11 cases only.

Comparison of the systolic pressure in the right ventricle with the systemic pressure. Of the 12 cases with severe pulmonary stenosis and intact ventricular septum catheterized, full electromanometric data were obtained in 9. In 6 the right ventricular pressure was considerably higher than the systemic systolic pressure (fig. 10). In 3 cases the right ventricular systolic pressure was lower than the systemic.

In the tetralogy the right ventricular systolic pressure is of the same order as

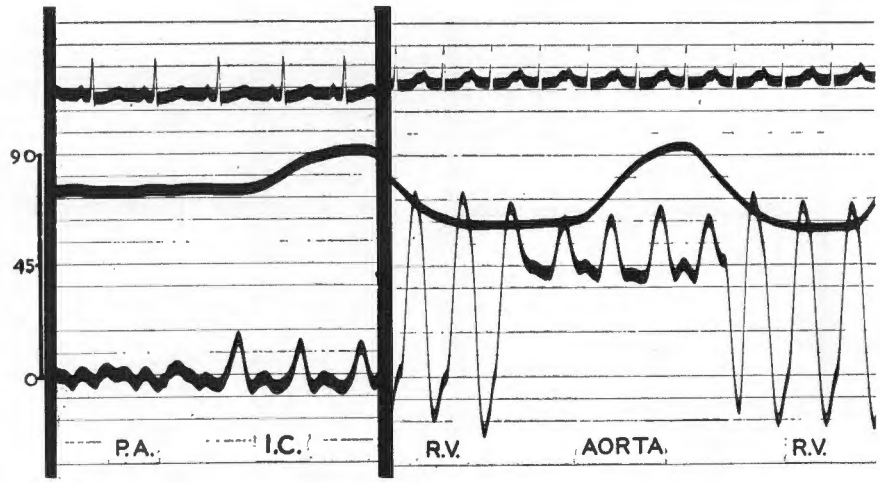

FIG. 9. The tetralogy of Fallot. A pulmonary artery pressure of 3, an infundibular chamber pressure of 18/ −2 and a right ventricular pressure of 74/ −12 to 0 mm Hg proves infundibular and pulmonary valve stenosis. The passage of the catheter from the right ventricle into the aorta proves that the ventricular septum is not intact. The diagnosis of the tetralogy of Fallot is thus established. The right ventricular and aortic systolic pressures are of the same order (case 21).

the systemic (fig. 8 and 9). In 10 cases where the aorta was entered there was never more than 10 mm Hg difference between the two systolic pressures. In these cases the aortic pressure was in good agreement with the systolic pressure as determined by the sphygmomanometer. In those cases where the aorta was not entered the right ventricular systolic pressure was usually of the same order, when compared with the systemic blood pressure as determined by the sphygmomanometer at the same time. There was one exception (case 40), a mild case with a right ventricular systolic pressure 15 mm Hg above the systemic blood pressure.

Thus when there is considerable difference between the right ventricular and systemic systolic pressures the diagnosis is almost always pulmonary stenosis with intact ventricular septum. In the tetralogy the pressures are usually of the same order. The effect of exercise on the systolic pressure in the right ventricle may be of considerable importance. In severe pulmonary stenosis with intact ventricular septum, the right ventricular systolic pressure may, by coincidence, be at the same level as the systemic but will reach a much higher level than the systemic pressure in response to exercise. In the tetralogy, however, no such disproportion will usually result. We have not employed exercise as a routine but in the occasional case it may well be crucial to the diagnosis.

These findings are in accord with the general experience of other workers (19, 20). Soulie *et al.* (5), however, have also observed an occasional case of the tetralogy of Fallot with a higher pressure in the right ventricle than in the aorta. It is conceivable that an unusually small ventricular septal defect with minimal overriding of the aorta may result in such a disparity in these pressures. In case

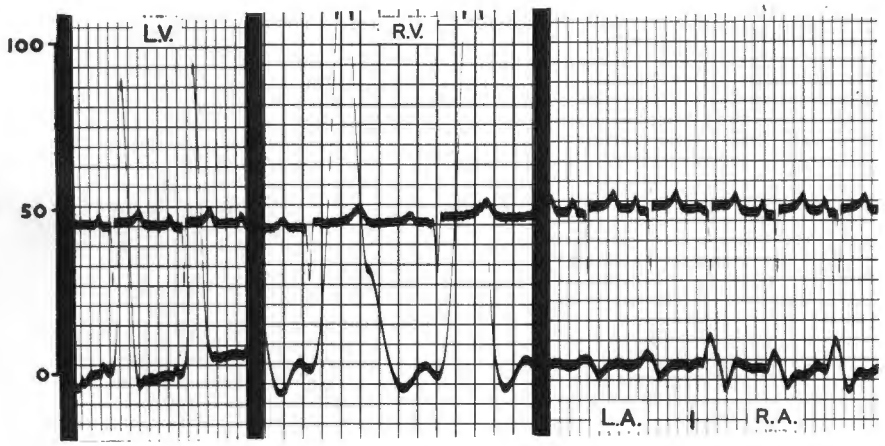

FIG. 10. Severe pulmonary stenosis with intact ventricular septum. The catheter has been passed through the defect in the atrial septum into the left side of the heart. The pressure in the left ventricle (*LV*) is 90/2 whereas that of the right ventricle is 150/2 mm Hg. The ventricular septum is thus intact. Cyanosis is due to a right-to-left atrial shunt, the "a" wave in the right atrium being higher than that of the left (7 and 3 mm Hg respectively (case 6)).

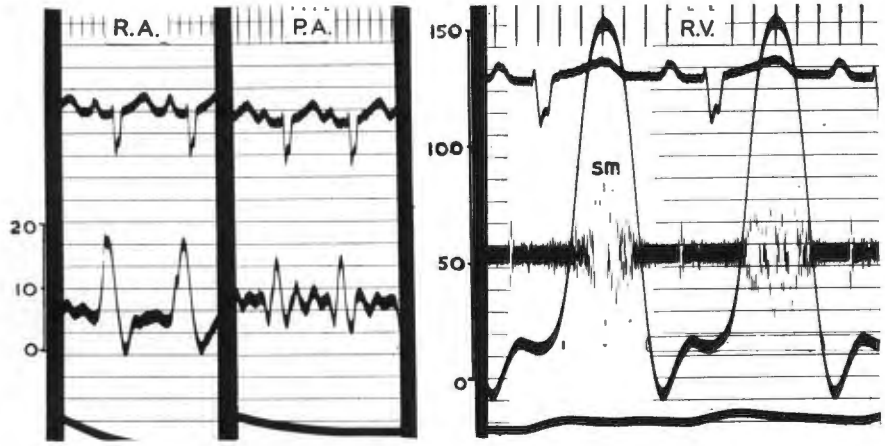

FIG. 11. Severe pulmonary stenosis with intact ventricular septum. A giant "a" wave of 13 mm Hg is recorded in the right atrium (*RA*). The mean pressure in the pulmonary artery (*PA*) is 8 mm Hg. The large "a" wave in the pulmonary artery tracing is presumably produced by right atrial contraction. This pulse wave is probably transmitted through the hole in the atrial septum into the left atrium and thence to the pulmonary artery via the pulmonary capillaries. The pressure in the right ventricle (*RV*) is 155/0 to 16, which is considerably higher than the systemic pressure of 115/85 mm Hg. The characteristic prolongation of the systolic murmur is also shown (case 5).

57 where the systolic pressure in the right ventricle was 9 mm Hg above the femoral artery at rest and 40 mm Hg above the systemic level for a short while after effort, the angiocardiogram showed no anteroposition and only slight early opacification of the aorta.

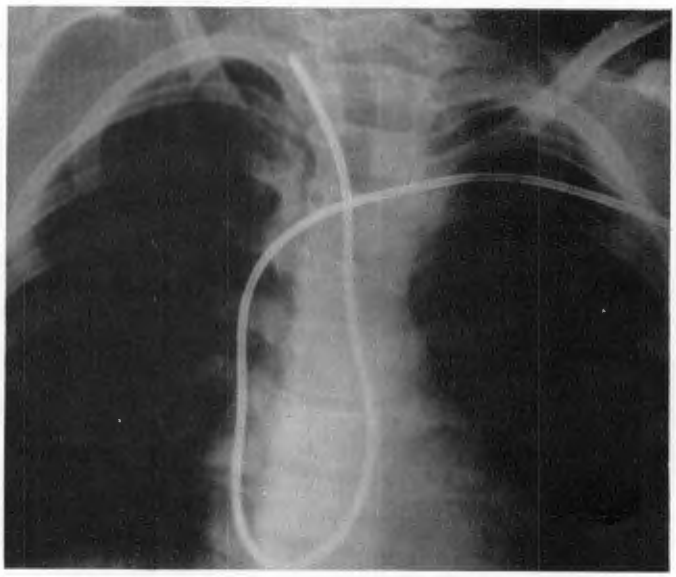

FIG. 12. The tetralogy of Fallot. The catheter has been passed into the aorta from the right ventricle. This excludes pulmonary stenosis with intact ventricular septum (case 47).

Right atrial pressure. Particular attention was paid to the height of the "a" wave. In 3 cases of severe pulmonary stenosis with intact ventricular septum, a giant "a" wave (10, 13, and 16 mm Hg, respectively) was present (fig. 11). In 5 cases the "a" wave measured 7 to 9 mm Hg and in 2 cases the "a" wave was only 5 and 3 mm Hg respectively.

In only 2 of the 22 cases of the tetralogy where the right atrial pressure was obtained with the electromanometer did the "a" wave exceed 5 mm Hg. In 1 (case 43) a giant "a" wave of 11 mm Hg was present. This case, however, was complicated by coarctation of the aorta, which resulted in a right ventricular pressure of 160/2 mm Hg. In the other case, (case 52) the mildest of the series, an "a" wave of 8 mm Hg was recorded. Thus the presence of a giant "a" wave excludes an uncomplicated case of the tetralogy of Fallot, and an "a" wave exceeding 5 mm Hg is a strong point against this diagnosis.

Passage of catheter into left atrium from right atrium. The catheter was passed from the right to the left atrium in 4 cases of severe pulmonary stenosis with intact ventricular septum, thus proving an interatrial communication. However, the presence of such a communication does not exclude the tetralogy because a patent foramen ovale or an atrial septal defect may also be present in this condition. Thus in 2 of our cases of the tetralogy, the left atrium was entered. However, if it can be shown that the pressure in the left atrium exceeds that of the right auricle (case 33) severe pulmonary stenosis with intact ventricular septum with reversed interatrial shunt can be excluded because in this condition the pressure in the right atrium always exceeds that of the left (fig. 10). However, Soulie *et al.* (5) have reported the occasional presence of a right-to-left gradient even in the tetralogy.

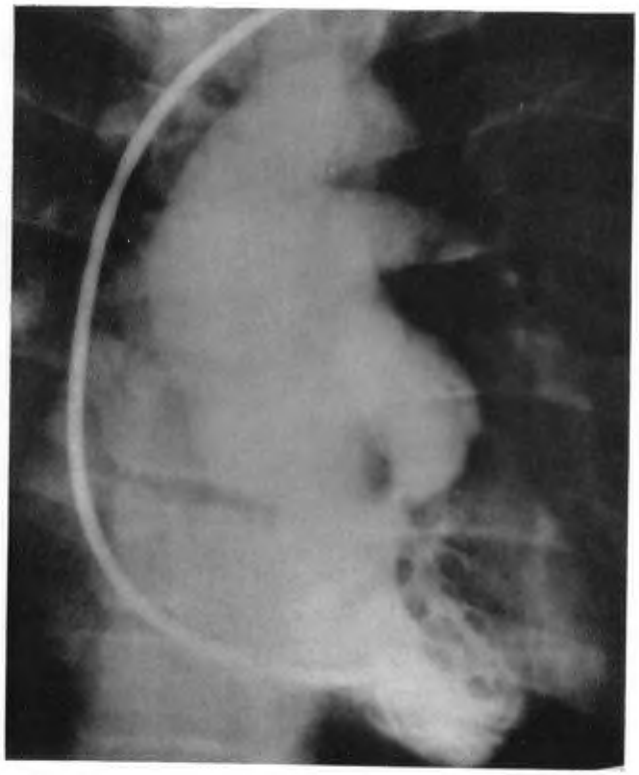

FIG. 13. Selective angiocardiogram from the right ventricle in the tetralogy of Fallot. Simultaneous filling of the aorta and the pulmonary artery excludes an intact ventricular septum. The infundibular stenosis and chamber are clearly demonstrated (case 33).

SELECTIVE ANGIOCARDIOGRAPHY FROM THE RIGHT VENTRICLE

In all 5 cases of severe pulmonary stenosis with intact ventricular septum on whom selective angiocardiography was performed no filling of the aorta was observed. In 11 of the 16 cases where this procedure was performed in the tetralogy the aorta was filled (fig. 13). Moreover, in the tetralogy the patient usually complained of the systemic effects of the dye almost immediately after the injection. In severe pulmonary stenosis with intact ventricular septum this effect was delayed or absent. Thus selective angiocardiography is a most useful method of establishing the diagnosis of the tetralogy of Fallot. However, if the aorta does not fill, the tetralogy can not be excluded.

In 6 cases of the tetralogy an infundibular stenosis and chamber were outlined, thus providing information of diagnostic value. Moreover, the demonstration of the abnormal local anatomy was of some assistance to the surgeon.

INTRAVENOUS ANGIOCARDIOGRAPHY

The role of intravenous angiocardiography in the diagnosis of the two conditions has been discussed in detail elsewhere (17). Provided one is aware of certain pitfalls (38), this method can afford conclusive proof of the diagnosis (39).

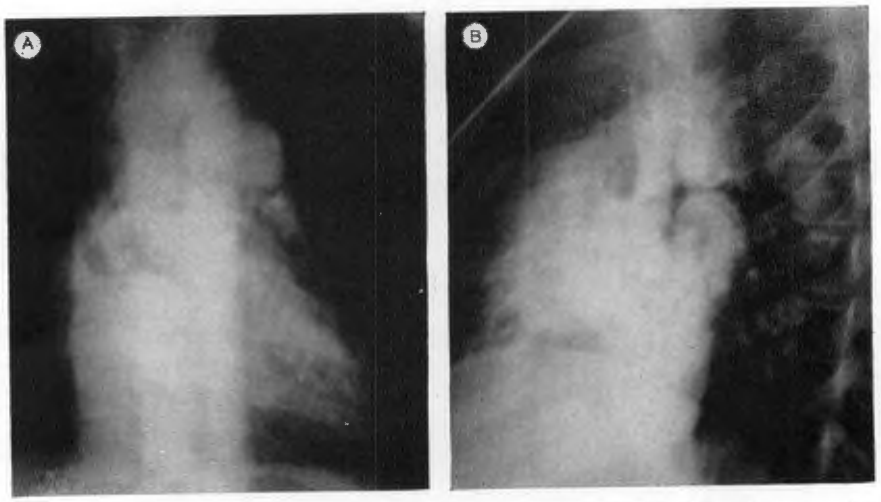

FIG. 14. Prograde angiocardiogram in severe pulmonary stenosis with intact ventricular septum. In the AP view (*A*) there is simultaneous and dense opacification of the aorta and the pulmonary artery, giving an appearance indistinguishable from the tetralogy. The oblique view (*B*) is essential to show that the aorta is filled from the left heart and not the right. All chambers of the heart are densely filled in the early series, proving a right-to-left shunt in the atria (case 9).

In the antero-posterior projection early opacification of the aorta and pulmonary arteries occurs in both conditions and the degree of the aortic opacification in severe pulmonary stenosis with intact ventricular septum may be comparable if the interatrial shunt is considerable (figs. 15 *A* and *C*, and 14 *A*).

In one of our early cases of severe pulmonary stenosis with intact ventricular septum (case 1) an erroneous diagnosis of the tetralogy of Fallot was made on these grounds.

Thus in no case should the diagnosis be based on the appearance of the antero-posterior angiocardiogram alone, when there is any evidence of premature opacification of the left heart. The crux of the angiocardiographic diagnosis is an early opacification of the left atrium in the left oblique projection (fig. 14 *B* and 15 *B*). In 5 out of 7 cases of severe pulmonary stenosis with intact ventricular septum on whom angiocardiograms were performed the right and left shunt through the atria was clearly demonstrated (fig. 14).

In the tetralogy of Fallot, slight fleeting filling of the left atrium may sometimes be seen due to a slight right-to-left interatrial shunt induced by angiocardiographic conditions (17, 40). This occurred in 5 of our cases but the degree of filling of the left auricle and left ventricle was so slight that the gross filling of the aorta shown in the same picture could not be accounted for by the interatrial shunt. In one of these cases (case 41) despite the large atrial septal defect shown at necropsy, the right-to-left interatrial shunt of diodone was small and fleeting (fig. 16).

Although early opacification of the left ventricle may occur in the tetralogy of Fallot through an interatrial or interventricular shunt, in none of our cases

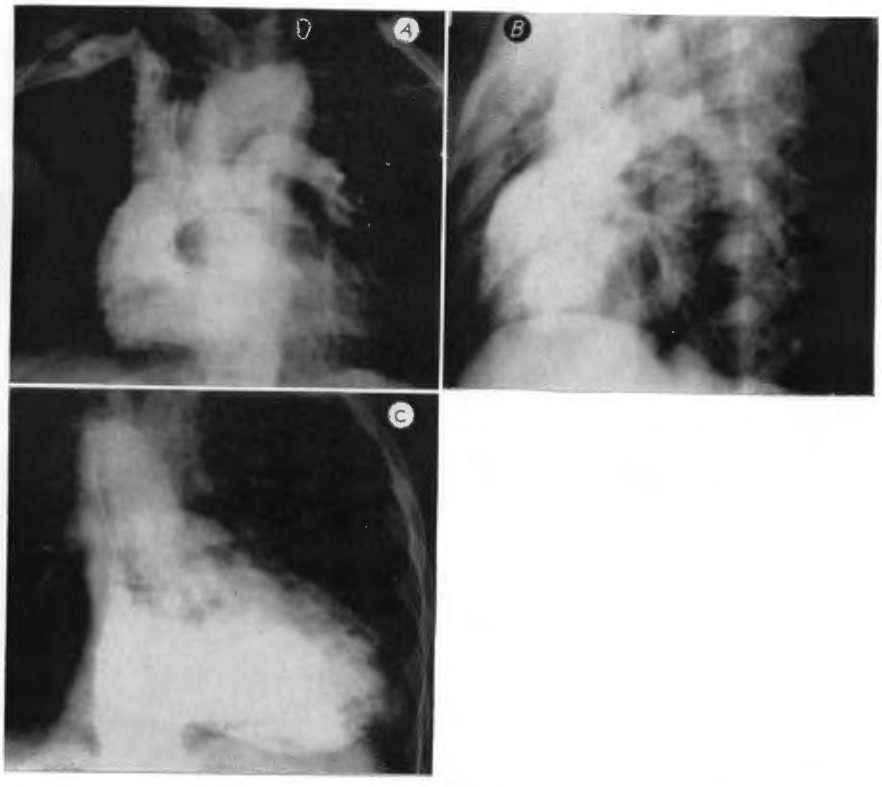

FIG. 15. Angiocardiogram in the tetralogy of Fallot. Simultaneous early filling of the aorta and pulmonary arteries is shown in both projections. The aorta is filled from the right ventricle because the left heart has not yet been opacified. While apparent in the antero-posterior projection (*A*), where the right ventricle does not form the left cardiac border, the absence of left heart filling is always more decisively shown in the left oblique projection (*B*). When the right ventricle forms the left border of the heart (*C*) the antero-posterior projection fails to differentiate the two conditions. However, the right-sided aorta strongly favors the tetralogy as does the disparity in size between the aorta and pulmonary artery. In this case valvular stenosis is clearly shown and there is no left pulmonary artery. (*A*, case 53; *B*, case 53; *C*, case 17).

was this premature opacification dense. On the other hand, early and dense opacification of the left ventricle was seen in 5 cases of severe pulmonary stenosis with intact ventricular septum, resulting in the remarkable finding of equal opacification of all four heart chambers in the same picture (fig. 14 *B*), as already stressed elsewhere (17). In 2 cases no early opacification of the left heart was observed.

As has been stressed in an earlier communication (17), attention must be directed not only to the early opacification of the aorta, but also to the density of the opacification and to the size of this vessel and its anatomic position. In the tetralogy of Fallot the early opacification of the aorta is usually as dense as that of the pulmonary artery. The aorta is often an abnormally large vessel, certainly larger than the pulmonary artery. Anteroposition is the rule and a

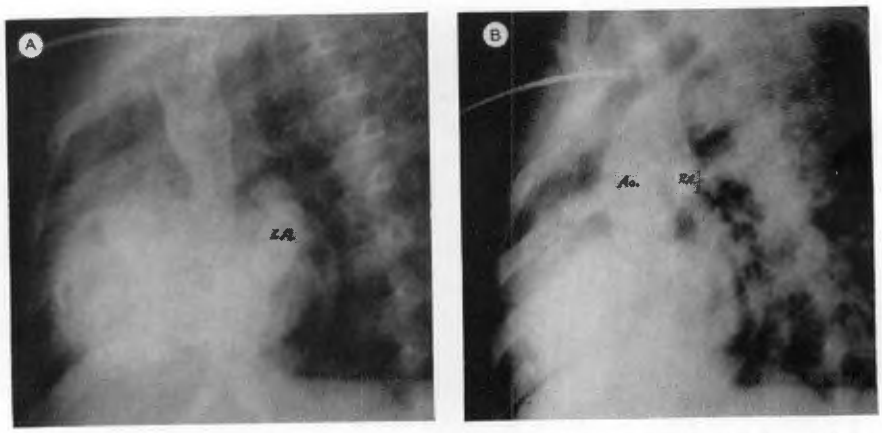

FIG. 16. Angiocardiogram in the tetralogy of Fallot associated with atrial septal defect (the pentalogy). In this combination the angiocardiogram even in the left oblique projection closely resembles pulmonary stenosis with intact ventricular septum (fig. 14 *B*). However, the volume of dye passing into the left heart (*A*) can not alone account for the early and dense opacification of the aorta (*B*) which is filled from both ventricles. Another feature favoring the tetralogy is the disparity in size between the aorta and pulmonary artery (case 41). (From Goetz, Nellen, Schrire, and Vogelpoel, 1955, courtesy of ANGIOLOGY.)

right-sided arch is not uncommon (fig. 15 *C*), and in our series it was present in 6 cases. On the other hand, in severe pulmonary stenosis with intact ventricular septum if the aorta is prematurely opacified, it is usually less dense than the pulmonary artery and is not abnormally large; in fact, the poststenotic dilatation of the pulmonary artery usually produces a shadow larger than the aorta (fig. 14 *A*). Anteroposition is not a feature and a right-sided arch is extremely uncommon (22, 41). Anomalies of the aortic arch and its branches are not uncommon in the tetralogy and these may occasionally be demonstrated by the angiocardiogram (fig. 15 *C*). The presence of such abnormalities favors the tetralogy. In one unusual case (case 43) coarctation of the aorta was found in association with the tetralogy of Fallot.

Pulmonary valvular stenosis with poststenotic dilatation occurs in both conditions. However, the degree of the dilatation is usually far greater in severe pulmonary stenosis with intact ventricular septum and in 1 case (case 7), it was in fact aneurysmal. In the tetralogy the poststenotic dilatation is not usually impressive and in only 2 cases (cases 38 and 62) was it a prominent feature (fig. 3). In infundibular stenosis poststenotic dilatation of the pulmonary artery usually is absent but may occur.

In the tetralogy of Fallot the right ventricle empties rapidly via the aorta and pulmonary artery. By contrast, in severe pulmonary stenosis with intact ventricular septum, the pulmonary artery is the sole outlet of the right ventricle and delayed clearing of the right heart is a constant feature. Thus dye is retained far longer in the right ventricle and pulmonary arteries in this condition.

We have often experienced difficulty in determining the site of the stenosis by intravenous angiocardiography. The infundibulum is situated well within

the cardiac shadow and unless the right ventricular outflow tract is clearly outlined the site and degree of the stenosis is impossible to determine. Narrowing and irregularity of the outflow tract is usually found in the tetralogy (39), the normal U-shape of the right ventricle being lost. Overlying shadows produced by the main and left pulmonary arteries add to the difficulties and may lead to errors in the localization of the stenosis. However, when infundibular stenosis is clearly demonstrated it may be helpful in the diagnosis as infundibular stenosis is so much more common in the tetralogy. The presence of infundibular stenosis is shown by the demonstration of an infundibular chamber, and was clearly shown in 9 cases of the tetralogy. However, it was not shown in several others in whom infundibular stenosis was proved by catheterization and necropsy. An opacified left pulmonary artery behind the outflow tract of the right ventricle may be mistaken for an infundibular chamber and this error was made in one of our cases in whom necropsy revealed valvular stenosis. Valvular stenosis can occasionally be demonstrated but is of no help in differential diagnosis.

OXYGEN SATURATION

Comparison of the oxygen saturation of the blood samples from right heart chambers and vessels is of little diagnostic value in the differentiation of the two conditions (5). If the left atrium is entered a right-to-left shunt may be demonstrated, but a normal oxygen saturation in a left atria sample does not exclude a reversed interatrial shunt, as the sample may be taken from a pulmonary venous stream before admixture. We have not found oxygen studies to be of value in the differential diagnosis but we have not investigated the effect of exercise, oxygen inhalation, or forced breathing in the two conditions. Selective dye dilution curves and circulation times from the right heart chambers appear to be promising techniques for accurate diagnosis but have not yet been performed in this laboratory.

DIAGNOSIS AT OPERATION

The diagnosis of the tetralogy of Fallot can be established if, during the procedure of pulmonary valvotomy or infundibular resection, the sound can be passed from the right ventricle into the aorta. In two of our cases (cases 45 and 51) the diagnosis was considered proved in this way as cardiac catheterization and angiocardiography had not been performed.

The recognition of an infundibular chamber normally presents little difficulty and its presence strongly favors the diagnosis of the tetralogy. Valvular stenosis, on the other hand, is of no diagnostic value.

SUMMARY

1. Fourteen cases of severe pulmonary stenosis with intact ventricular septum and right-to-left interatrial shunt and 48 cases of the tetralogy of Fallot have been analyzed to assess the points of value in the differential diagnosis.

2. The methods used in establishing conclusive proof of the diagnosis in each case are described.

3. The most important and constant clinical differentiating features are the findings on auscultation. Thus, in severe pulmonary stenosis with intact ventricular septum the systolic murmur at the site of maximal intensity is so prolonged that it extends beyond and obscures the normal aortic component of the very widely split second sound. It stops, however, before the markedly delayed diminutive pulmonary component, which may or may not be audible. In the tetralogy of Fallot on the other hand, the systolic murmur starts soon after the first sound, reaches maximal intensity by midsystole and then diminishes markedly usually ending before the single loud, often palpable aortic component of the second sound. Other auscultatory findings of some importance are described.

4. Examination of the neck veins is second only to auscultation in importance in the clinical differentiation. A giant "a" wave excludes uncomplicated tetralogy of Fallot where the "a" wave is usually normal. A dominant "a" wave strongly favors severe pulmonary stenosis with intact ventricular septum.

5. In severe pulmonary stenosis with intact ventricular septum the heart is usually normal in size but may be considerably enlarged; there is usually a marked sustained lift over the right ventricular outflow tract and the second heart sound is not palpable. In the tetralogy the heart is normal in size as a rule and the lift over the second right ventricle is insignificant. However, the second sound is often easily palpable and a systolic thrust in the pulmonary area, presumably due to the anteroposed aorta, is occasionally felt.

6. A delayed onset of central cyanosis favors severe pulmonary stenosis with intact ventricular septum but may occasionally occur in the tetralogy. Cyanosis developing in the first year favors the tetralogy but may also occur in severe pulmonary stenosis with intact ventricular septum. The intensity of cyanosis at rest is on the whole greater in the tetralogy than in severe pulmonary stenosis with intact ventricular septum.

7. A history of squatting occurs more commonly in the tetralogy than in severe pulmonary stenosis with intact ventricular septum, but is of no help in the diagnosis of the individual case.

8. Dyspnea, clubbing, polycythemia, effort syncope, and stunting of growth are common to both conditions.

9. A history of angina pectoris favors severe pulmonary stenosis with intact ventricular septum.

10. Whereas right atrial and right ventricular hypertrophy are electrocardiographic features common to both conditions, the pattern of extreme right ventricular hypertrophy favors severe pulmonary stenosis with intact ventricular septum.

11. In a large proportion of cases the diagnosis can be suggested on radiologic grounds alone. In severe pulmonary stenosis with intact ventricular septum, the heart is usually larger and there is marked poststenotic dilatation of the pulmonary arteries. In the tetralogy the heart is often sabot shaped. The aorta is generally unusually wide and may be right-sided. However, many features overlap in both conditions. Moreover, in a number of cases the cardiac silhouette is within normal limits. Pulmonary oligemia and right ventricular hypertrophy are common to both conditions.

12. The diagnosis can usually be made by cardiac catheterization. The demonstration of an infundibular stenosis favors the tetralogy but valvular stenosis is common to both. Passage of the catheter from the right ventricle into the aorta excludes severe pulmonary stenosis with intact ventricular septum. The presence of an "a" wave of 9 mm Hg or more excludes uncomplicated tetralogy of Fallot. Passage of the catheter from the right atrium to the left does not prove the diagnosis of severe pulmonary stenosis. A pressure gradient from right-to-left atrium and/or the demonstration of a right-to-left interatrial shunt favors the latter diagnosis.

13. Selective angiocardiography is a useful method for establishing the diagnosis of the tetralogy of Fallot. The aorta usually can be filled by injecting diodone into the right ventricle and the infundibular chamber can often be outlined.

14. Intravenous angiocardiography usually produces simultaneous opacification of the aorta and pulmonary arteries in both conditions. Differentiation of the two is best seen in the left oblique projection. In severe pulmonary stenosis with intact ventricular septum, marked early opacification of the left atrium and left ventricle accounts for the premature opacification of the aorta. In the tetralogy the aorta is filled from the right ventricle. In the anteroposterior projection the infundibular chamber can sometimes be outlined favoring the tetralogy. An unusually large aorta and anomalies of the aortic arch favor the tetralogy.

15. An accurate diagnosis can usually be made at the bedside. Cardiac catheterization and angiocardiography provide special anatomic information useful to the surgeon and may be essential for the diagnosis in the occasional case.

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Louis Vogelpoel, M.B., M.R.C.P.
Dept. of Medicine
University of Cape Town
Cape Town, South Africa

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CHAPTER III

ASSESSMENT OF SEVERITY BY AUSCULTATION AND PHONOCARDIOGRAPHY IN PULMONARY AND INFUNDIBULAR STENOSIS WITH INTACT VENTRICULAR SEPTUM

FOREWORD

In this chapter and in Chapter IV, the main purpose has been to study the effect on the systolic murmur and heart sounds of increasing severity of stenosis in pulmonary stenosis and Fallot's tetralogy. If the thesis outlined in Chapter I, pages 11-14 is correct, then increasingly severe stenosis should exert an opposite effect on the murmur length in the two conditions, lengthening it when the septum is intact and shortening it in the tetralogy. It will be shown that this is true; moreover, in each condition, the relationship between murmur length and severity is sufficiently precise to enable accurate prediction of severity from auscultation. Other criteria, also of value, are described.

INTRODUCTION.

The complete diagnosis in a case of pulmonary stenosis must include correct assessment of the anatomical situation as well as its severity. In Chapters I and II it was shown that severe pulmonary stenosis with intact ventricular septum could be differentiated from Fallot's tetralogy by the striking difference in the duration of the systolic murmur. It was also suggested that the severity of the stenosis influences the duration of the murmur in opposite fashion in the two conditions. Increasingly severe stenosis appeared to lengthen the murmur when the ventricular septum was intact but shortened it when a large septal defect was present (Fallot's tetralogy). This was additional support for the thesis that the systolic murmur was influenced by a different mechanism in the two conditions.

The purpose of this chapter is to draw attention to the value of auscultation and phonocardiography in diagnosing the severity of stenosis when the ventricular septum is intact. Their value in Fallot's tetralogy will be described in Chapter IV. Reliable criteria based on the murmur length and width of splitting of the second sound will be defined enabling accurate prediction of the severity of the stenosis. These criteria are of considerable value in assessing the result of surgery, as described in Chapter V.

Severity of stenosis in cases with intact ventricular septum is most precisely determined by cardiac catheterization, but it is believed that auscultation and phonocardiography are superior to other clinical methods such as electrocardiography and radiology.

In the tetralogy, however, it is not sufficiently appreciated that electrocardiography, radiology and even cardiac catheterization are usually unhelpful in assessing severity, whereas auscultation and phonocardiography will be shown to be accurate, simple and invaluable for this purpose.

Diagnosis of the severity of the stenosis is of great importance since the symptomatology, natural history and management is determined by the degree of stenosis in both conditions. While this statement is obviously true when the ventricular septum is intact, it also holds for the tetralogy because surgical relief of the stenosis alone results in disappearance of symptoms and cyanosis, despite persistence of the ventricular septal defect[15, 22].

MATERIAL AND METHODS.

Forty-three cases of pulmonary valvular stenosis and 8 of infundibular stenosis with intact ventricular septum were studied. The diagnoses were confirmed in all by cardiac catheterisation and angiocardiography, and in 19 cases at operation, using methods previously described[1, 2]. One case came to necropsy. All cases of pulmonary stenosis associated with a left-to-right shunt in the atria or ventricles were excluded from this study. Mild pulmonary stenosis was included only if the right ventricular pressure was elevated above 30 mm.Hg.; below this the value idiopathic dilatation of the pulmonary artery was diagnosed. No case in frank cardiac failure was included.

Full clinical examination with special attention to auscultation was carried out in all cases, after which data were compared and finally checked with the phonocardiogram (PCG). Particular attention

was paid to the intensity and duration of the systolic murmur at the site of its maximal intensity. The intensity was graded from 1 - 6 and the duration analysed by noting whether the crescendo was in early, mid or late systole, whether the murmur ended before, at or extended beyond the aortic component of the second sound and whether this sound was clear, partially buried or obscured by the murmur. The presence or absence of splitting of the second heart sound was noted and, if present, the degree of splitting on held expiration graded from 1 - 4 and the intensity of each component noted. The first sound was studied during respiration and held expiration for its intensity, width of splitting and the presence or absence of pulmonary or aortic ejection sounds. The presence or absence of sounds and murmurs in diastole was also noted.

High frequency (logarithmic) sound tracings which give an accurate graphic representation of human hearing[12, 19, 20] were recorded in every case and frequently repeated from time to time, particularly in those cases subjected to surgery. A modified two channel Sanborn Stethocardiette was used in the early cases but a six-channel E.E.P. recording apparatus with two PCG channels was later substituted. Sound tracings were recorded synchronously with E.C.G., indirect carotid and jugular tracings. In most cases sound recordings were repeated during cardiac catheterisation to obtain synchronous PCG, right ventricular or pulmonary artery tracings with external carotid artery tracings. Recordings were made in the mitral area (MA), fourth intercostal space just to the left of the sternum (4LS), the third left intercostal space (3LS), pulmonary area (PA) and aortic area (AA). The amplification chosen was purely qualitative,

designed to give the best recording for the particular purpose. Thus, to record a very soft sound, greater amplification was used; conversely to measure more accurately the site in systole of the crescendo of a very loud murmur, less amplification was used. The degree of amplification was always noted so that subsequent recordings, in particular those taken after surgery, could be taken at the same amplification for comparison. This method was roughly quantitative when used on the same patient, provided no marked changes occurred in chest wall thickness, but a method of sound calibration would have been desirable. However, as this study was chiefly concerned with changes in duration of murmur and width of splitting of the second heart sound, accurate measurements of intensity were not required.

Mitral and tricuspid components of split first sounds, aortic and pulmonary ejection sounds and aortic and pulmonary components of split sounds were identified by the methods described in Chapter I and always measured during held expiration unless otherwise stated. Tracings recorded at high speed (80 mm. per sec.) were essential for accurate study. The intervals were always measured from the onset of the deflections whether recorded in the PCG, ECG, indirect or direct pulse recordings.

The systolic murmur was analysed in suitable tracings recorded during expiration at the site of maximal intensity of the murmur. The crescendo and duration of the murmur were measured from the first component of the first sound to the peak and the end of the murmur respectively. The time taken for the systolic murmur to reach its crescendo was expressed as a percentage of the time between the first heart sound and the aortic second sound (left ventricular systole) (Diagram 1 (a)). Thus, if the crescendo occurred in mid-systole, it would be expressed as 50%, whereas if it occurred at the aortic second sound it would be 100%. Similarly, the total duration of the murmur was expressed as a percentage of the time between the

first heart sound and the aortic sound and if it extended beyond the aortic sound some figure above 100% would be obtained (Figs. 2 and 5). The degree to which the aortic second sound was buried by the murmur was also expressed as a percentage. This was obtained by expressing the mean amplitude of the murmur where it transected the sound, as a percentage of the mean amplitude of the sound (Diagram 1 (b)). The degree of burying thus varied from 0 - 100% (Table 1, and Fig. 4). All measurements were made in at least 10 different systoles and the mean taken.

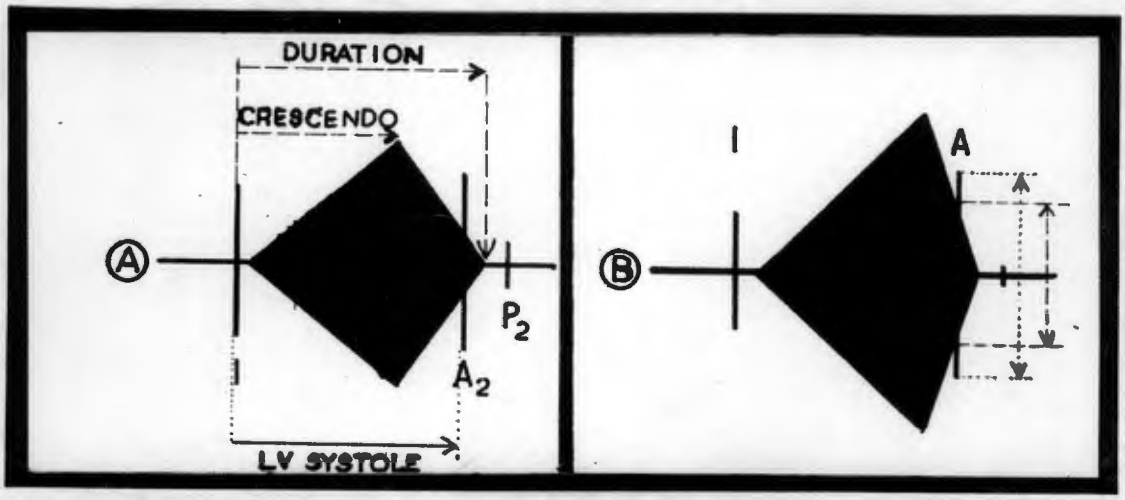

Diagram 1. (A) Shows method of measuring the systolic murmur (crescendo and duration) and left ventricular systole (1 - A). (B) shows method of measuring the degree of burying the aortic sound by the murmur. See text for details.

Routine electrocardiograms included the standard and unipolar limb leads and the praecordial leads V1 to V7. V3R was often included. The degree of right ventricular hypertrophy was graded from 1 - 4 in severity. Routine radiological investigation included fluoroscopy and skiagrams.

The severity of valvular or infundibular stenosis with intact ventricular septum was assessed by the right ventricular pressure measured during cardiac catheterisation under barbiturate or morphine sedation. An arbitrary grading was used as follows: when the systolic pressure was under 60 mm.Hg., stenosis was considered mild (14 cases), between 60 and 120 mm.Hg., moderate (10 cases), between 120 and 180 mm.Hg., severe (15 cases) and over 180 mm.Hg., very severe (4 cases) (Table 1). Eight cases of infundibular stenosis were similarly graded (Table 1). There was one mild case, 4 moderate cases, 1 severe case and 2 very severe cases. In both the latter, the pressures exceeded 200 mm.Hg., and in both a very small ventricular septal defect of no dynamic significance was found at surgery.

RESULTS AND DISCUSSION.

(A) VALVULAR STENOSIS

In pulmonary stenosis with intact ventricular septum increasingly severe stenosis results in progressive increase in pressure and duration of right ventricular systole[1,2,11].* When stenosis is severe, both the pressure and duration of right ventricular systole greatly exceed that of the left. The duration of the right ventricular systole in pulmonary stenosis can be detected clinically by the duration of the systolic murmur and the width of splitting of the second heart sound. It is now well recognised that with increasingly severe stenosis the murmur becomes more prolonged and the splitting wider[1,5,24,25]. Conversely, production of mild stenosis by a valvotomy promptly shortens the murmur and reduces the width of splitting, thereby neatly confirming these views [(Chapter V) and (Fig. 6)].

* Footnote: This statement holds only for cases not in right ventricular failure. Once failure, with or without tricuspid incompetence occurs and a fall in cardiac output supervenes, the correlation between the pressure and duration of right ventricular systole with severity of stenosis will clearly become changed.

TABLE 1

ANALYSIS OF AUSCULATATORY AND PCG FINDINGS IN PULMONARY AND INFUNDIBULAR STENOSIS WITH INTACT VENTRICULAR SEPTUM.

Severity mm.Hg	No.of Cases	Systolic Murmur				A2 in Pulm.Area (Auscultation).	P2	Width of Split (in exp) (Sec).	Aortic Ejection Sound	Pulm. Ejection Sound
		Intensity	Crescendo (% LV systole)	Duration (% LV systole)	% Burying of A2 by SM					
VALVULAR STENOSIS										
Mild (RVP<60)	14	2-5	32-65 Mean 51	76-100 Mean 96	0-42 Mean 15	N	N	0.02-0.09 Mean 0.05	0	43%
Moderate (RVP 60-120)	10	3-5	53-89 Mean 67	94-117 Mean 103	0-83 Mean 37	N	Soft	0.05-0.12 Mean 0.07	0	40%
Severe (RVP 120-180)	15	3-5	62-93 Mean 77	100-125 Mean 115	36-100 Mean 78	Partially buried in in 6. Buried 8.	Soft (Absent in 2).	0.06-0.12 Mean 0.08	0	Click-like 1st Sound 55%
V.Severe (RVP>180)	4	4-5	71-88 Mean 80	120-125 Mean 123	100	Buried	V.Soft (Absent in 1).	0.09-0.10 Mean 0.10	0	Click-like 1st Sound 50%
TOTAL	43									
INFUNDIBULAR STENOSIS										
Mild (RVP<60)	1	5	50	100	20	N	N	0.07	0	0
Moderate (RVP 60-120)	4	4-5	48-69 Mean 60	115-117 Mean 116	56-100 Mean 70	N	Soft	0.09-0.12 Mean 0.10	0	0
Severe (120-180)	1	5	74	126	100	Almost buried	0	0.12	0	0
V.Severe (RVP>180)	2	5	80-85	128-133	100	Buried	Very soft (Absent in 1)	0.14	0	0
TOTAL	8									

In health, the two components of the second heart sound are fused or closely split on expiration (up to 0.03 sec)[5], but separate during inspiration, due to delay in the pulmonary component. In pulmonary stenosis splitting is abnormally wide due to greatly delayed closure of the pulmonary valve from prolongation of right ventricular systole[1,12]. Since the aortic component marks the end of left ventricular systole and the pulmonary component the end of right ventricular systole, measurement of the width of separation of the two components gives a useful indication of the degree of prolongation and indirectly the pressure of right ventricular systole[5]. The duration of right ventricular systole can also be determined by the duration of the murmur using new methods of measurement (vide supra). Since the murmur becomes prolonged with increasing duration of systole, it extends up to, into or beyond the aortic second sound depending on the severity of the stenosis. Prolongation of right ventricular systole can therefore be measured by relating the duration of the murmur to the duration of left ventricular systole (time interval between first and aortic second sound). The ratio so obtained can be used to assess the severity of stenosis. The degree to which the aortic second sound is buried by the murmur reflects the intensity of the murmur at the termination of left ventricular systole providing another but indirect method of assessing the length of murmur.

In this study the duration of right ventricular systole determined by these methods has been correlated with the right ventricular systolic pressure in order to define criteria for assessing the severity of stenosis by auscultation and phonocardiography. The findings are analysed in Table 1 and Figs. 1 - 5.

Mild pulmonary stenosis - There were 14 cases with right ventricular systolic pressure under 60 mm.Hg. All had a soft to loud (grade 2-4) systolic murmur which reached a crescendo in midsystole (range 32-65% of left ventricular systole; mean 51%), and ended before or at the aortic component (range 76-100%; mean 96%). The aortic component was always clearly audible, the degree of burying by the murmur being 0-42%, with a mean of 15%. The second sound was abnormally widely split in expiration (range 0.02-0.09 sec.; mean 0.05 sec.) and the pulmonary component not reduced in intensity. A pulmonary ejection sound was sometimes found (43% of cases) but not invariably, as stated by Leatham and Weitzman[5].

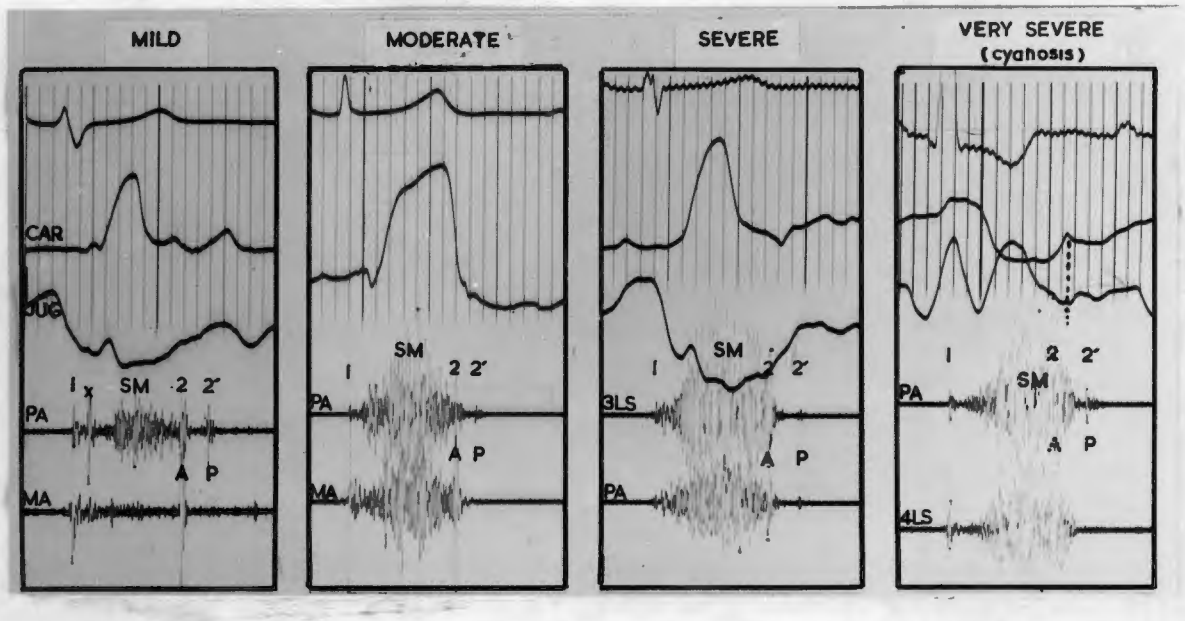

Fig. 1. Pulmonary Stenosis With Intact Ventricular Septum.

In the mild case (RVP 42/4, PAP 16/6 mm.Hg.) the crescendo of the systolic murmur was in midsystole and the murmur ended at the aortic component (A2). The second sound was widely split (0.09 sec.) partly due to gross post-stenotic dilatation. There was a pulmonary ejection sound (X). In the moderately severe case (RVP 95/10, PAP 17/10 mm.Hg.) the murmur was louder and extended a short distance beyond the aortic component, but did not obscure it. The pulmonary component was soft and delayed (0.07 sec.) after the aortic component. In the severe case (RVP 120/4, PAP 18/10 mm.Hg.) the crescendo of the loud murmur was later, and the murmur extended well beyond the aortic component which it partially obscured. The pulmonary component was very soft and delayed 0.09 sec. In the very severe case (RVP 225/5, PAP 20/10 mm.Hg. with RL atrial shunt) the murmur was so prolonged that it extended far beyond the aortic component which it completely obscured. The murmur ended before an easily audible pulmonary component which was followed by trivial pulmonary incompetence. The very wide splitting could not be heard but synchronous PCG's at the pulmonary and mitral area disclosed splitting of 0.11 sec.

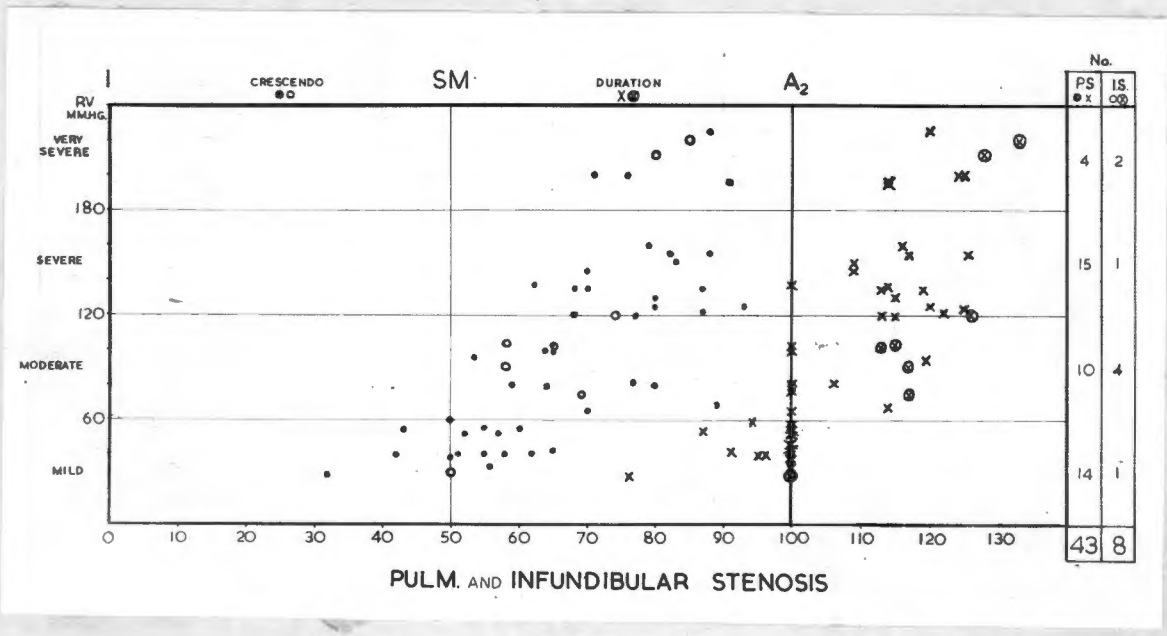

Fig. 2. The relation of the crescendo (●) and duration (X) of the systolic murmur in 43 cases of pulmonary stenosis and 8 cases of infundibular stenosis (O and ⊗ respectively) to the duration of left ventricular systole (1-A2). The severer the stenosis, as judged by the right ventricular systolic pressure, the greater the duration of right ventricular systole as reflected by the crescendo and duration of the systolic murmur. The duration of the murmur appears greater in infundibular stenosis than in valvular stenosis of comparable severity.

Moderate pulmonary stenosis - There were 10 cases with a right ventricular systolic pressure between 60 and 120 mm.Hg. The systolic murmur tended to be louder than in mild cases (grade 3-5), the crescendo later than midsystole (range 53-89%; mean 67%) and the duration greater, often extending beyond the aortic second sound (range 94-117%; mean 103%). The aortic component was always audible, the degree of burying by the murmur being 0-83% with a mean of 37%. The second sound was widely split in expiration (range 0.05 - 0.12 sec; mean 0.07 sec.) and the pulmonary component softer than normal. A pulmonary ejection sound was heard in 40% of cases.

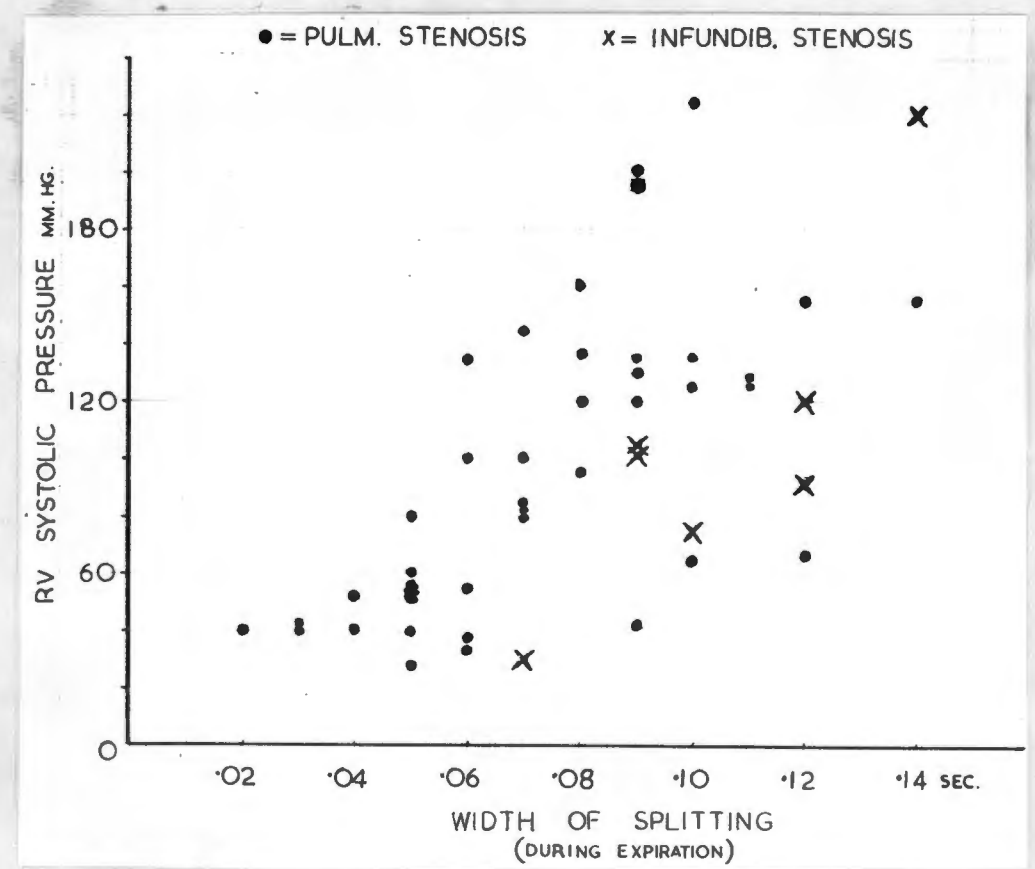

Fig. 3. Relation of the width of splitting (delay in pulmonary valve closure) to the right ventricular systolic pressure in pulmonary valvular stenosis (●) and infundibular stenosis(X) to right ventricular systolic pressure. Unusually wide splitting was found in infundibular stenosis and in those cases of valvular stenosis associated with marked post-stenotic dilatation.

Severe pulmonary stenosis - There were 15 cases with a right ventricular systolic pressure between 120 and 180 mm.Hg. Five were cyanosed from a right-to-left interatrial shunt. The systolic murmur was loud (grade 3-5) in intensity, similar to the moderate and very severe groups. The crescendo occurred later than in moderate cases (62-93%; mean 77%) and the duration greater, extending well beyond the aortic component of the second sound (range 100-125%; mean 115%). The murmur appeared kite-shaped rather than diamond-shaped. The aortic component was partially buried by

the murmur in 6 cases and totally obscured in 8. The degree of burying ranged between 36 and 100% with a mean of 78% Fig. 4 shows that whenever the aortic sound was completely obscured by the murmur, the right ventricular pressure was above 120 mm.Hg. The murmur always ended before the pulmonary component, which was abnormally soft in 12 cases and inaudible in two. Splitting on expiration tended to be wider than in moderate cases, averaging 0.08 sec. with a range of 0.06 - 0.12 sec. Splitting could not be heard when the aortic component was buried but could be demonstrated and measured on the PCG (Fig. 6).

The first sound in the third left interspace was abnormally loud on expiration in 8 cases (55%). The loud sound coincided with the second component of a closely split first sound. Whether this was due to loud tricuspid valve closure or an unusually early pulmonary ejection sound could not be determined, but one favours the latter for the following reasons. The sound was sharp and click-like in quality. Its behavior with respiration was similar to the pulmonary ejection sound found in milder cases of pulmonary stenosis, being very loud at the onset of expiration yet often absent during inspiration (see Fig. 9, Chapter I). In severe pulmonary stenosis where the pulmonary diastolic pressure is low and, in consequence, the isometric contraction time of the right ventricle short, a pulmonary ejection sound would be early. It may indeed occur so early that confusion with tricuspid valve closure might result. Furthermore, in a severe case converted to a mild one by a successful valvotomy, the pre-operative PCG revealed a loud "second component" of a closely split first sound, whereas the post-operative PCG showed a clear pulmonary ejection sound following normal splitting of the

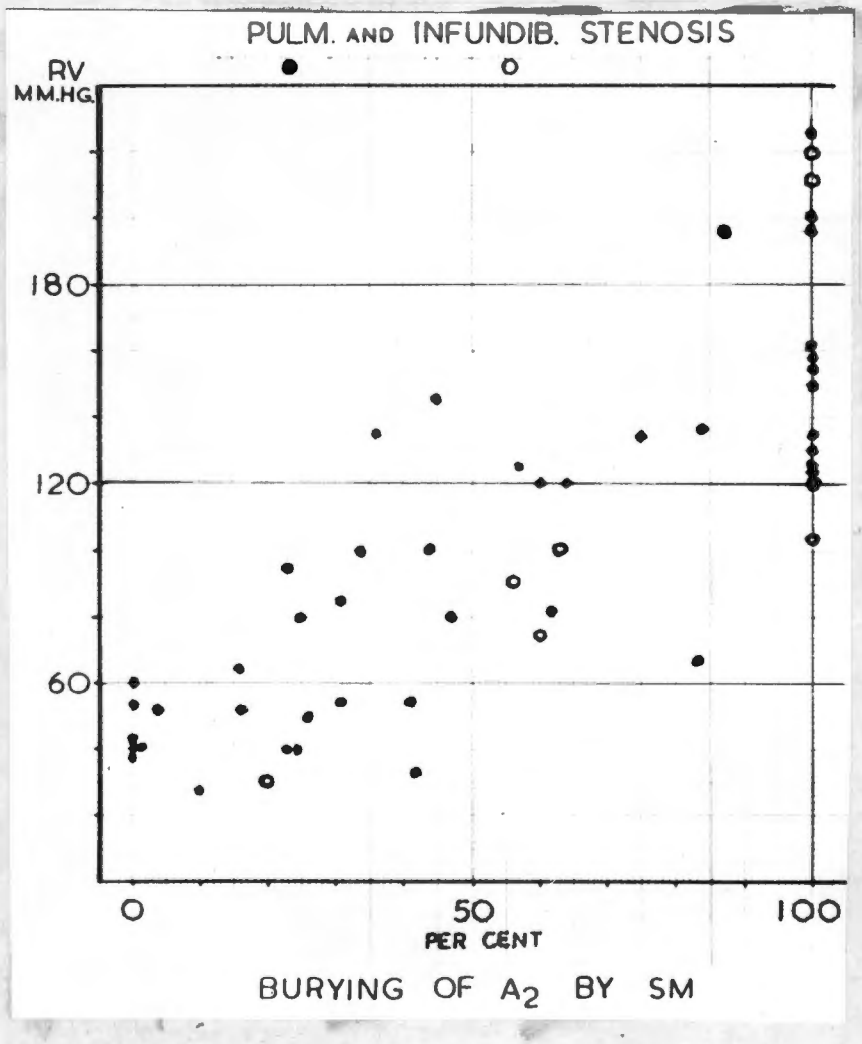

Fig. 4. The degree of burying of the aortic component of the second sound by the systolic murmur in relation to the severity of the stenosis. This expresses the loudness of the murmur where it transects the aortic sound as a percentage of the amplitude of the sound. In both pulmonary and infundibular stenosis, the degree of burying steadily increases with increasing severity of the stenosis. In severe cases (RVP above 120 mm.Hg.) the sound is usually partially or totally obscured. If the aortic sound is completely obscured the RVP is above 120 mm.Hg.

first heart sound (Fig. 6). It was felt that an increase in isometric contraction time of the right ventricle would accompany conversion to mild stenosis and that this might shift a pulmonary ejection sound to a later position in systole, thereby clearly separating it from the first sound and making it recognisable as a pulmonary ejection sound.

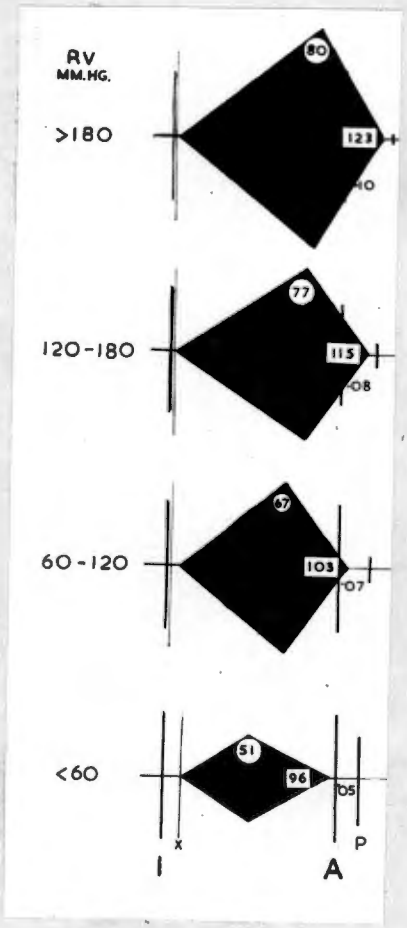

Fig. 5. This diagram illustrates the progressive prolongation of murmur length and width of splitting with increasing grades of severity of pulmonary stenosis with intact ventricular septum. The mean time of the crescendo and duration of the murmur, each expressed as a percentage of the duration of left ventricular systole, is indicated and drawn to scale for each group, as well as the mean width of splitting. With increasing severity the murmur becomes kite-shaped due to delay in the crescendo and marked lengthening of the murmur. The murmur progressively obscures more of the aortic component (A) but always ends before the pulmonary component (P) which becomes more delayed and softer. The pulmonary ejection sound (X) follows the first sound in the mild cases, but in severe grades coincides with the first sound as indicated.

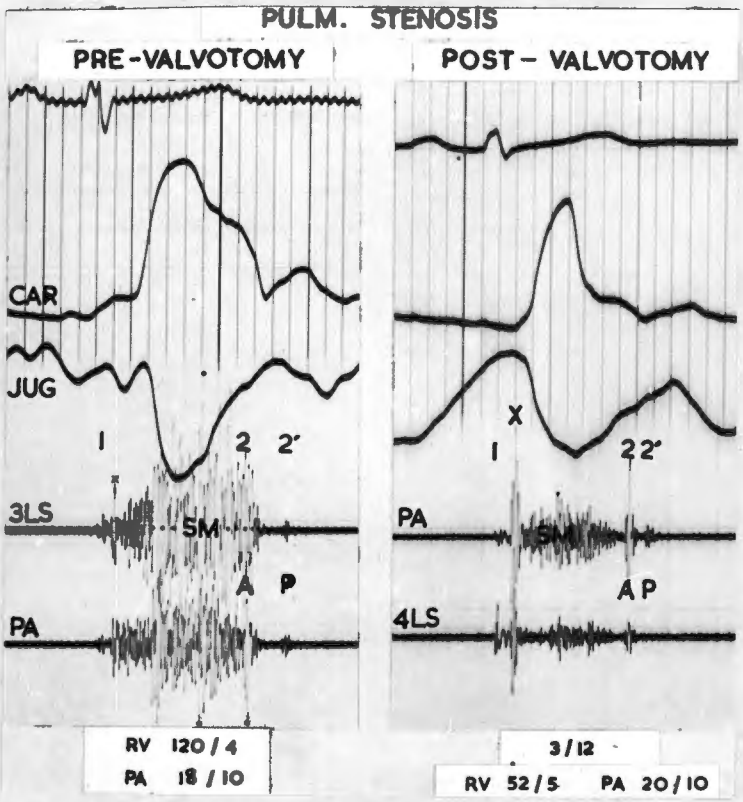

Fig. 6. Pulmonary stenosis before and after valvotomy. Prior to surgery the murmur was very loud and prolonged almost completely obscuring the aortic component at the site of maximal intensity (3LS). There was wide splitting (0.09 sec.) and a sharp click-like first sound on expiration. The features were those of severe stenosis and the RVP was 120/4 mm.Hg. and PAP 18/10 mm.Hg. After valvotomy the murmur became softer and much shorter, the degree of splitting much less (0.04 sec.) and a striking pulmonary early systolic sound (X) emerged. The features were now those of mild stenosis and an excellent result was predicted. This was confirmed on re-catheterisation 3 months after valvotomy (RVP 52/5; PAP 20/10 mm.Hg.)

Very severe pulmonary stenosis - There were 4 cases with a right ventricular pressure exceeding 180 mm.Hg. In two, the pressure was above 200 mm.Hg. Two cases were cyanosed from a right-to-left interatrial shunt. The systolic murmur was very loud (grade 4-5), extremely prolonged and kite-shaped with the crescendo occurring very late (range 71-88%; mean 80%) and the duration invariably extending well beyond the aortic component (range 120-125%; mean 123%). In every case the aortic component was completely buried

by the murmur at the site of maximal intensity. The murmur always ended before the pulmonary second sound, which was abnormally soft and hence heard only in the pulmonary area. In 1 case it was inaudible and unrecordable.

Splitting could never be appreciated by the ear because the aortic component was completely obscured by murmur in the pulmonary area, which was the only site at which the very soft pulmonary component could be heard. At sites where the aortic component was audible, due to less intense murmur, the pulmonary component was inaudible. However, by using synchronously recorded PCG's from PA and MA, the width of the splitting could be measured, provided the pulmonary component was recordable. In the 3 cases the width of splitting was very great, being 0.09, 0.10 and 0.10 sec. respectively. Since the width of splitting in cases with a buried aortic sound could not be heard, the only auscultatory guide to the excessive prolongation of right ventricular systole was the length of the murmur. The finding of a loud, very prolonged systolic murmur completely burying the aortic component but ending before a diminutive pulmonary component was sufficient to predict a right ventricular pressure exceeding 120 mm.Hg. (Fig. 4). The pulmonary component was always easy to distinguish from the aortic because it was so soft and always followed the end of the murmur.

A pulmonary ejection sound was not heard, but in 2 cases the first sound had a sharp click-like quality during expiration, similar to that found in severe stenosis. Other auscultatory findings of lesser value in assessing the severity of the stenosis were also found. An atrial sound and a presystolic murmur to the left of the sternum may occur in severe stenosis (see Fig. 8, Chapter I). This was ascribed to severe right atrial hypertrophy.

where the giant "A" wave exceeded the pulmonary diastolic pressure. The pulmonary valve could thus be opened by this wave and pulmonary ejection initiated before the onset of right ventricular systole, resulting in the presystolic sound and murmur. A pulmonary incompetent murmur occurred in three cases, but was of no value in the assessment of the severity of the stenosis occurring in moderate, severe and very severe cases.

COMMENT.

While auscultation alone permitted an accurate prediction of the grade of severity, study of the graphic recording made the assessment more certain. The length of the murmur was found to be of greater value than the width of splitting since it was easier to assess on auscultation. In the analysis of the P.C.G., measurement of murmur length was also more dependable than the width of splitting (Fig. 7., compare Figs. 2 and 3).

Leatham and Weitzman[5] found a surprisingly close relation between the width of splitting and the right ventricular systolic pressure, bearing in mind that the PCG and cardiac catheterisation were usually recorded on separate occasions. They emphasised the value of this method, since prolongation of right ventricular systole is measured in relation to left ventricular systole in the same patient and in the same cardiac cycle. However, the same advantage holds for measurements of the length of murmur. Their findings were confirmed in the severe cases but I found several important exceptions in the mild and moderate grades (Fig. 3). In a mild case (RVP 42/4; PAP 16/1 mm.Hg.) the width of splitting on expiration was 0.09 sec. (Fig.7). In a case of moderate severity (RVP 67/10; PAP 13/5 mm.Hg.) the width of splitting was 0.12 sec. and in a third case also of moderate severity (RVP 65/0; PAP 17/2 mm.Hg.), the split measured

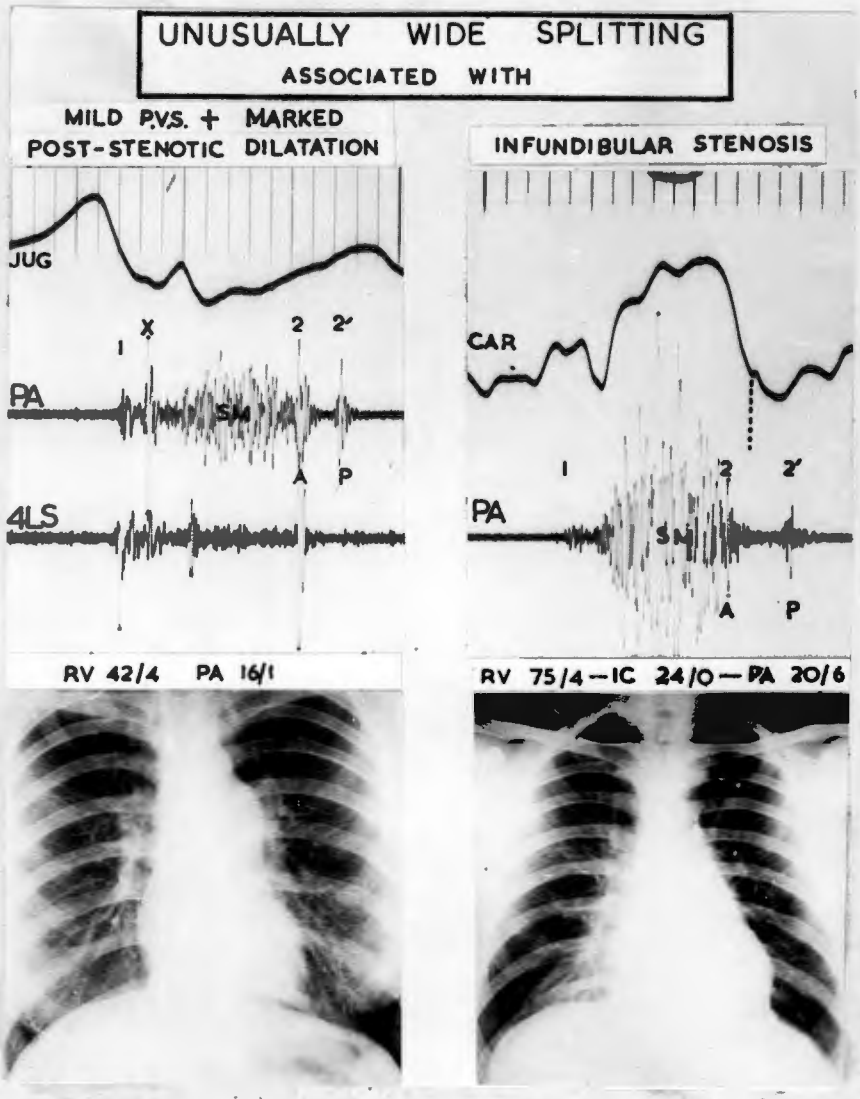

Fig. 7. Unusually wide splitting in pulmonary and infundibular stenosis. In valvular stenosis the length of the murmur was that of mild stenosis yet the delay in pulmonary valve closure was exceptionally great (0.09 sec.) and attributed in part to the associated marked post-stenotic dilatation. The severity of the stenosis was correctly predicted by the length of the murmur but not by the width of splitting. In the case of the moderate infundibular stenosis the severity was correctly predicted by the length of the murmur but not by the gross splitting (0.12 sec.) The greater delay of pulmonary valve closure in infundibular stenosis cannot be attributed to post-stenotic dilatation but is probably due to delayed emptying of the infundibular chamber. Note the pulmonary ejection sound in mild valve stenosis and its absence in infundibular stenosis.

0.10 sec. In these cases, prediction of the right ventricular pressure from the width of splitting on expiration alone would have given an unreliable estimate of severity, but using the criteria of murmur length, correct prediction was possible.

The reason for the exceptionally wide splitting found in these cases was obscure, as the usual causes could be excluded. Thus there was no right bundle branch block to cause delay in onset of right ventricular systole, no shortening of left ventricular systole and no case had a left-to-right shunt. However, a striking feature common to all 3 cases was gross post-stenotic dilatation of the pulmonary artery suggesting that this might be the determining factor (Fig.7). In support of this possibility is that dilatation of this magnitude was never encountered in the severer cases where the width of splitting more accurately reflected the severity. It is well known that the degree of post-stenotic dilatation bears no relation to the severity of stenosis[2]. It is in fact apt to be much greater and more variable in the milder cases where the lack of correlation with width of splitting is most apparent. It is believed that the elastic recoil of the pulmonary artery may be an important, hitherto unrecognised factor in influencing the time of closure of the pulmonary valve. In a greatly dilated pulmonary artery with thin, inelastic walls, not only would there be greater delay in the filling of the vessels during ejection but the elastic recoil after ejection would be less vigorous. This might delay pulmonary valve closure quite independently of the duration and pressure of right ventricular systole. The low pulmonary diastolic pressure found in these cases may support such a mechanism, since none had pulmonary incompetence. It is of interest that I have found abnormally wide splitting in a few cases of idiopathic dilatation of the pulmonary artery where no factors other than the dilated artery could account for the delay (up to 0.05 sec. in expiration in one case).

The disadvantage of assessing the severity from the width of splitting alone lies in the fact that in severer cases where the

correlation is good, splitting is usually inaudible, whereas in the milder cases where splitting is easily heard, the correlation is less reliable. If the murmur is relatively short, suggesting mild stenosis but the splitting wide, suggesting severe stenosis, more reliance should be placed on the murmur. Such cases usually have mild or moderate stenosis with marked post-stenotic dilatation.

There were 2 cases where the length of the murmur was much shorter and the width of splitting narrower than expected for the height of right ventricular pressure. Both cases had left ventricular hypertrophy (moderate systemic hypertension (200/125 mm.Hg.) in one and severe aortic stenosis (LVP 250/10; brachial arterial P. 85/60 mm.Hg.) in the other. The reason for the shorter murmur, and hence shorter duration of right ventricular systole, was not solely due to moderate prolongation of left ventricular systole. Possibly the hypertrophied left ventricle (and interventricular septum) enabled the right ventricle in some obscure fashion, to achieve a high pressure (150 in the first case, 145 in the second) without the expected prolongation of systole.

The pulmonary ejection sound was of some value in grading the severity of the stenosis. If it occurred well after the first sound producing "wide splitting" of the first sound in the pulmonary area, the stenosis was mild or moderate, but never severer than this (Fig. 7). If, however, the first sound was either single or very closely split being sharp and click-like on expiration, the stenosis was usually severe (Fig. 6).

B. <u>INFUNDIBULAR STENOSIS WITH INTACT VENTRICULAR SEPTUM</u>.

Whereas infundibular stenosis is much more commonly associated with a ventricular septal defect than with an intact ventricular septum, the latter situation is certainly encountered.

With increasingly severe infundibilar stenosis the pressure and duration of right ventricular systole progressively increases similar to that found in valvular stenosis. Thus a similar correlation between the auscultatory findings and the right ventricular pressure would be anticipated. This was, in fact, found to be the case. In our small series of 8 cases a full spectrum of severity was fortunately encountered. Thus, there was one mild case, 4 moderate cases, one severe case and 2 very severe cases (Table 1 and Figs. 2-4, 8). In both of the latter there was an associated small ventricular septal defect of no physiological significance. Similar small defects could not be detected in the other cases, but it is appreciated that the detection of minute septal defects can be extremely difficult. Additional confirmation of an intact or physiologically intact ventricular septum was obtained by the marked intensification of the murmur after amyl nitrite inhalation which excluded Fallot's tetralogy (3,23) (see Chapter VI).

Mild Infundibular stenosis - In the one case the right ventricular pressure was 30/0, the infundibular pressure was 15/0 and the pulmonary artery pressure 15/6 mm.Hg. The systolic murmur was very loud (grade 5), heard best in the third left interspace, with a crescendo in midsystole (50%) and ending at the aortic second sound (duration 100%). The aortic second sound was clearly audible, being only 20% obscured by the murmur. Both components of the second sound were of normal intensity and splitting was unusually wide (0.07 sec.) compared to cases of valvular stenosis of comparable severity (Figs. 3 and 8). There was no pulmonary ejection sound.

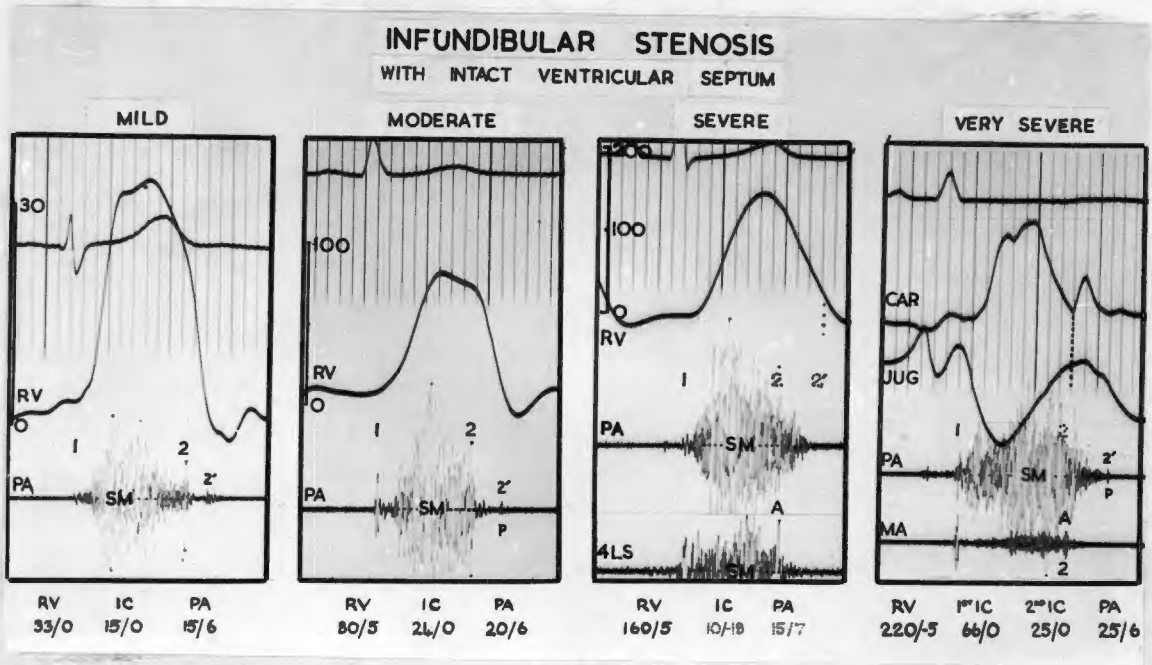

Fig. 8. Infundibular stenosis with intact ventricular septum. The crescendo and duration of the systolic murmur became more delayed and the degree of splitting of the second sound wider with increasing severity of the stenosis just as in valvular stenosis. In the severe and very severe cases, the aortic component was completely obscured by the very prolonged murmur and the great width of splitting could not be heard; however, the synchronously recorded PCG from the mitral area (MA) where the murmur was much less loud, disclosed the site of the buried aortic component in the murmur, and the width of splitting could thus be measured (0.14 sec.). In infundibular stenosis the delay of pulmonary valve closure was greater than in valve stenosis of equivalent severity and there was no pulmonary ejection sound.

Mild infundibular stenosis - In the one case the right ventricular pressure was 30/0, the infundibular pressure was 15/0 and the pulmonary artery pressure 15/6 mm.Hg. The systolic murmur was very loud (grade 5), heard best in the third left interspace, with a crescendo in midsystole (50%) and ending at the aortic second sound (duration 100%). The aortic second sound was clearly audible, being only 20% obscured by the murmur. Both components of the second sound were of normal intensity and splitting was unusually wide (0.07 sec.) compared with cases of valvular stenosis of comparable severity (Figs. 3 and 8). There was no pulmonary ejection sound.

Moderate infundibular stenosis — There were 4 cases with right ventricular systolic pressures between 60 and 120 mm.Hg. None had additional valvular stenosis. One case had a right-to-left atrial shunt. The systolic murmur was very loud in all (grade 4-5) and more prolonged than in the mild case, with the crescendo at or after midsystole (range 48-69%), and the duration exceeding that of the left ventricular systole (range 115-117%) mean 116%). The aortic second sound was audible, being only partially obscured by the murmur (range 56-100%; mean 70%). The pulmonary second sound was softer than normal and the width of splitting very wide (0.09 - 0.12 sec; mean 0.10 sec.) (Fig. 7). A pulmonary ejection sound was absent. The site of maximal intensity was in the third left interspace in all so that distinction from valvular stenosis could not be made. The greater duration of the murmur (Fig. 2) and width of splitting compared to cases of valvular stenosis (Fig. 3) is noteworthy.

Severe infundibular stenosis - There was only one case with a right ventricular pressure of 120/1 mm.Hg. The pressure in the infundibular chamber was 21/1, and in the pulmonary artery 16/10 mm.Hg. Central cyanosis was absent. The systolic murmur was very loud (grade 5), maximal in the third left interspace with the crescendo after midsystole (74%), ending well after the aortic second sound (126%). The aortic component was completely obscured (100%) but the pulmonary component though inaudible, was recorded, the width of splitting (0.12 sec.) being exceptionally great. There was no pulmonary ejection sound.

Very severe infundibular stenosis - There were 2 cases both with right ventricular systolic pressures well above 180 mm.Hg. Both cases were of special interest since small ventricular septal defects

were discovered at ventriculotomy. Because of their small size and physiological insignificance, the dynamics and physical signs were those of severe stenosis with intact ventricular septum.

The first case had very severe stenosis as judged by the pressure of 220/-5 in the low right ventricle, which far exceeded the systemic pressure of 135/100 mm.Hg. There were two pressure zones in the infundibular chamber, being 25/0 and 66/0 mm.Hg. The pulmonary arterial pressure was 24/6 mm.Hg. No shunt was detected and the septum was considered intact. At ventriculotomy using cardio-pulmonary by-pass, severe, low infundibular stenosis was found with a minute septal defect (2 mm. in diameter) opening into the infundibular chamber; the septum proximal to the stenosis was intact.

The systolic murmur was very loud (grade 5) and very prolonged (Fig. 8 and Fig. 5, Chapter V). The site of maximal intensity was low (fourth left interspace). The crescendo occurred well beyond midsystole (85%) and the duration far exceeded left ventricular systole (133%). The aortic sound was completely buried in the murmur. A very soft pulmonary second sound was audible. Splitting could not be heard, but the PCG showed great delay in pulmonary valve closure (0.14 sec.) (Figs. 2,3 and 8). There was no pulmonary ejection sound.

It may be argued that the small septal defect distal to the stenosis contributed a loud pansystolic murmur which would fuse with and distort the shape of the stenotic murmur. Indeed, the murmur of a small defect is frequently loud and has a late systolic crescendo[23]. However, such a murmur, being dependent on a left-to-right shunt, would end very soon after aortic valve closure and thus offer no contribution beyond this. Therefore the great prolongation of the murmur beyond the aortic second sound must be a function of the stenotic murmur, reflecting greatly prolonged right ventricular systole from very severe infundibular stenosis with intact proximal ventricular septum.

The second case will be considered separately since the septum proximal to the stenosis, though not anatomically intact, was believed to be physiologically intact.

VERY SEVERE INFUNDIBULAR STENOSIS WITH FUNCTIONALLY INTACT VENTRICULAR SEPTUM.

This case had a right ventricular pressure far exceeding the left and a small right-to-left interatrial shunt through a patent foramen ovale was demonstrated at cardiac catheterisation. The systolic murmur was very loud (grade 5), maximal in the pulmonary area and very prolonged, with the crescendo well after midsystole (80%), ending well after the aortic sound (120%). The aortic sound was completely buried and a pulmonary sound was neither audible nor recordable (Fig. 9). There was no pulmonary ejection sound. The diagnosis of very severe pulmonary stenosis with intact ventricular septum was therefore made. At ventriculotomy, under hypothermia, a high infundibular stenosis was found, the pressure being 215/5 in the right ventricle, 10/-18 in the infundibulum and 15/7 in the pulmonary artery. A catheter was passed into the aorta from the right ventricle, the pressure being much lower than in the right ventricle.

Following the resection, the murmur shortened considerably and moderately wide splitting emerged both suggesting that moderately severe stenosis had been produced. Catheterisation performed 7 weeks after surgery showed a right ventricular shunt proving the presence of a small ventricular septal defect (Fig. 9). The defect was clearly of no physiological significance since the murmur shortened appropriately with the drop in right ventricular pressure from 215 to 70. Had the defect been large, as in Fallot's tetralogy, an

infundibular resection would not have shortened the murmur (see Chapter V). The case masqueraded as severe infundibular stenosis with intact ventricular septum, since the septum was, in fact, functionally intact. A similar case with necropsy proof has been reported by McCord et al[21].

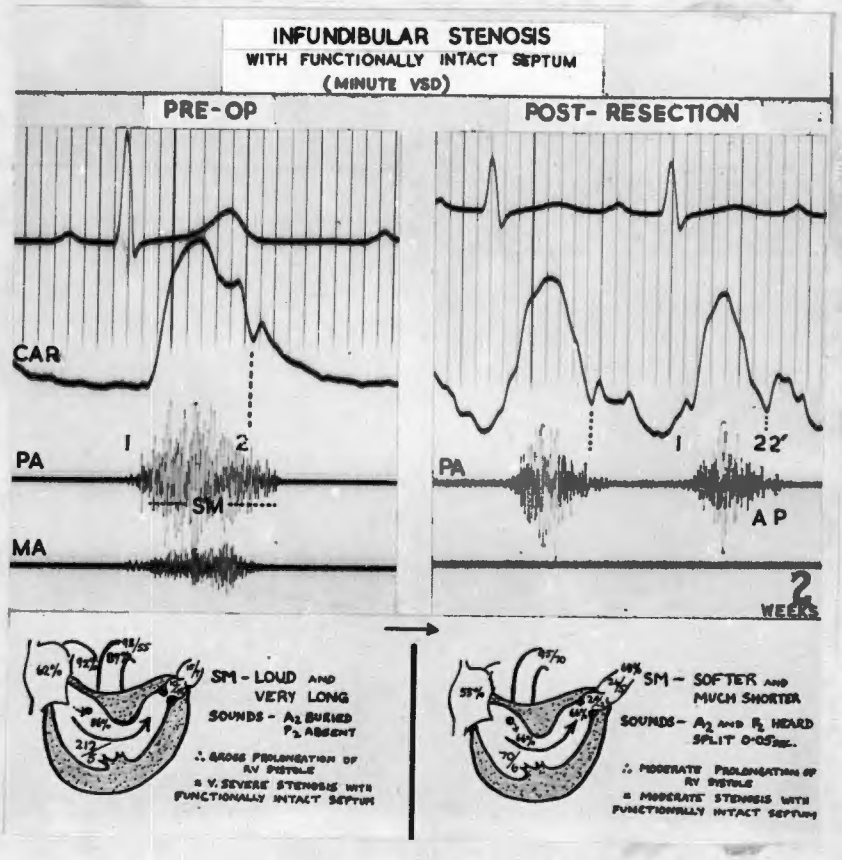

Fig. 9. Infundibular stenosis with functionally intact ventricular septum. Owing to the small size of the septal defect the dynamics and murmur length pre- and post-resection were those of intact ventricular septum. Note the rapid shortening of the greatly prolonged systolic murmur which far exceeded the duration of left ventricular systole. The post resection murmur length and width of splitting were those of moderately severe stenosis and re-catheterisation 2 weeks after surgery confirmed this as well as a small left-to-right shunt.

COMMENT.

These findings confirm the belief that infundibular stenosis, whether high or low, influence the auscultatory findings in the same way as valvular stenosis, provided the ventricular septum is anatomically and functionally intact. By using the length of the systolic murmur, the degree of burying of the aortic second sound and the width of splitting, the severity of the stenosis can be predicted as in the case of valvular stenosis (Figs. 2-5). Differentiation between infundibular and valvular stenosis can be most difficult, yet clearly the distinction is of great practical importance. The site of maximal intensity of the murmur proved of little value, since it was in the fourth left interspace in only one case. In the remainder it was loudest in the third left interspace, a site frequently shared by valvular stenosis. However, a number of new auscultatory signs emerged which were of value in differentiating the two conditions.

A pulmonary ejection sound or a sharp click-like first sound was never encountered in infundibular stenosis in contrast to its frequent occurrence in valvular stenosis. This may be due to the much less marked post-stenotic dilatation of the pulmonary artery in infundibular stenosis.

In infundibular stenosis the width of splitting appeared to be much greater than in valvular stenosis of comparable severity (Fig. 3). Thus, in the mild case the splitting measured 0.07 sec., in the 2 moderate cases it was as much as 0.10 and 0.12 sec. (Fig. 7) respectively, and in the severe case it was 0.12 sec. and in the very severe case 0.14 sec. The reason for the excessive delay in pulmonary valve closure in infundibular stenosis is obscure. Clearly it can not

be ascribed to abnormality in the pulmonary artery since post-stenotic dilatation was not a feature of these cases (Fig. 7). The mechanism is probably related to the duration of ejection of blood into the pulmonary artery. This may well be more prolonged in infundibular than in valvular stenosis due to delay in emptying of the abnormal, often dilated, infundibular chamber so frequently present. Delay in emptying of this chamber would be revealed by delayed closure of the valve and not by the murmur since the chamber lies distal to the stenosis.

I was unable to confirm the suggestion[10] that in infundibular stenosis with intact septum the crescendo of the murmur occurs earlier than in cases of valvular stenosis. However, it did appear to be true in the tetralogy, where infundibular stenosis caused an earlier crescendo and more rapid diminuendo than in those cases with valvular stenosis (see Chapter IV). Fig. 2 shows that in stenosis with intact ventricular septum there is good agreement between the time of the crescendo in valvular and infundibular stenosis of comparable severity. However, the duration of the murmur appears to be longer in infundibular stenosis. This may reflect an increase in the severity of the stenosis with contraction of the outflow tract of the right ventricle. The infundibular region is one of the last portions of the right ventricle to contract during systole,[6,7,13,14] and dynamic narrowing of the outflow tract may increase the stenosis during early or midsystole. This has been shown to occur by Rodbard and Shaffer[7] who compared the pressure curves recorded simultaneously in the right ventricle and infundibular chamber. In 10 out of 13 cases of infundibular stenosis the pressure in the two chambers began to rise together during the isometric contraction and for a variable

time during the rapid ejection phase, but thereafter the infundibular pressure began to fall, even though the right ventricular pressure continued to rise. The pressures did not become coincident again until the end of ejection. I confirmed this and in a few cases found that the duration of systole in the infundibular chamber is considerably longer than in the proximal chamber (Figs. 6 and 7, Chapter IV). In the tetralogy, sudden increase in stenosis with infundibular contraction has the very disadvantageous effect of diminishing the flow into the pulmonary artery and increasing the shunt down the aorta (see Chapter IV). This is reflected by the earlier crescendo and rapid diminuendo of the murmur and occasionally complete disappearance of murmur when severe spasm of the infundibular muscle causes a cyanotic or syncopal attack[8]. However, when the ventricular septum is intact, the right ventricle proximal to the stenosis has no escape route and is able to hypertrophy and adapt itself much more adequately to the stenosis whether this remains fixed or increases during systole. That systole is prolonged is shown by the greatly prolonged systolic murmur and the excessive width of splitting, though part of latter may be caused by delayed contraction in the infundibular chamber.

It is possible that gross subvalvular muscle hypertrophy in cases of severe valvular stenosis[6,16,18] might cause additional functional or acquired infundibular stenosis. In severe cases of valvular stenosis, however, I have been unable to detect any altered relation between severity of stenosis and length of systole or change in the site of murmur which would suggest additional infundibular stenosis. Acquired subvalvular stenosis is probably only detectable by auscultation when the murmur fails to shorten after a satisfactory

valvotomy (see Chapter V). In such cases the pressure gradient shifts from valvular to infundibular level and dynamics become those of infundibular stenosis[6].

SUMMARY.

1. A Clinical and phonocardiographic study has been made on pulmonary and infundibular stenosis with intact ventricular septum, in order to determine the value of auscultation and phonocardiography in assessing the severity of the stenosis. There were 43 cases of pulmonary valve stenosis with intact ventricular septum, 8 cases of infundibular stenosis with intact ventricular septum.

2. The severity of the stenosis, as determined by the right ventricular pressure, was correlated with the duration of right ventricular systole, as determined both by the length of the systolic murmur and width of splitting of the second heart sound. It was shown that increasingly severe stenosis resulted in progressive lengthening of the murmur in relation to the aortic second sound and delay in pulmonary valve closure. Criteria were defined whereby the severity of the stenosis could be predicted; these proved more accurate than other clinical methods.

3. In mild stenosis (RVP under 60 mm.Hg.), the murmur was soft to loud in intensity, reached a crescendo in midsystole and ended before or at the aortic component of the second sound. The second sound was always abnormally split (av. 0.05 sec.) and there was frequently a pulmonary ejection sound. In moderately severe stenosis (RVP 60-120 mm.Hg.), the murmur was louder, the crescendo and duration greater, extending a short way beyond the aortic component which it never

obscured. Splitting was wider (av. 0.07 sec.) and the pulmonary component reduced in intensity. There was frequently a sharp, click-like first sound on expiration. In severe stenosis (RVP 120/180 mm.Hg.) the murmur was loud with great delay in the crescendo and duration resulting in a kite-shaped rather than diamond-shaped configuration. It invariably exte ded well beyond the aortic component, which it either partially or completely buried. The murmur always ended before a very soft pulmonary component which was widely separated from the aortic component (av. 0.08 sec.). In very severe stenosis (RVP above 180 mm.Hg.) the murmur was loud and so prolonged that it invariably obscured the aortic component, but ended before a very delayed (av. 0.10 sec.) diminutive pulmonary component which may or may not be heard. Whenever the aortic component was completely buried by the murmur, the great width of splitting could not be heard on auscultation and phonocardiography was required for its detection. Thus, the length of murmur and the degree to which the aortic sound was buried were more useful auscultatory guides than the width of splitting in severe grades of stenosis. Whenever the aortic component was buried, a right ventricular pressure exceeding 120 mm.Hg. could be predicted.

4. Unusually wide splitting of the second sound was encountered in a few mild and moderately severe cases of valve stenosis. These cases all had pronounced post-stenotic dilatation of the pulmonary artery to which the delay in pulmonary valve closure was attributed. In these cases prediction of severity from murmur length was more reliable than from width of splitting.

5. Valvular and infundibular stenosis differed only in a few features. In infundibular stenosis, a pulmonary ejection sound was never encountered and the width of splitting was much greater than in valvular stenosis of comparable severity. The mechanism is discussed. The site of maximal intensity of the murmur was seldom helpful in differentiating valvular from infundibular stenosis. The increase in murmur length with increasing severity of stenosis was similar in both conditions.

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CHAPTER IV.

ASSESSMENT OF SEVERITY BY AUSCULTATION AND PHONOCARDIOGRAPHY IN FALLOT'S TETRALOGY.

FOREWORD.

The purpose of study in this chapter has already been outlined in the foreword to Chapter III. It also draws attention to the value and importance of auscultation and phonocardiography in assessing the severity of Fallot's tetralogy. In the tetralogy, unlike stenosis with intact ventricular septum, it is not sufficiently appreciated that electrocardiography, radiology and even cardiac catheterisation are usually unhelpful in evaluating the severity. However, it will be shown that the length of the murmur and other auscultatory signs are accurate, simple and invaluable for this purpose. Since the symptomatology, natural history and management are determined by the degree of stenosis, the importance of correct diagnosis of the severity needs no emphasis.

INTRODUCTION.

In the preceding chapter it was shown that increasingly severe stenosis caused progressive prolongation of right ventricular systole as reflected by progressive lengthening of the systolic murmur and delay in pulmonary valve closure. The opposite effect on the murmur will be shown to occur in Fallot's tetralogy, supporting the belief that the systolic murmur is influenced by different dynamic mechanism in the tetralogy. The main thesis can be stated as follows:

In the tetralogy, unlike pulmonary stenosis with intact ventricular septum, the dynamic situation is completely altered by the presence of a large ventricular septal defect, which offers to the right ventricle an escape route of much lower resistance than its stenosed outflow tract, and hence the right ventricular systolic pressure cannot significantly exceed the systemic pressure*. Thus the right ventricular pressure is determined not by the severity of the stenosis, but by the systemic resistance. Pulmonary blood flow is therefore dependent on two main factors, namely, the systemic resistance and the severity of the stenosis. For a given degree of stenosis, pulmonary blood flow will be influenced by the systemic resistance. If systemic resistance is high, the right ventricular pressure rises and increased pulmonary flow results[22](see Chapter VII); if the systemic resistance falls, following inhalation of amyl

*

Footnote. This argument holds for the majority of cases of tetralogy where the ventricular septal defect is large. It is appreciated that in the rare case of an exceptionally small septal defect[12](see Chapter III), or a large defect rendered functionally small by a tricuspid or endocardial flap valve,[6, 20] right ventricular pressure may adjust more satisfactorily to the stenosis by producing a higher pressure and a better gradient.

nitrite, for example, the right ventricular pressure likewise falls causing decreased pulmonary flow with shortening and softening of the murmur (Chapter VI).

Conversely, for a constant systemic resistance, pulmonary blood flow diminishes with increasing severity of stenosis as shown by the inverse relation between the length and loudness of the murmur and severity of stenosis (Chapter I). Thus the severer the stenosis the shorter, softer and more limited to early systole the murmur became. This is because the right ventricular pressure becomes progressively more inadequate the severer the stenosis; hence flow into the pulmonary artery becomes restricted to the early ejection phase of systole. During this phase the ventricle contains most blood and attains its maximal pressure; thereafter pulmonary blood flow falls off sharply since most of the stroke volume is discharged down the aorta. An important additional mechanism causing rapid fall-off in pulmonary blood flow and murmur in early systole may be the sudden increase in the stenosis produced by infundibular contraction later in systole[6,7,8,15,16] (Figs. 6,7). Clearly the influence of infundibular contraction on pulmonary flow will be more critical the severer the stenosis (Figs. 7,10). By the time the aortic valve closes, both ventricles have discharged most of their blood down the aorta; hence the murmur usually ends before the aortic sound in severe cases. Conversely, it was shown that the milder the stenosis the longer the systolic murmur became[1]. This is because the right ventricular pressure produces a more satisfactory gradient the milder the stenosis. Thus the closer the pulmonary stenotic resistance approaches the systemic resistance, the longer the duration of effective flow through the stenosed region and hence the longer the systolic murmur, which now extends into the aortic second sound.

These suppositions[1,2] will be confirmed in two ways; firstly, by correlating the auscultatory and PCG findings with the severity of the tetralogy and, secondly, by observing the marked increase in duration of the systolic murmur that follows when a successful pulmonary valvotomy or infundibular resection results in a mild tetralogy (Fig. 2 and Chapter V).

MATERIAL AND METHODS.

Sixty-two cases of Fallot's tetralogy were studied. The diagnosis was confirmed in all by cardiac catheterisation and/or angiocardiography, using methods previously described[2] and by operation (27 cases) and necropsy (19 cases). By Fallot's tetralogy is meant severe infundibular or valvular stenosis with large ventricular septal defect and right and left ventricular pressures of the same order. Even in acyanotic cases the stenosis is relatively severe, permitting bi-directional ventricular shunt or at most, a small left-to-right shunt (up to 2 litres/min. at rest). Cases of large septal defect with large left-to-right shunt and mild pulmonary stenosis or small septal defects with mild pulmonary stenosis have been excluded. Such situations, in my view, are not true examples of acyanotic Fallot's tetralogy, and have been described elsewhere[21,23].

The methods used in clinical examination, auscultation and phonocardiographic technique and measurement have already been described in Chapter III.

The severity of Fallot's tetralogy could not be as simply assessed as in pulmonary stenosis with intact ventricular septum. The right ventricular systolic pressure remains at systemic level whether the stenosis is mild or severe, and thus fails to reveal the severity of the condition (Chapter II). On the other hand, if the pulmonary

blood flow and the degree of right-to-left shunt down the aorta could be accurately measured, a reasonable assessment of the severity of the condition would be possible. However, my experience is similar to others[10] in that using the Fick principle, calculations of blood flow in the tetralogy were not dependable for this purpose (see Comment).

For these reasons a clinical method of appraisal had to be used. The disability and degree of cyanosis were graded from 0-4, corresponding to nil, mild, moderate, severe and extreme. Disability and cyanosis often corresponded to the same grading and this correlated well with the degree of polycythaemia. However, cyanosis was occasionally disproportionate to the disability, particularly in adults, of whom there were many in this series. When cyanosis was severe, yet symptoms mild and physical development normal, the degree of disability influenced the grading more than the cyanosis. On the other hand, in infants and physically retarded children, it was difficult to apply the same method of grading used in ambulant children and adults. In this series there were very few infants but it is appreciated that grading is much more difficult in this age group, where haemodynamic adjustments are still taking place. However, it was not difficult to distinguish the extreme case with repeated cyanotic attacks from the mild case who was barely cyanosed and thriving, albeit a little slower than normal. It was generally simple especiallly after several visits to the clinic and effort tests to classify a given case.

Extreme cases (6) were uncommon, but readily recognised by their total disability and severe cyanosis (grade 4). Mild cases (21), although seldom completely symtpom-free, were able to live normal lives did not often squat, were normally developed, were able to walk a

reasonable distance on the level without stopping and cyanosis was usually slight. Six of these cases were acyanotic at rest and in several, cyanosis would have been missed were it not for its appearance after effort or inhalation of amyl nitrite[3](Chapter VI). In two cases, cyanosis was grade 3, but the cases were classified as mild. The first, aged 30, was virtually symptom-free and doing an active day's work, as was the other, aged 19; both were normally developed. Moderate cases (17) were moderately disabled usually with grade 2, or occasionally with grade 3 cyanosis and clubbing. Severe cases (18) were usually deeply cyanosed (grade 3-4) and severely disabled, but not as totally incapacitated as the extreme case. In three cases, the cyanosis was only grade 1, but disability was severe. Two of these had syncopal attacks on slight effort and the third, an infant aged 2, the youngest in the series, had very frequent syncopal and cyanotic attacks at rest and was physically retarded.

RESULTS AND DISCUSSION.

The systolic murmur varied in intensity from grade 1 to grade 5. However, the intensity was of little value in assessing the severity, except in extreme tetralogy where the murmur was never louder than grade 2 (Table 1). Of far greater importance was the duration of the systolic murmur in relation to the aortic second sound at the site of maximal intensity of the murmur. This could be assessed with sufficient accuracy by auscultation, but sound tracings were always used to measure the length of murmur and degree to which the murmur

TABLE 1

ANALYSIS OF AUSCULTATORY AND PCG FINDINGS IN FALLOT'S TETRALOGY

SEVERITY	No. of Cases	Systolic Murmur				A 2 Heard	P2 on PCG	P 2 Heard	Width of Split (in exp) Sec.	Aortic Ejection Sound	Pulm. Ejection Sound
		Intensity (1-6)	Crescendo (% LV systole)	Duration (% LV systole)	% Burying of A2 by SM						
EXTREME	6	1-2	26-30 Mean 27	38-55 Mean 45	0	6	0	0		6	0
SEVERE	18	2-5 Mean 3	22-60 Mean 34	68-100 Mean 87	0-25 Mean 4	18	0	0		5	0
MODERATE	17	3-5 Mean 4	30-87 Mean 45	80-101 Mean 96	0-24 Mean 10	17	3	1	0.09	0	0
MILD	21	3-5 Mean 4	48-83 Mean 69	92-118 Mean 102	0-100 Mean 32	20	18	10	0.07-0.12 Mean 0.09	2	0
TOTAL	62										

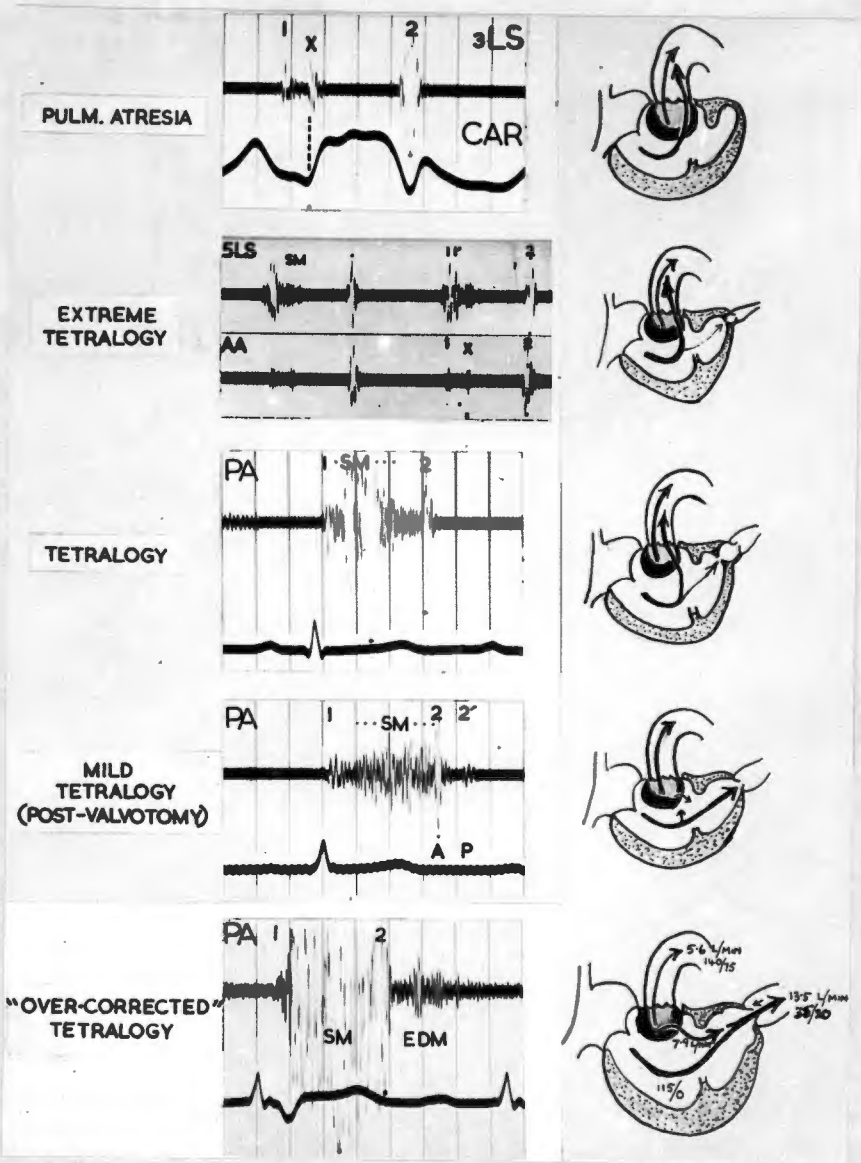

Fig. 1. The relation between severity of stenosis and length and loudness of the murmur. In pulmonary atresia there is usually no systolic murmur but invariably a loud aortic ejection sound (X). In extreme tetralogy the murmur is soft, short and confined to early systole and there is usually an aortic ejection sound. In severe and moderate cases the murmur is loud but reaches a crescendo by mid-systole and diminishes rapidly to end before or at the loud aortic second sound. In mild cases the murmur is loud and more prolonged, extending into and occasionally slightly beyond the aortic component. A soft pulmonary component (P) is frequently recorded or often heard well after the aortic component (av. 0.09 sec.) and reflects a relatively high diastolic pressure. In "over-corrected" tetralogy caused by excessive removal of the stenosis by valvotomy, complicated by bacterial endocarditis, a large left-to-right shunt developed through the large ventricular septal defect. A loud, pansystolic murmur and pulmonary incompetence developed. The diagrams reflect the influence of the severity of the stenosis on the pulmonary blood flow and the ventricular shunt.

buried the aortic second sound (see Methods). The data thus obtained were correlated with severity of the tetralogy, as determined by the clinical method used (see Methods). Figs. 1,3 and 5 show that the severer the tetralogy the shorter, earlier and softer the systolic murmur. The murmur thus behaves in opposite fashion to pulmonary stenosis with intact ventricular septum, where increasingly severe stenosis results in a longer, later and louder murmur (Fig. 5).

Extremely severe tetralogy - There were 6 cases, 2 with valvular stenosis, 3 with infundibular stenosis and 1 with both. Necropsy confirmed both the severity and site of stenosis in 4 cases and in the fifth case, extreme valvular stenosis was found at valvotomy, following which, the case was converted into a mild tetralogy (Fig. 2).

All had a soft systolic murmur (grade 1-2) confined to early systole, with the murmur ending long before the aortic second sound. The time of the crescendo ranged between 26 to 30% (mean 27%) of the left ventricular systole and the murmur ended at midsystole (range 38 to 55%; mean 43%) (Table 1,3 and 5). The aortic second sound was loud and in no case was the pulmonary component recorded. An aortic early systolic ejection sound was heard and recorded in all, and could be distinguished from pulmonary ejection sound by its much wider range of audibility, lack of variation with respiration and later onset in systole[4,19], giving the impression of "wide splitting" of the first sound at all areas. Confusion with the pulmonary ejection sound heard in pulmonary stenosis with intact ventricular septum never arose because the sound was only heard in mild and

moderate cases, all of whom were acyanotic*.

The aortic ejection sound in the tetralogy is thought to be produced by several factors (Chapter I). The aorta is dilated and nearer the chest wall than normal, because it is dextro and anteroposed and crossed by a pulmonary artery much smaller than normal. Furthermore, the severer the pulmonary stenosis the greater the stroke volume discharged into the aorta, and the greater the likelihood of production of an ejection sound. However, its presence in milder cases may be obscured by the loud pulmonary systolic murmur commencing earlier in systole (ejection into the pulmonary artery precedes ejection into the aorta because the pulmonary diastolic pressure is much lower (Fig. 7)). We believe that a clearly audible

*

Footnote. I am in agreement with Leatham and Weitzman (5) that there is little need to distinguish between an aortic and pulmonary ejection sound in the severely cyanosed cases with pulmonary stenosis(4). However, accurate distinction may be of paramount importance in differentiating severe tetralogy and pulmonary atresia from cyanotic heart disease associated with pulmonary hypertension. In both groups a short, early systolic murmur and a loud, unsplit second sound may be heard; but the first group has an aortic and the second a pulmonary ejection sound. The pulmonary ejection sound associated with pulmonary hypertension may closely simulate the aortic sound since it occurs later in systole than in cases without pulmonary hypertension(4). There is also much less variation with respiration and it may occasionally be so loud that it becomes audible at all areas (personal observation). Hence great care must be exercised before assuming that an ejection sound in a cyanotic patient is of aortic of pulmonary origin, since on this decision the auscultatory diagnosis may either be correct or seriously misleading.

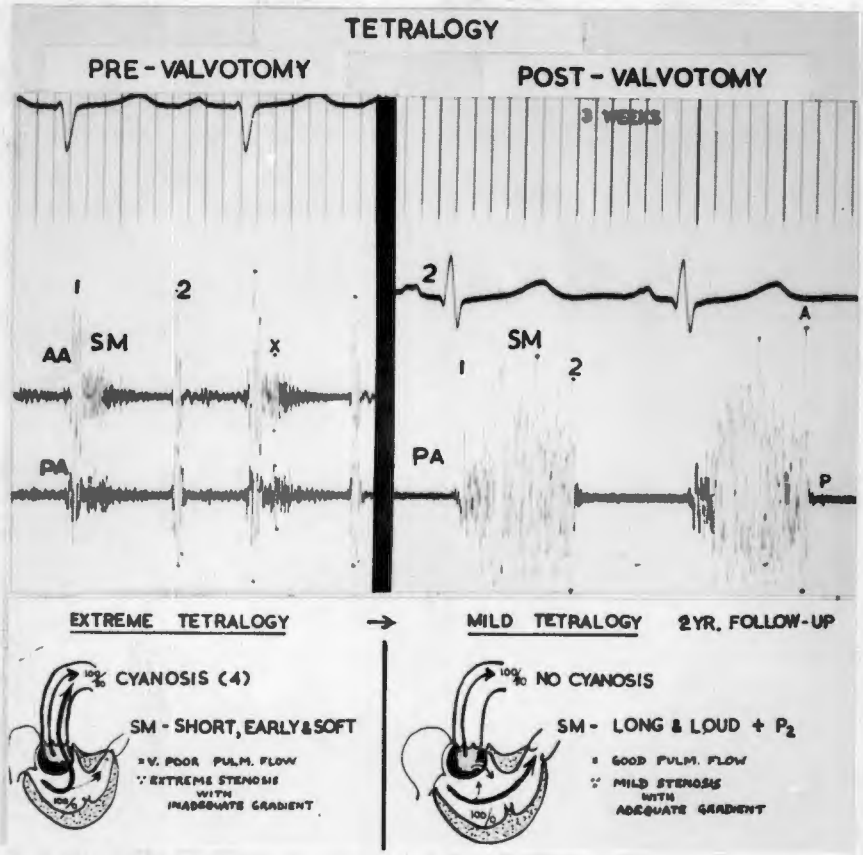

Fig. 2. <u>**The effect of a successful valvotomy on the length and loudness of the systolic murmur.**</u> Extreme valvular stenosis rendered mild by valvotomy resulted in pronounced lengthening and intensification of the murmur and emergence of a very soft delayed pulmonary component. This proves that the murmur length and loudness are inversely related to the severity of the stenosis in the tetralogy and that the murmur is produced by the stenosis and not by the septal defect. The pre- and post-valvotomy sound tracings were recorded during expiration at the same attenuation. Each vertical line in this and subsequent tracings measures 0.04 sec.

aortic ejection sound usually indicates a severe tetralogy. In pulmonary atresia, where the entire stroke volume of both ventricles is discharged into the very dilated aorta, a striking aortic ejection sound was the rule (Fig. 1), as first described in an earlier publication[1]. Pulmonary atresia has not been included in this series, although it might well be regarded as the most extreme grade of tetralogy. However, when there is no communication between the pulmonary artery and the right ventricle, there can be no pulmonary

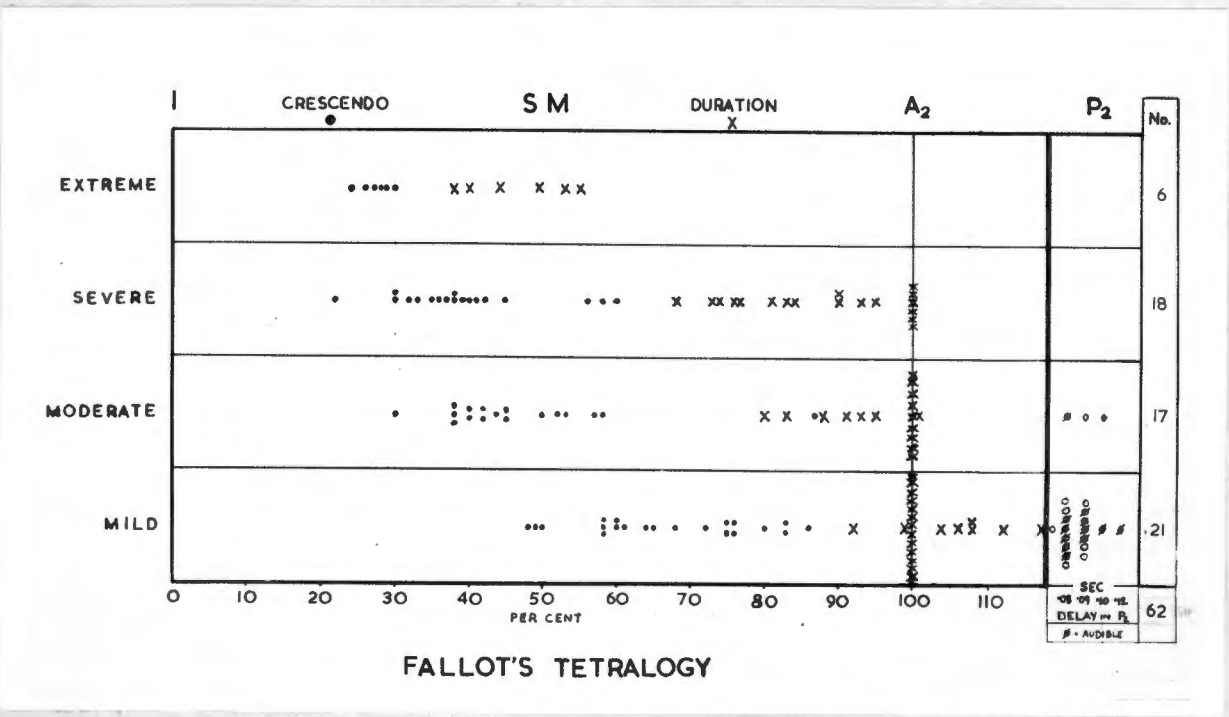

Fig. 3. The time of the crescendo and duration of the systolic murmur in relation to left ventricular systole (I-A2) in 62 cases. The severer the stenosis as judged by the disability and cyanosis, the earlier the crescendo and the shorter the murmur, proving the inverse relation between pulmonary flow, as reflected by the murmur, and the severity of the stenosis. In mild cases, although the murmur usually ends in and may be loud at the aortic component, it rarely extends much beyond it. In 18 of 21 mild cases, a delayed, soft, pulmonary component was recorded, and in 11 of these it was audible. A very soft pulmonary component was recorded in 3 moderately severe cases, being audible in 1.

stenosis, and hence the natural history and signs are dependent on factors not germane to the present discussion. The only relevant features are the almost invariable presence of a loud aortic ejection sound (11 of the 12 cases) and the frequent absence of a systolic murmur, supporting the belief that the ventricular septal defect plays no part in the genesis of the systolic murmur when the pressures in both ventricles are at the same level.

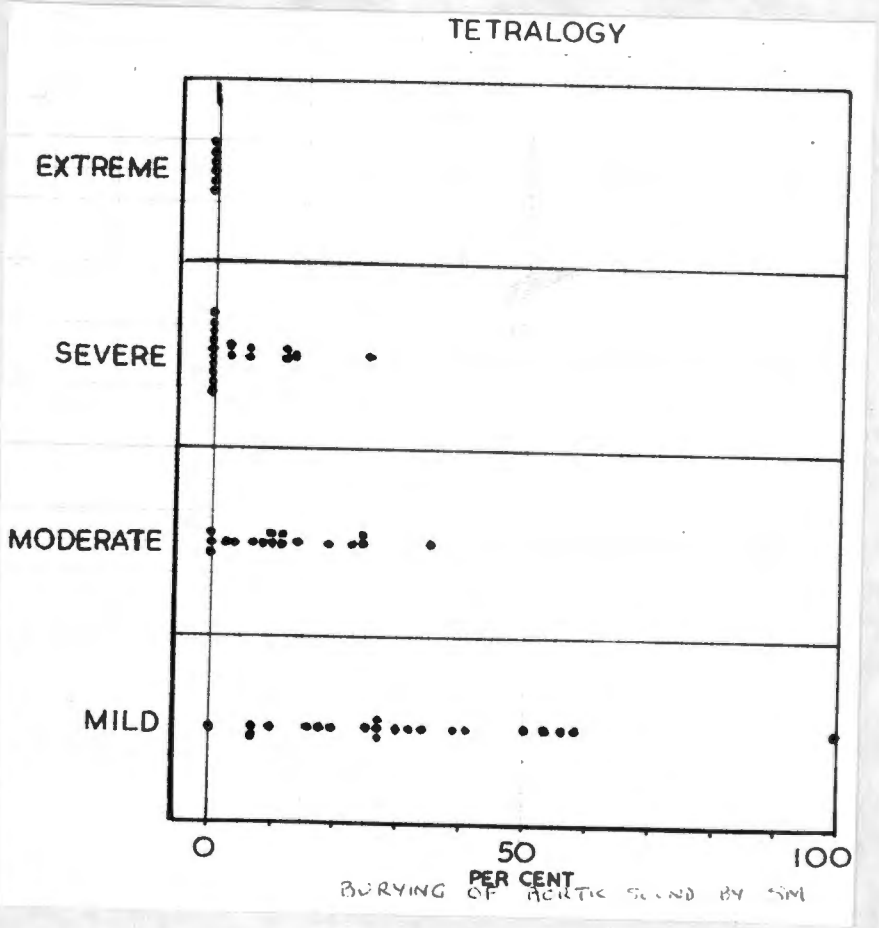

Fig. 4. The degree of burying of the aortic second sound by murmur in 62 cases. This expresses the loudness of the murmur where it transects the aortic sound, as a percentage of the sound. The murmur was loudest at the aortic sound in the milder cases, but in only 5 did it exceed 50% of the sound, and in only 1 case was the sound totally hidden by the murmur.

Severe tetralogy - There were 18 cases in this category; 12 had infundibular stenosis, 2 were thought to have valvular stenosis and 4 had infundibular and valvular stenosis. All had grade 3 disability and all but 3 were deeply cyanosed and clubbed. The 3 exceptions were mildly cyanosed, but had syncopal attacks in addition to marked disability. One was deeply cyanosed and died in a cyanotic attack.

The systolic murmur, which was loud in all except 2 cases (grade 2-5, mean 3) reached a crescendo before midsystole and ended

well before the loud aortic second sound. PCG analysis revealed that crescendo occurred between 22 and 60% (mean 34%) of left ventricular systole and the duration of the murmur ranged between 68 and 100% (mean 87%) (Table 1, Figs. 3 and 5). There was virtually no burying of the aortic second sound by the murmur (range 0-25); mean 4%) (Fig. 4). The pulmonary second sound was never recorded and an aortic ejection sound was recorded in 5 cases, though heard in only one.

Four cases had cyanotic or syncopal attacks. In 3 auscultation during an attack revealed disappearance of the murmur, despite the presence of marked tachycardia and a good pulse volume. These observations were consistent with the suggestion that such attacks may be due to temporary spasm of the infundibular portion of the right ventricle. One case died in a cyanotic attack and severe infundibular stenosis was found at necropsy (Fig. 10). Infundibular stenosis was also present in the other cases.

Moderate tetralogy - There were 17 cases; 10 had infundibular stenosis, one was thought to have valvular stenosis, 4 had valvular and infundibular stenosis and in the remaining cases the site could not be determined. The systolic murmur, which was loud in all (grade 3-5), reached a crescendo at about midsystole and, to the ear, usually ended before or at the aortic second sound, which was never obscured by the murmur. The second sound was loud and wide splitting was audible in only one case. PCG analysis revealed that the crescendo occurred between 30 and 87% (mean 45%) of left ventricular systole, and the duration between 80 and 101% (mean 96%) (Table 1, Figs 3 and 5). The degree of burying of the aortic second sound by murmur was always very slight (range 0-24%; mean 10%), and this could not be appreciated by ear. A pulmonary second sound was recorded in

only 3 cases. It was extremely soft, occurring 0.09 sec. after the aortic component in all and just audible in one. In no case was an aortic ejection sound recorded.

Mild tetralogy - There were 21 mild cases; infundibular stenosis was present in 10, infundibular and valvular stenosis in 2 and in 9 valvular stenosis was thought to be present. The high incidence of valvular stenosis in this group is noteworthy. All cases had mild disability; cyanosis was absent at rest in 6, but could be brought out by exercise and amyl nitrite(3). Cyanotic attacks never occurred in this group.

The systolic murmur was loud in all (grade 3-5), reached a crescendo after midsystole and extended into the aortic second sound. However, this sound was totally obscured by the murmur in only one case. A very soft second sound was audible in the pulmonary area in no less than 11 cases. It was always widely separated from the aortic component, causing wide splitting. In 3 cases it was quite loud and in one striking loud (see Chapter I, Fig. 6).

PCG analysis revealed that the crescendo occurred later in systole than in moderate tetralogy, ranging from 48 to 83% (mean 69%) and the duration longer ranging from 92 to 118% (mean 102%). The murmur was also louder at the second sound, though in only one case sufficiently loud to obscure the sound completely, the degree of burying ranging from 0 to 100% (mean 32%) (Fig. 4). This was in striking contrast to the severer grades of pulmonary stenosis with intact ventricular septum, where this sound was often totally obscured by the much more prolonged murmur (Fig. 5). The aortic component remained audible in the mild tetralogy both because this sound was usually louder than in pulmonary stenosis and more important,

the murmur was not so prolonged. The murmur continued for a short distance beyond the aortic sound in only 5 cases of mild tetralogy (Fig. 3). Moreover, this was usually difficult to hear (Fig. 6) and required an amplified PCG for confirmation.

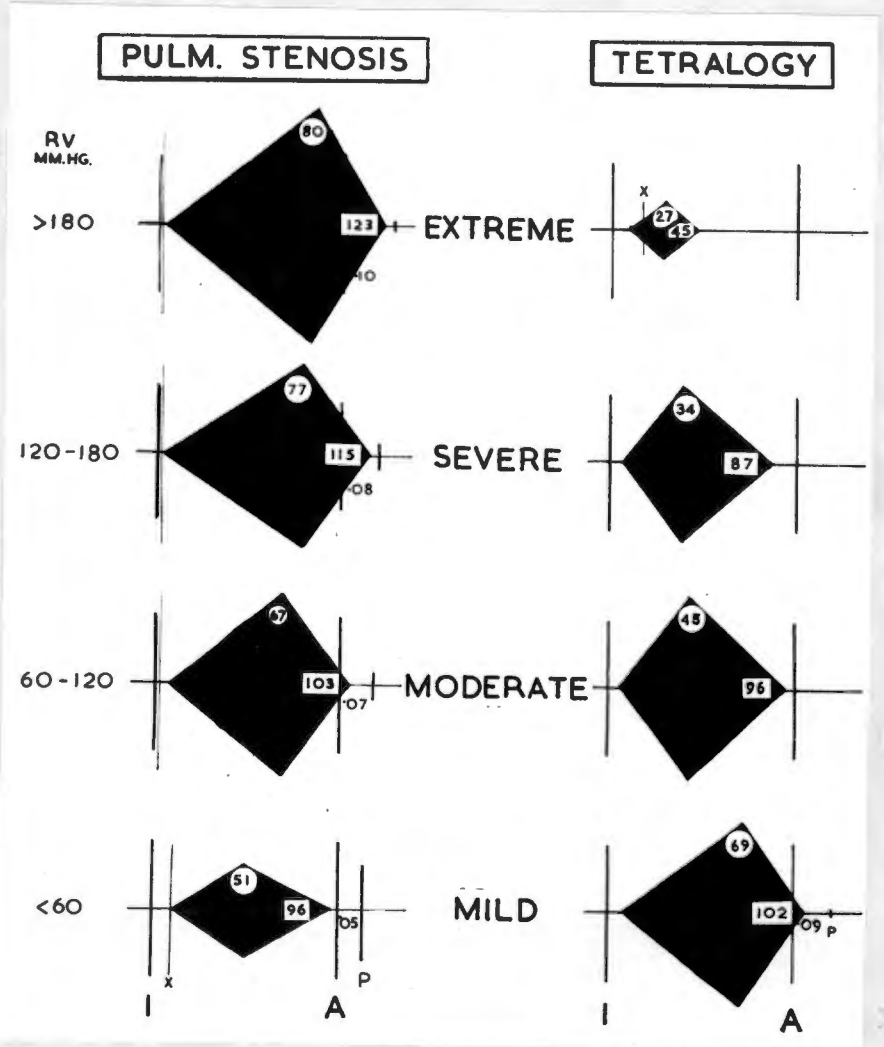

Fig. 5. This diagram illustrates the opposite effect induced on the murmur length by increasingly severe stenosis in pulmonary stenosis with intact ventricular septum and Fallot's tetralogy. The crescendo and duration of the murmur, each expressed as a percentage of the duration of left ventricular systole, has been drawn to scale using the mean times, as indicated, in each category of severity. The mean width of splitting of the second sound is also indicated. Increasingly severe pulmonary stenosis with intact septum causes a kite-shaped murmur due to great lengthening and delay in the crescendo. In severe stenosis the murmur usually totally obscures the aortic component (A) but always ends before the soft delayed pulmonary component (P). Increasing severity in the tetralogy causes the murmur to become shorter, softer and more confined to early systole and in extreme cases an aortic ejection sound usually emerges. A soft, pulmonary component producing wide splitting is heard only in the mild cases. The murmur configuration of mild tetralogy is usually indistinguishable from moderately severe pulmonary stenosis.

An aortic ejection sound was recorded but not heard in three cases, being almost buried in the loud murmur which had commenced before it. A pulmonary ejection sound or sharp click-like first sound was never recorded or heard in contrast to its frequent occurrence in mild and moderate pulmonary stenosis with intact ventricular septum. This may be related to the greater post-stenotic dilatation and the larger stroke volume ejected into the pulmonary artery in the latter condition.

A very soft, pulmonary second sound was recorded in 18 out of 21 cases, being audible in 11 (Fig. 3). Splitting was always wide, varying from 0.07 to 0.12 seconds (mean 0.09 sec). PCG proof that the sound was the pulmonary component was based on its localisation to the pulmonary area, its occurrence before the summit of the V wave in the synchronously recorded phlebogram[1] and its intensification after phenylephrine (Chapter VII). Of the 18 cases with a recordable pulmonary component, the stenosis was infundibular in 7, valvular and infundibular in 2, and valvular in 9. The sound was loudest when the stenosis was valvular. A recordable or audible pulmonary component always reflected an unusually high pulmonary arterial pressure for tetralogy. Vogelpoel and Schrire were the first to draw attention to the presence of splitting of the second sound and its significance in the tetralogy in an earlier publication (See Chapter I), and further experience has confirmed the view that a recordable or audible pulmonary component is a valuable indication that the stenosis is mild in the tetralogy, since it denotes a relatively high pulmonary arterial pressure. That the component is a sensitive indication of the pulmonary arterial pressure in the tetralogy can be shown by its variable audibility with respiration, its temporary disappearance when

pulmonary blood flow and pressure are reduced following amyl nitrite inhalation[3] and by its intensification when pulmonary blood flow and pressure are increased after phenylephrine. (See Chapters VI and VII).

I believe that the murmur in mild tetralogy can never be as prolonged as in severe pulmonary stenosis with intact ventricular septum despite the fact that splitting of the second sound, when measurable is always as wide (av. 0.09 sec.) (Fig. 5). When the septum is intact the right ventricle can discharge its contents only through the stenosed outlet, hence the greatly prolonged systole and murmur when stenosis is severe. In the tetralogy, however, the large septal defect permits an alternative escape route so that by the time of aortic valve closure, the right ventricle has discharged most of its blood. Thereafter, despite persistence of a pressure gradient across the stenosis during the 0.09 sec. before pulmonary valve closure, little flow occurs. This is because the ventricle proximal to the stenosis is relaxing and contains little residual blood available for flow. Pulmonary valve closure is always delayed because time is required for the right ventricular pressure to drop from aortic to pulmonary diastolic pressure level. Since the pulmonary diastolic pressure is low and often at right atrial level the time interval between the aortic and pulmonary second sounds expresses the isometric relaxation time of the right ventricle in the tetralogy. The time is of the same order as that between the aortic sound and mitral opening snap in mitral stenosis.

Another important factor causing delay in pulmonary closure in the tetralogy may be abnormally prolonged contraction of the infundibular chamber in cases with infundibular stenosis. In the absence of additional valve stenosis, delayed emptying of the infundibular chamber would be detected not by murmur but by delay in

pulmonary valve closure. Fig. 6 shows that systole is in fact more prolonged in the infundibular chamber than in the proximal right ventricle. This case was an acyanotic tetralogy with infundibular stenosis. There was a 2.0 litre/min. left-to-right ventricular shunt. A large ventricular septal defect and relatively mild infundibular stenosis was found at ventriculotomy. Accurately superimposed sound and pressure tracings showed that the crescendo of the murmur occurred at midsystole coinciding with the peak rise in infundibular pressure and nadir of the Venturi wave in the pulmonary artery. Thereafter, the pressure in the infundibular chamber suddenly fell away while the pressure in the proximal ventricle continued to rise. The decrescendo of the murmur coincided with the fall-off in infundibular pressure and decending limb of the Venturi wave in the pulmonary artery. This suggested that the stenosis was suddenly increased during systole of the infundibular chamber with abrupt reduction in volume rate of pulmonary flow. The murmur ceased shortly after the aortic second sound, but the pulmonary valve closed as late as 0.09 sec. after aortic valve closure, presumably due to prolonged systole in the chamber. Similar pressure and murmur changes have been found in other cases of infundibular stenosis, where tracings could be accurately superimposed. Fig. 7 illustrates a severe case of tetralogy where the crescendo and sudden pressure drop in the infundibular chamber occurred earlier in systole (30%). Having severe stenosis the influence of contraction of the chamber was presumably critical at an earlier period of systole than in the mild case discussed above. However, despite the severer stenosis the duration of systole in the infundibular chamber also continued beyond that of the proximal ventricle. Had pulmonary valve closure been recordable, wide splitting would have been anticipated.

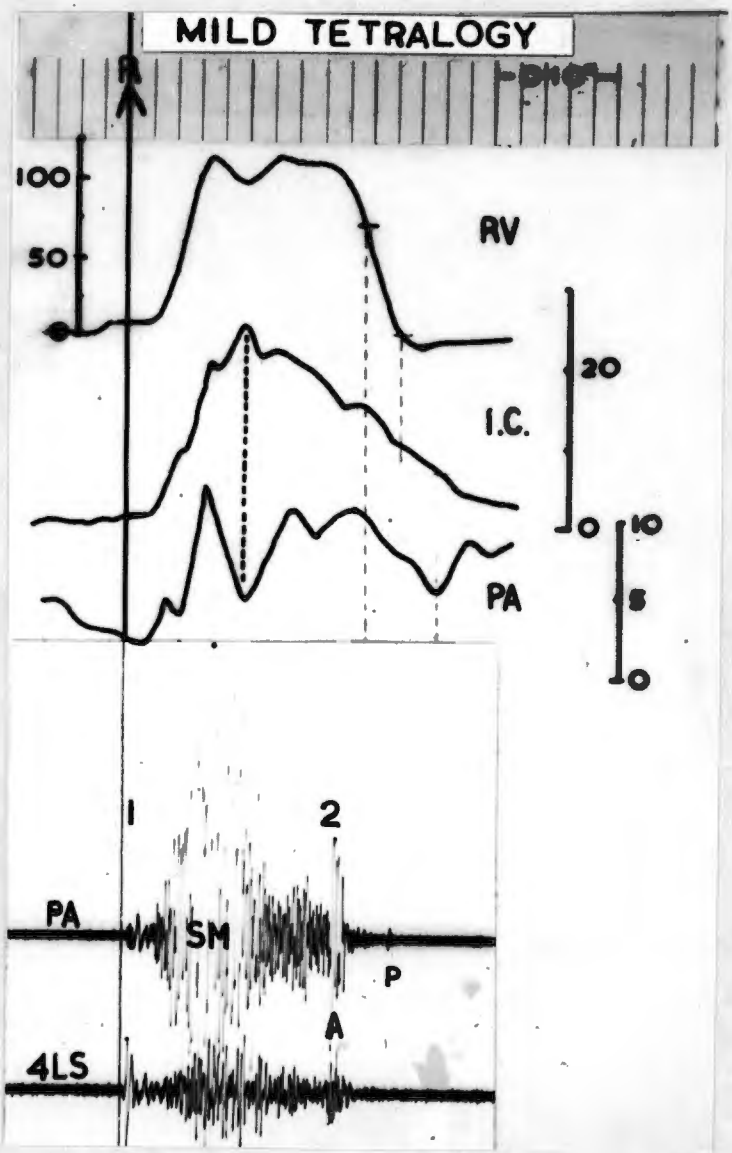

Fig. 6. The influence of infundibular contraction on the crescendo and duration of the systolic murmur in a mild case of Fallot's tetralogy with infundibular stenosis. Allowing for a 0.02 sec. delay in transmission of pressure down the catheter, the peak of the crescendo coincided with peak rise of infundibular pressure (I.C.) and nadir of the Venturi wave in the pulmonary arterial tracing (PA), suggesting maximal pulmonary flow at this point. Thereafter, infundibular pressure fell while the proximal right ventricular pressure (RV) continued to rise. The rapid diminuendo of the murmur and disappearance of Venturi wave, suggested abruptly reduced volume rate of pulmonary blood flow, probably due to increase in stenosis during infundibular contraction. Pulmonary valve closure (P) was delayed 0.09 sec. after aortic valve closure (A), presumably from prolonged isometric relaxation time and prolongation of systole in the infundibular chamber, about 0.06 sec. beyond the proximal right ventricle. The figure has been constructed by superimposing sound and pressure recordings of identical cycle lengths and accurately mounted in relation to the R wave (R) of the same ECG lead.

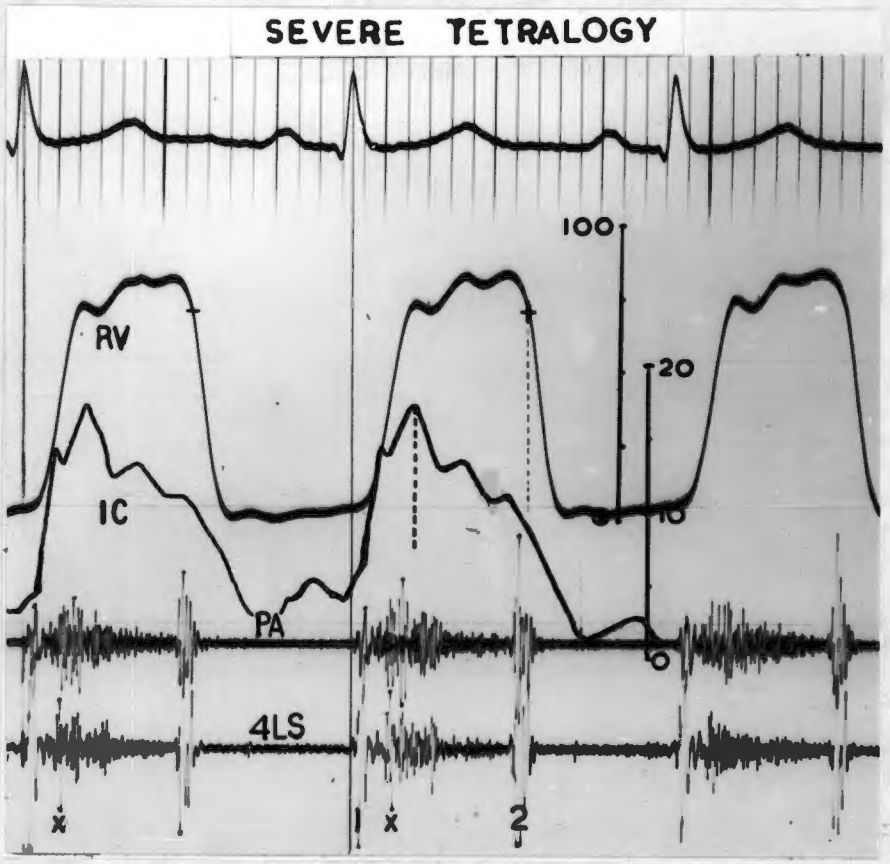

Fig. 7. The influence of infundibular contraction on the murmur in a severe case with infundibular stenosis. See text for discussion.

The incidence of valvular stenosis was much higher amongst the mild cases of tetralogy, whereas it was rare in the severer groups. This supports the belief that infundibular contraction greatly handicaps pulmonary flow when infundibular stenosis is present. Valvular stenosis would not be increased during contraction of the out-flow tract and this may account for the tendency of the murmur to be longer with a later crescendo in mild cases with valvular stenosis. Even in mild cases with infundibular stenosis the crescendo tended to occur earlier with a more pronounced diminuendo than in valvular stenosis (compare Figs. 6 and 8(b), both of whom were asymptotic at rest).

Diastolic murmurs were encountered in only 2 of the 62 cases. The first had aortic incompetence since the early diastolic murmur followed the aortic second sound(Fig. 8(a)). She had infundibular stenosis of moderate severity as shown by the loud systolic murmur with early crescendo and rapid diminuendo. The diastolic murmur being aortic, gave no guide as to the severity of the stenosis. The second case (Fig. 8(b)), had pulmonary incompetence which proved a useful guide to the severity. The murmur could be distinguished from aortic incompetence by its delayed onset following the delayed and audible pulmonary second sound, occurring 0.08 sec. after the aortic sound. He had relatively mild valvular stenosis as shown by the loud systolic murmur with late crescendo and partial burying of the aortic sound. He was cyanotic at rest. The soft pulmonary second sound and incompetent murmur were of additional value, reflecting a relatively high pulmonary arterial pressure of 25/5 with a right and left ventricular pressure of 80/0 mm.Hg. Pulmonary incompetence not infrequently develops after surgery[8] (Chapter V), and may follow an attack of bacterial endocarditis (Fig. 1, bottom row).

Mitral mid-diastolic flow murmurs were not audible in the cyanotic cases of tetralogy because none had a large left-to-right ventricular shunt. This murmur, however, is a useful indication of a large left-to right ventricular shunt, being usually present in cases of large septal defect with mild pulmonary stenosis. Such cases, being excluded from this series by my definition of Fallot's tetralogy, will be discussed elsewhere[21, 23].

Continuous murmurs from well developed bronchо-pulmonary collateral circulation were never heard in this series in contrast to their frequent occurrence in pulmonary atresia.

Diastolic sounds being rarely heard in the tetralogy[1] proved of no value in assessing the severity.

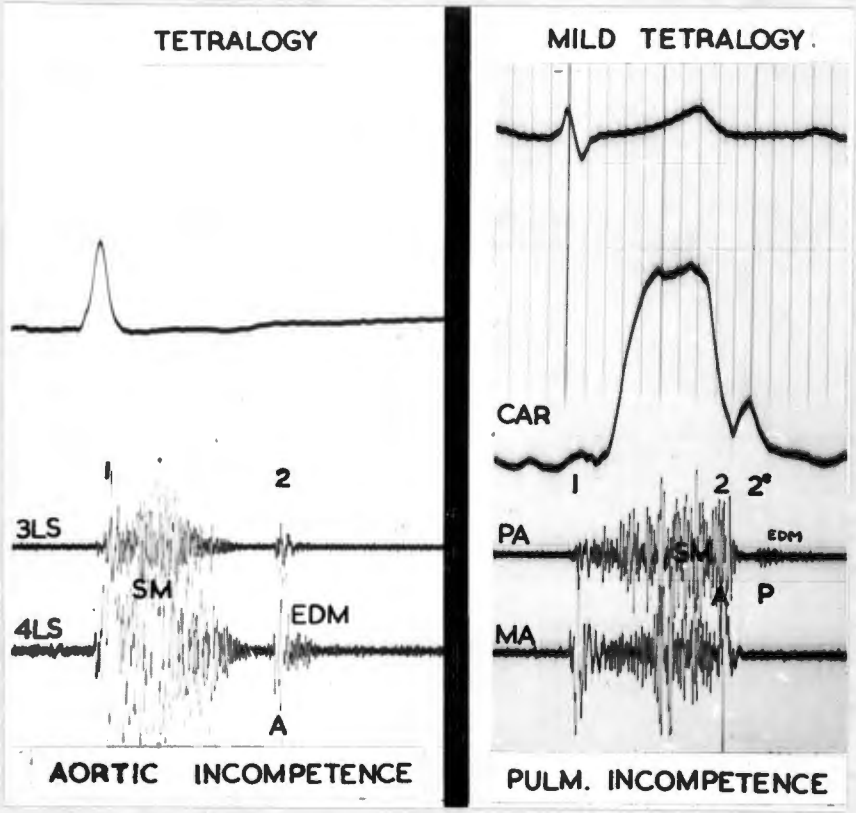

Fig. 8. Diastolic murmurs in Fallot's tetralogy. The first case had moderately severe infundibular stenosis and aortic incompetence. The diastolic murmur in the second was of pulmonary origin since it commenced with the delayed soft pulmonary second sound (2, P), 0.08 sec. after the aortic second sound (2, A). The audible pulmonary sound and murmur proved helpful in predicting a normal pulmonary arterial pressure. He had relatively mild valvular stenosis and was acyanotic at rest.

COMMENT.

I believe that the auscultatory criteria for assessing the severity of Fallot's tetralogy are of great value because they reflect the rate and volume of blood flow through the stenosed orifice. Hitherto objective methods have been limited to measurement of the left-to-right shunt down the aorta, since there has been no available simple method of assessing the pulmonary flow. Such criteria as the degree of central cyanosis, polycythemia, clubbing and fall in arterial oxygen saturation during effort and the Valsalva manoeuvre, using ear oximitry, chiefly measure the right-to-left shunt (Fig. 9).

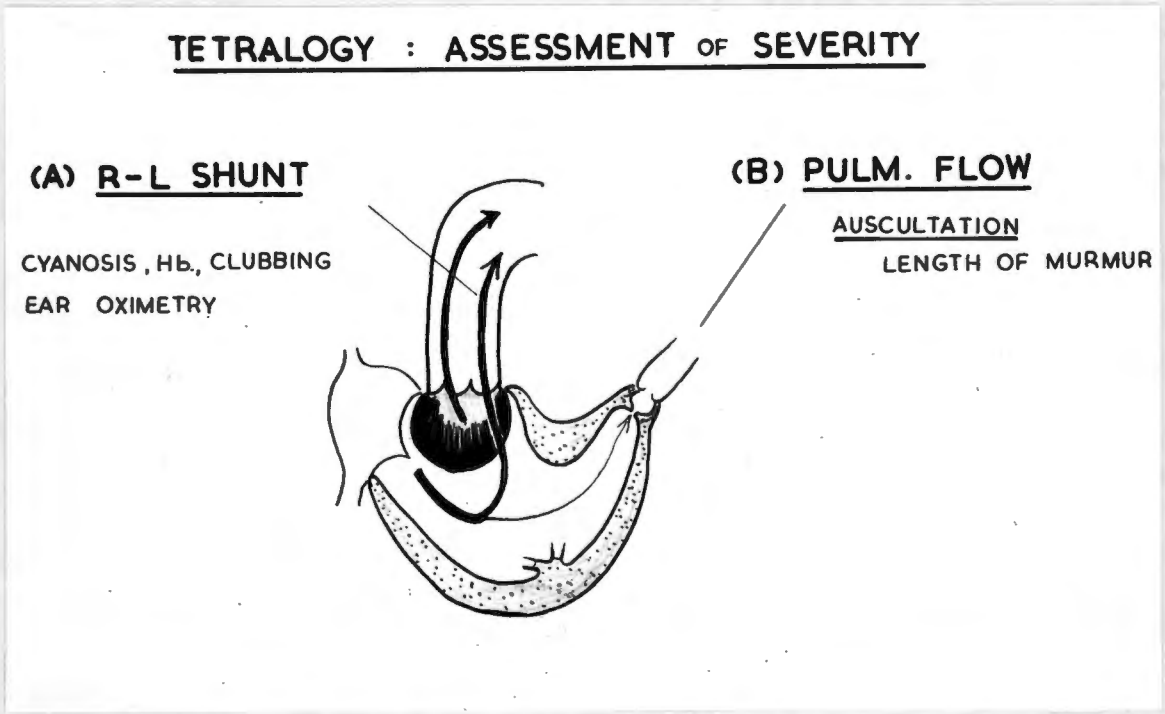

Fig. 9. This diagram illustrates the methods used at the bedside for objective assessment of severity in Fallot's tetralogy. Hitherto, most methods have depended on measurement of the degree of right-to-left shunt down the aorta but auscultation conveys accurate information about the volume rate of pulmonary blood flow and hence the severity of the stenosis.

In practice, however, the length of murmur alone will suffice, since in the tetralogy, the less the pulmonary blood flow the greater the right-to-left shunt. Little experience is required to recognise and predict that a case with a loud, prolonged systolic murmur, extending into, but not obscuring, the aortic component, whether associated with a soft pulmonary component or not, has good pulmonary blood flow. Cases showing these features are always virtually asymptomatic and often acyanotic at rest, and, in fact frequently masquerade as cases of moderate pulmonary valvular or infundibular stenosis with intact ventricular septum (Fig. 5) or small isolated ventricular septal

defects requiring amyl nitrite for differentiation[3, 21]. They have relatively mild stenosis, sufficient to maintain balanced pressures in the ventricles with a slight left-to-right or right-to-left shunt, and a virtually normal pulmonary blood flow and pressure. Conversely, severer cases with shorter murmurs ending before a single second sound are easily recognised and the severity of the stenosis can be readily predicted from the degree of shortening of the murmur.

It must be emphasised that the auscultatory assessment of severity should be made in a relaxed subject, examined at rest. This is because pulmonary blood flow is dependent not only on the severity of stenosis but also on the right ventricular pressure, which, in turn, is determined by the systemic resistance. Marked changes in the latter may induce changes in the murmur independently of the stenosis. In Chapter VI it will be shown that the brisk fall in systemic resistance following amyl nitrite inhalation, induces a fall in right ventricular pressure despite the increased venous return to this chamber and the presence of pulmonary stenosis. This is due to the efficient escape route provided by the large ventricular septal defect. The fall in right ventricular pressure reduces pulmonary flow which is reflected by a marked temporary shortening and softening of the murmur. It is obvious that reduced systemic resistance from other causes will likewise shorten the murmur. Thus I have frequently observed marked shortening and softening in cases over-sedated with morphine, pethedine or barbiturates during cardiac catheterisation. In such cases, measurements of pulmonary blood flow and arterial oxygen saturation were often excessively low and might explain the inaccuracy of these methods in assessing the severity of Fallot's tetralogy by cardiac catheterisation[10]. Conversely, increased

systemic resistance results in elevation of right ventricular pressure which causes greater pulmonary blood flow[22], a longer murmur and less cyanosis (Chapter VII). The favourable combination of coarctation of the aorta with Fallot's tetralogy has been described in Chapter I and the marked intensification of the murmur and increase in arterial oxygen saturation following pressor agents will be shown in Chapter VII. Squatting probably achieves its beneficial effect by combining increased systemic resistance with increased venous return and I have observed increase in loudness of the murmur during squatting. Partial clamping of the aorta during surgery is known to improve pulmonary blood flow whereas excessive drop in systemic pressure has the opposite and highly undesirable effect.

There are other variables which may influence pulmonary blood flow and murmur. Changes in cardiac rate, venous return and blood viscosity must also play a greater or lesser part in the individual case. There is also the possibility that the state of tonus in the infundibulum may vary and so alter the degree of stenosis. However, the great merit of the murmur is that its length and loudness accurately reflects the volume rate of blood flow through the stenosis at the given moment. For this reason, auscultation is a particularly sensitive means of detecting both the severity of the stenosis and spontaneous fluctuations in pulmonary blood flow. Auscultation has, in fact, thrown considerable light on the mechanism of cyanotic and syncopal attacks to which severe cases of tetralogy are prone. In 4 cases examined during such attacks the murmur softened and shortened and at times completely disappeared (Fig. 10). The presence of marked sinus tachycardia and a normal pulse pressure excluded acute hypotension as a cause of gross reduction in the gradient across the

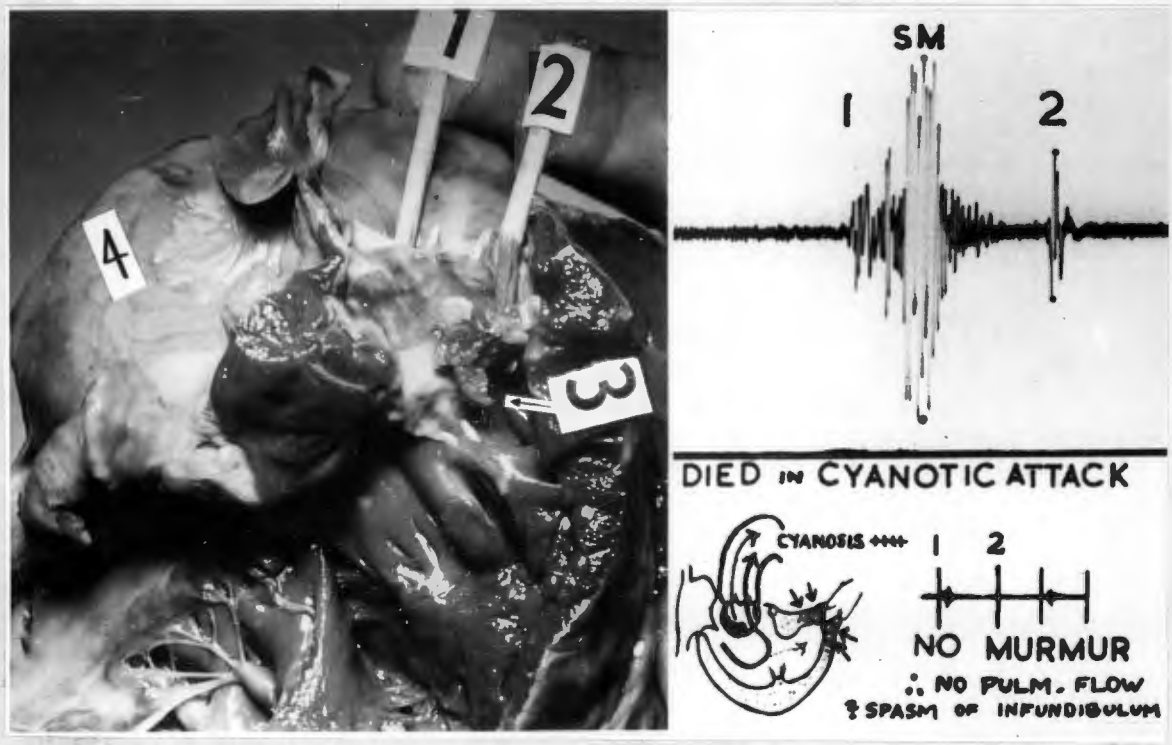

Fig. 10. Severe Fallot's tetralogy. Two days before death the systolic murmur was loud but the crescendo occurred before midsystole followed by a rapid diminuendo with and cessation well before the loud aortic sound. These were the features of severe tetralogy. This child had had numerous cyanotic attacks for 2 years and had died in an attack. During an attack the murmur disappeared despite a good pulse pressure. The concept of spasm of the infundibulum causing functional atresia, disappearance of the murmur and a greatly increased right-to-left shunt is depicted in the diagram. The necropsy specimen shows the small infundibular chamber (2), between the pulmonary valves (1) and the severe infundibular stenosis. Small fleshy vegetations (3) are present in the chamber and thick contractile muscle surrounds the chamber. The tricuspid valve is shown in the lower left corner and the aorta (4) lies above.

stenosis. In the presence of normal blood pressure and hence right ventricular pressure, disappearance of the murmur could only mean a greatly increased stenosis during the attack. On recovery from the attack, cyanosis lessened, consciousness returned while the murmur

reappeared and returned to its original state, suggesting release of superadded functional obstruction. That increased tonus or even spasm may occur in the infundibular portion of the right ventricle in Fallot's tetralogy has been well established[6, 9] and has been postulated as the mechanism of cyanotic attacks by Brock[6] and Wood[8, 9]. I believe that the shortening, softening and eventual disappearance of the systolic murmur in the face of the normal blood pressure confirms this suggestion. Brock[6] believes that cyanotic attacks are due to increase in tonus of an already diminutive outflow tract which diminishes the lumen even further, as if by sphincteric action. Cyanosis is at once deepened by the marked increase in right-to-left shunt and the diminished blood flow to the lungs. The cases most prone to frequent, and perhaps fatal, cyanotic attacks are those in whom the stenosis is initially severe, where even a slight increase in tonus is sufficient to induce an attack. Wood[9] studied 5 cases of Fallot's tetralogy, either in an actual attack of syncope or in an episode of spontaneous dyspnoea and cyanosis short of syncope. The blood pressure did not fall in any and in one case methedrine was without effect on the very low arterial oxygen saturation (10%), even though the blood pressure rose from 100 to 150 mm.Hg. This proved that peripheral vasodilatation had not caused the attack; moreover, it strongly supported the contention of severe functional infundibular stenosis where even a right ventricular pressure of 150 mm.Hg. failed to increase pulmonary blood flow. In all patients there was shortening softening and eventual disappearance of the systolic murmur, according to the degree of fall in arterial oxygen saturation. When consciousness was lost, no murmur could be heard at all, suggesting that there was then a state of pulmonary "atresia". Unconsciousness

was attributed to the extremely low arterial oxygen saturation. He concluded that the most likely mechanism accounting for these observations is that during the attacks the infundibulum contracts more completely than usual and tends to block the outflow to the lungs. This would cause the murmur to shorten, and to disappear when the obstruction was complete.

If these views are correct then therapy should be aimed at release of the increased tonus in the infundibulum. Tonus must relax spontaneously in the majority of cases, possibly due to profound anoxia of the myocardium during the attack. Taussig observed that morphine has a most beneficial effect in relieving the attacks, but the mode of action is obscure. Could it be that it releases the tonus of the infundibulum? Wood[9] has shown that cyclopropane relieved the functional obstruction in one case of Fallot's tetralogy. Braude and Zion[24] reported success with intravenous procaine in a mild, acyanotic case of Fallot's tetralogy who developed severe infundibular spasm during cardiac catheterisation. This well documented case proved beyond reasonable doubt that infundibular spasm caused the cyanotic attack, since a normal blood pressure was maintained throughout while the murmur, which had been loud and long with an audible pulmonary component, disappeared. Procaine resulted in a temporary marked improvement in cyanosis, quick restoration of consciousness and return of the murmur to its former loudness. However, morphine was ultimately required for complete recovery since procaine released spasm only for a few minutes.

The various factors which influence the blood flow through the stenosis and hence the systolic murmur in Fallot's tetralogy are summarised in Table 2.

TABLE XI

FACTORS INFLUENCING PULMONARY BLOOD FLOW IN FALLOT'S TETRALOGY.

(A) THE RIGHT VENTRICULAR - PULMONARY ARTERIAL PRESSURE GRADIENT

(1) Increased by: (murmur gets longer and louder; right-to-left shunt diminishes).

(a) Lessening the severity of the stenosis.

Surgery: infundibular resection or valvotomy S.B.E.
Relaxants of tonus of infundibulum, ? morphia, cyclopropane, oxygen, procaine.

(b) Increasing systemic peripheral resistance.

Hypertension.
Pressor Agents.
Squatting.

(c) Combining (a) and (b).

(2) Decreased by: (murmur gets shorter and softer; right-to-left shunt increases).

(a) Increasing severity of the stenosis

Increased tonus or spasm of the infundibulum causing cyanotic attacks.

(b) Decreasing systemic peripheral resistance.

Inhalation of amyl nitrite.
Oversedation.

(c) Combining (a) and (b).

(B) BRONCHO-PULMONARY COLLATERAL CIRCULATION.

(systolic murmur gives no information).

Spontaneous development seldom effective except in pulmonary atresia.

Increased by Blalock-Taussig and Pott's operations.

SUMMARY.

1. A clinical and phonocardiographic study has been made on 62 cases of Fallot's tetralogy in order to determine the value of auscultation and phonocardiography in assessing the severity of the stenosis.

2. The severity of the tetralogy, as determined by clinical methods was correlated with the length and loudness of the murmur and other auscultatory signs.

3. Increasingly severe stenosis was shown to be associated with a shorter, earlier and softer systolic murmur. In extreme tetralogy, the murmur was invariably soft and very short, being confined to early systole and ending in midsystole. An aortic ejection sound was usually audible and the second sound invariably loud and single. In severe tetralogy, the murmur was usually loud and short, with its crescendo before midsystole and termination before the aortic second sound. A pulmonary component was never audible. In moderate cases, the murmur was loud and longer, with its crescendo at midsystole and termination before or at the aortic second sound, which was never obscured by the murmur. A very soft, pulmonary component was only rarely recorded. In mild cases, the murmur was loud and more prolonged with the crescendo in the latter half of systole and extension into, but rarely much beyond the aortic component. Although at times loud at the aortic component, the murmur totally obscured this sound in only one case. A pulmonary component was frequently recorded and often heard; it was extremely soft and localised, but occasionally relatively loud. Splitting was always wide (av. 0.09 sec.). The loud, long

murmur reflected good pulmonary flow and the audible or recordable pulmonary component a relatively normal pulmonary arterial pressure.

4. Since the length and loudness of the systolic murmur reflects the volume rate of blood ejected through the stenosis, auscultation is believed to be a most valuable method of assessing both the severity of stenosis and fluctuations in blood flow which may result from changes in systemic resistance and tonus of the infundibulum of the right ventricle. The change in murmur during cyanotic or syncopal attacks has thrown considerable light on the mechanism of such attacks, as discussed.

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CHAPTER V

ASSESSMENT OF POST-OPERATIVE RESULT BY AUSCULTATION AND PHONOCARDIOGRAPHY

In the preceding chapters it was shown that increasingly severe stenosis exerted an opposite effect on the systolic murmur in pulmonary stenosis with intact ventricular septum and in Fallot's tetralogy. The murmur became longer and louder when the ventricular septum was intact, but shorter, softer and earlier when a large septal defect (Fallot's tetralogy*) was present (Fig. 1). Conversely, production of mild stenosis by a successful valvotomy or infundibular resection, was also shown to produce an opposite effect on the murmur in the two conditions, shortening and softening it when the septum was intact and prolonging and intensifying it in the tetralogy. The opposite behavior of the murmur with changing severity of the stenosis clinches the thesis that the murmur is determined by, and accurately reflects the different dynamic situation in the two conditions[1].

*

Footnote. Again, by Fallot's tetralogy is meant severe infundibular or valvular stenosis with large ventricular septal defect and right-to left ventricular pressures of the same order. Even in acyanotic cases the stenosis is relatively severe permitting bi-directional ventricular shunt or at most, a small left-to-right shunt at rest (see Fig. 11). This definition is, of course, arbitrary but for this work it has been necessary to avoid classing as tetralogy, combinations of V.S.D. with large left-to-right shunt and mild stenosis, or small V.S.D. and mild stenosis. The case material in this thesis illustrates the clinical and haemodynamic spectrums of pulmonary stenosis and ventricular septal defect described by McCord et al[14] and it is agreed that the term Fallot's tetralogy may have overserved its usefulness and perhaps should be dropped. However, for convenience and sentimental reasons I have retained it to cover the spectrum within the limits just defined.

The purpose of this paper is to emphasise the value of auscultation and phonocardiography in evaluating the post-operative result. The severity of stenosis after a pulmonary valvotomy or infundibular resection can be assessed by the same criteria defined in Chapters III and IV for diagnosing the pre-operative severity. This method will be shown to be one of the earliest and most reliable means of evaluating the result of this type of operation.

The different effect of the three operations for Fallot's tetralogy on the systolic murmur will be used to support the thesis that in the tetralogy the murmur length is inversely related to the severity of the stenosis provided the septal defect is large and the systemic resistance constant (see Chapters VI and VII). A successful valvotomy or infundibular resection (Brock operation) alone causes great lengthening of the murmur since the stenosis has been rendered mild, while the septal defect remains unchanged. A successful Blalock-Taussig operation will be shown to have no effect on the murmur length, since both stenosis and septal defect remain unchanged. A successful repair operation with closure of the defect and removal of the stenosis produces a short ejection systolic murmur of mild stenosis with intact ventricular septum or possibly no murmur at all.

Material and Methods.

The effect of surgery on the auscultatory and phonocardiographic (PCG) findings was studied in 16 cases of pulmonary valvular stenosis submitted to valvotomy and 2 cases of infundibular stenosis with functionally intact ventricular septum submitted to infundibular resection. There were 23 cases of Fallot's tetralogy. Of these a

pulmonary valvotomy, infundibular resection or dilatation (Brock operation) was performed in 13, a Blalock-Taussig operation in 7 and 3 had the septal defect closed and the stenosis resected. The method of auscultation and phonocardiographic technique and measurements was identical to that already described in Chapter III. It is necessary to re-emphasise that pre- and post-operative sound recordings were always made at the same site on the chest wall and at the same amplification during held expiration. This method was roughly quantitative when used on the same patient, provided no marked changes occurred in chest wall thickness, but a method of sound calibration would have been desirable.

Pre- and post-operative severity of valvular or infundibular stenosis with intact ventricular septum was confirmed in most cases by the right ventricular pressure, while in the tetralogy, a clinical method was used. These will be discussed in detail below under the appropriate headings to avoid repetition.

PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM.

The effect of surgery on the auscultatory and PCG findings was studied in 16 cases submitted to pulmonary valvotomy. A "blind" transventricular operation was performed in 7 and an open trans-arterial pulmonary valvotomy in 9, using hypothermia in 5 and cardio-pulmonary bypass in 4. In one of the latter, infundibular resection for gross secondary infundibular hypertrophy was required. The length of the systolic murmur and the width of splitting of the second sound was used to predict whether mild or moderate pulmonary stenosis or little change had been produced by the operation. The criteria used were those described above (see summary in Chapter III), and summarised Fig. 1.

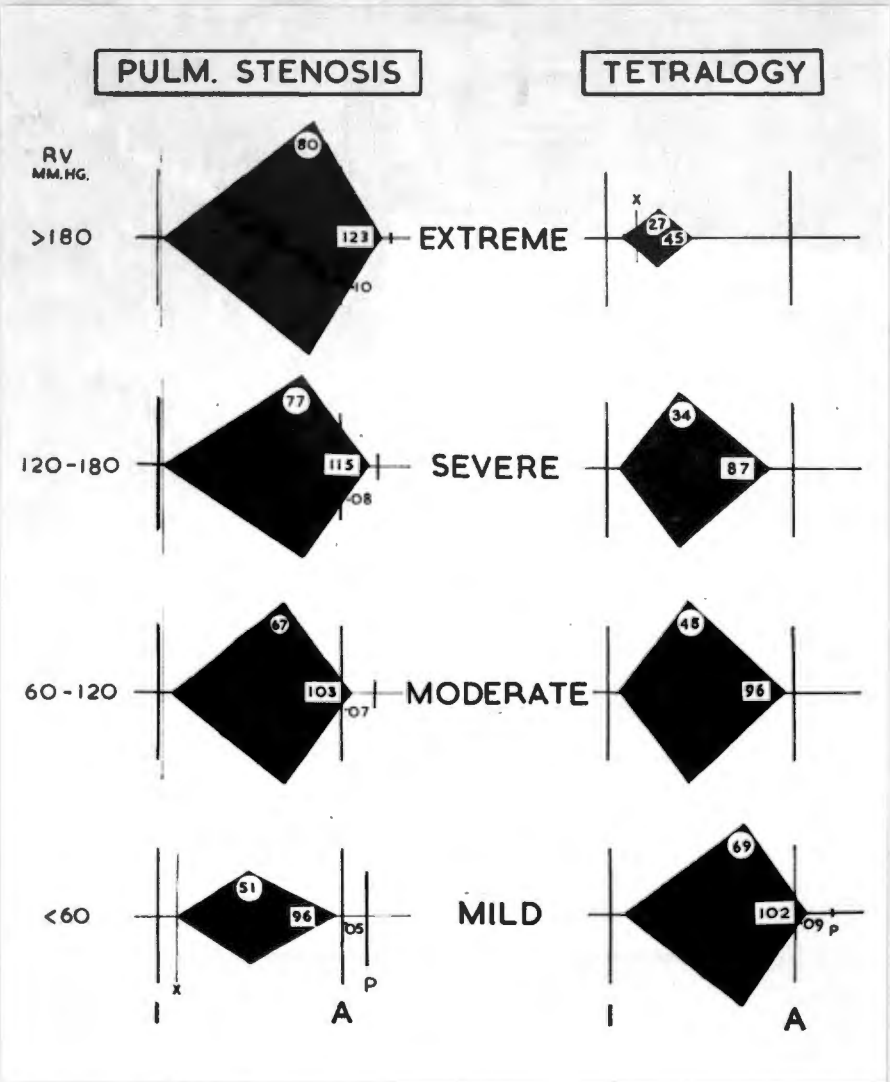

Fig. 1. This diagram depicts the opposite effect induced on the murmur length by increasingly severe stenosis in pulmonary stenosis with intact ventricular septum and Fallot's tetralogy. The mean time of the crescendo and duration of the murmur, each expressed as a percentage of the duration of left ventricular systole, is indicated and drawn to scale for each category of severity. The mean width of the splitting of the second sound is also indicated. Increasingly severe stenosis with intact septum causes a kite-shaped murmur due to great lengthening with delay in crescendo. In severe stenosis the murmur usually engulfs the aortic second sound (A) but always ends before the soft delayed pulmonary component(P). Increasing severity in the tetralogy causes the murmur to become shorter, softer and more confined to early systole and in extreme cases an aortic ejection sound usually emerges. A very delayed pulmonary component, producing wide splitting is heard only in mild cases.

The assessment of the post operative severity of stenosis made by these criteria was checked against right ventricular and pulmonary arterial pressures obtained either at operation immediately after valvotomy (not always reliable) or, preferably, by cardiac catheterisation a few months after surgery. Eight cases were re-catheterised, the cases being selected to cover the full range of results as predicted by auscultation. The result was considered excellent when the right ventricular pressure was reduced to below 40 mm.Hg., good if under 60 (i.e. mild pulmonary stenosis), fair if above 60 or below 100 mm.Hg. (i.e. moderate pulmonary stenosis), especially if reduced from a very high level, and bad if the pressure remained above 100 mm.Hg. even if reduced from a high level.

RESULTS.

Of the 8 cases re-catheterised after surgery, 4 had right ventricular pressures below 60 mm.Hg. (54/0, 52/5, 52/7 and 40 mm.Hg.) 2 had pressures of moderate severity (82/0 and 80/0 mm.Hg.) and 2 remained in the severe category (150/0 and 125/7 mm.Hg.). The prediction of severity from the murmur length and width of splitting proved correct in these cases.

In 4 of the remaining 8 cases not re-catheterised, right ventricular pressures recorded immediately after the valvotomy had to be used for proof of the success of the valvotomy. The pressures fell from 120/5 to 42/10, 160/0 to 60/0, 196/-2 to 30/2, and 125/15 to 62/4 mm.Hg. respectively. In the latter case, infundibular resection was required because of gross subvalvular muscle hypertrophy causing failure of pressure to drop below 105/10 mm.Hg. despite complete transarterial pulmonary valvotomy under direct vision.

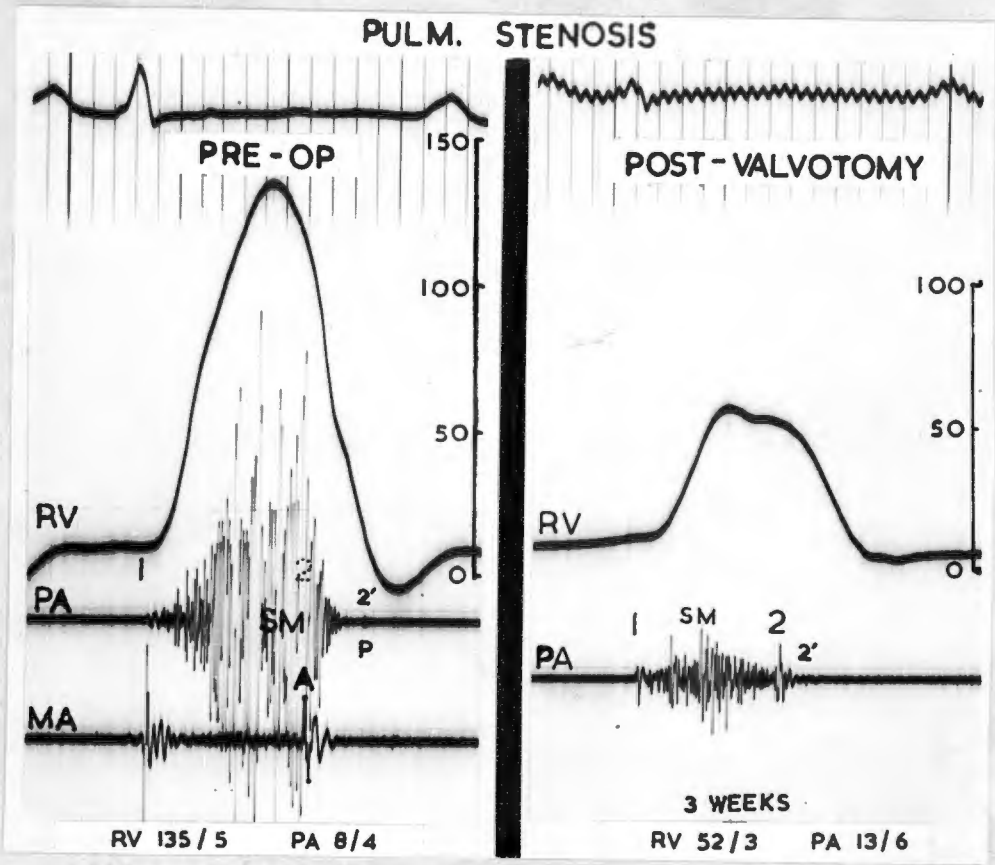

Fig. 2. Pulmonary stenosis before and after valvotomy. This case illustrates the rapidity with which the murmur length and loudness and width of splitting change after successful valvotomy, enabling early confirmation or prediction of the result at the bedside. The very loud, prolonged systolic murmur, which completely obscured the aortic sound before operation, became much shorter and much softer, ending at the aortic component soon after surgery. Splitting, which could not be heard at this early stage, had narrowed from 0.11 to 0.05 sec. Re-catheterisation 3 weeks after surgery confirmed the good result predicted. The RVP had fallen from 135/5 to 52/3 mm.Hg. The pre- and post-operative PCG's were taken at the same site and amplification in this and subsequent tracings. Each vertical line in this and subsequent tracings measures 0.04 sec., unless otherwise indicated.

These cases all developed pronounced shortening and softening of the murmur, with the crescendo in midsystole and cessation before, or at the aortic component, indicating mild stenosis. Reduction of splitting was equally impressive, but required time to appreciate, since during

the first few post-operative weeks the soft pulmonary component was often inaudible due to damping from pericardial reaction and other factors. For the same reason, shortening of the murmur was much more reliable than the degree of softening in the early post-operative period.

In 4 cases, no post-operative pressure data were available. In one of these a good result was predicted and born out by a 2 year follow-up, during which the cardiac symptoms, the giant A wave and cyanosis from a right-to-left interatrial shunt, disappeared. In the remaining three the murmurs became so short and soft that conversion to very mild stenosis seemed obvious.

The marked shortening and softening of the murmur following successful valvotomy is shown in Fig. 2, which also emphasises how rapidly the change develops permitting early prediction of the post-operative right ventricular pressure. Before valvotomy the loud, prolonged, kite-shaped murmur extended well beyond, and buried, the aortic component, but ended before a very soft and greatly delayed (0.11 sec.) pulmonary component. These features indicated marked prolongation of right ventricular systole from severe pulmonary stenosis and the right ventricular pressure was 135/5 mm.Hg.). Transarterial valvotomy under direct vision, using hypothermia and inflow occlusion, was performed, following which the murmur became much shorter and softer and splitting narrowed to 0.05 sec. These findings clearly indicated mild stenosis with little prolongation of right ventricular systole. This prediction was verified by a right ventricular pressure of 52/3 mm.Hg. at re-catheterisation, 3 weeks after valvotomy.

Fig. 9 (top row) shows the post-operative murmurs in 4 cases. In the first case the result was bad. Pre-operative auscultation

had shown a very prolonged murmur completely obscuring the aortic component and the PCG revealed very wide splitting (0.14 sec.). The prediction of very severe stenosis was confirmed by a right ventricular pressure of 160/20 mm.Hg. Following blind, transventricular valvotomy, the murmur shortened only slightly, so that the aortic component could just be heard. Splitting was still considerable (0.11 sec.). Central cyanosis and a giant A wave persisted. The auscultatory findings were now those of severe pulmonary stenosis and a bad result was predicted. During the follow-up, the length of the murmur and width of the splitting remained unchanged and cardiac catheterisation three years after the operation confirmed the unsatisfactory pressure of 125/7 mm.Hg. The bad result did not necessarily indicate an inadequate valvotomy, since it is known that gross irreversible subvalvular muscular hypertrophy can persist after complete valvotomy resulting in secondary infundibular stenosis[7,10]. Withdrawal pressures at catheterisation showed the gradient at valve level but this method can be misleading in determining the exact site of stenosis. Unfortunately, a blind transventricular valvotomy was used so that the precise reason for the bad result is not yet known in this case. However, auscultation accurately reflected the failure of right ventricular pressure to fall.

In the second case shown in Fig. 9 (top row, second from the left) the murmur extended into and partially buried the aortic second sound and splitting was 0.07 sec. Being the features of moderately severe stenosis, a fair result was predicted. Moreover, there was no change in murmur length or splitting over a 2 year follow-up. The pre-operative right ventricular pressure was 200/15 mm.Hg. and the post-operative pressure at re-catheterisation, 2 years after the blind valvotomy was 60/0 mm.Hg., confirming the forecast made from auscultation.

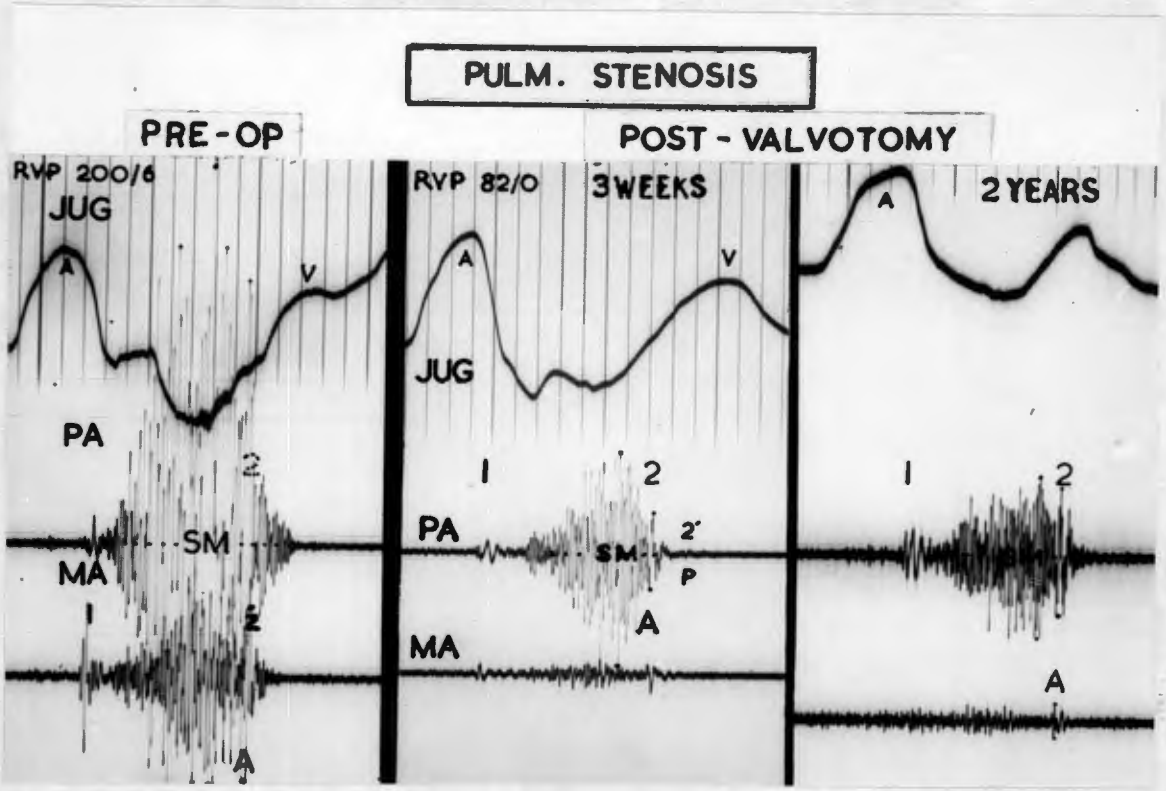

Fig. 3. Pulmonary stenosis before and after valvotomy. 3 weeks after an open, transventricular valvotomy, the grossly prolonged and loud, pre-operative murmur of very severe pulmonary stenosis (RVP 200/6 mm.Hg.) softened and shortened and a very soft inaudible pulmonary component became recordable. However, only a fair result was predicted because the murmur did not shorten enough. Its crescendo occurred well beyond mid-LV systole, the aortic sound was partially buried and splitting was wide (0.07 sec.), all suggesting moderately severe stenosis and confirmed by RVP 82/0 mm.Hg. 3 weeks after surgery. Follow-up for 2 years failed to show any further shortening of murmur and the pulmonary sound remained inaudible, suggesting persistence of high RVP from incomplete valvotomy.

Fig. 3 shows a similar result. Although the grossly prolonged and loud murmur of very severe stenosis had shortened considerably and a previously unrecordable pulmonary second sound emerged, the degree of shortening was not good enough. The crescendo was in late systole and the aortic component partially obscured; splitting was wide (0.07 sec). These were the features of moderately severe stenosis and recatheterisation 3 weeks after the open transventricular valvotomy confirmed a right ventricular pressure of 82/0 mm.Hg. During a 2 year follow-up the murmur length and width of splitting remained unchanged suggesting that there had been no regression of secondary infundibular hypertrophy.

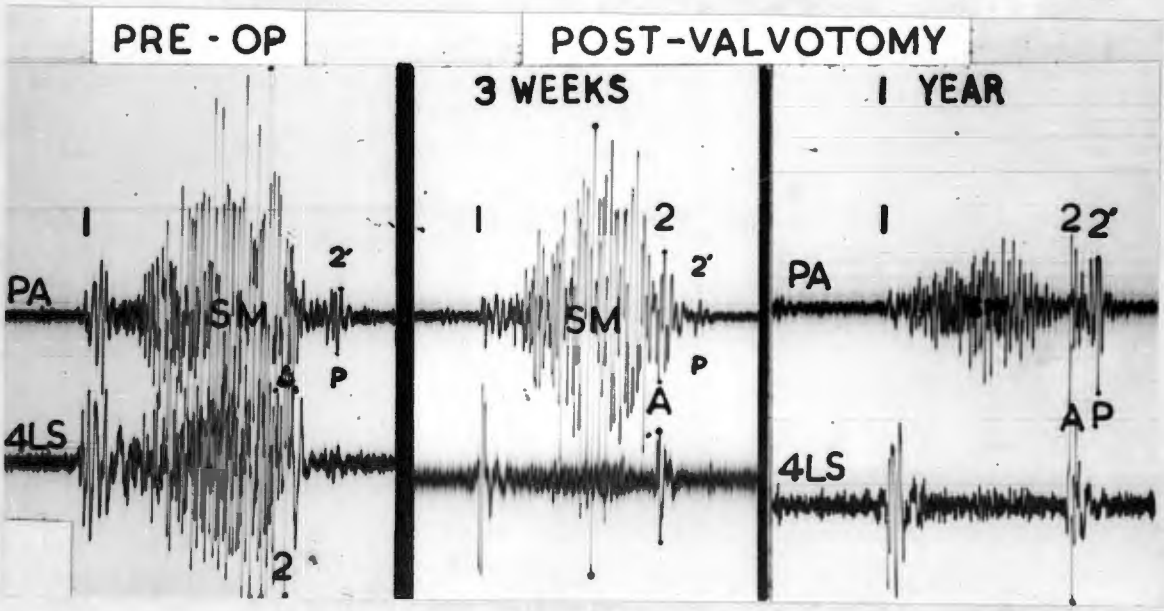

Fig. 4. Spontaneous regression of secondary infundibular stenosis after successful valvotomy. Shown by gradual shortening, softening of the murmur, narrowing of the split second sound and return to normal intensity of the pulmonary component. See text for details.

Gradual regression of secondary infundibular hypertrophy may occur after successful valvotomy. Such cases initially have a disappointing drop in right ventricular pressure despite the certainty of complete valvotomy done under direct vision. Brock[6]

has attributed this to gross concentric muscular hypertrophy of the outflow tract which causes infundibular stenosis once the valve stenosis has been relieved. However, the hypertrophied muscle may regress with time, resulting in a gradual drop in right ventricular pressure[7, 10]. This favourable trend is detectable by serial auscultation and phonocardiography as shown in Fig. 4. This case had severe pulmonary stenosis with a right ventricular pressure of 135/4 mm.Hg. and the appropriate murmur and width of splitting. Complete valvotomy under direct vision using cardio-pulmonary by-pass without hypothermia, resulted in a pressure drop to only 70/0 mm.Hg. The outflow tract was hypertrophied when palpated via the pulmonary artery but not judged sufficiently stenosed to warrant ventriculotomy and infundibular resection. The murmur length and width of splitting 3 weeks later suggested moderately severe stenosis in keeping with the disappointing drop in pressure at operation. However, 1 year later, both murmur length and splitting had diminished to a degree suggesting very mild stenosis. This was confirmed by re-catheterisation which now showed a right ventricular pressure of 40/0 mm.Hg. The ultimate result was therefore excellent.

In the third case shown in Fig. 9 (top row, third from the left), the post-operative murmur length, width of splitting and pulmonary ejection sound[4, 5] indicated mild stenosis. The good result predicted was confirmed by the right ventricular pressure drop from 135/5 to 52/3 mm.Hg., determined at cardiac catheterisation. In the last case shown in Fig. 9 (top row, fourth from the left), the murmur became very soft and short and the width of splitting much reduced (0.05 sec.). These features were those of very mild stenosis or even idiopathic dilatation of the pulmonary artery without stenosis and such a result was considered excellent.

In no case was the murmur completely abolished and in only 2 cases did the reduction in width of splitting on expiration return to normal (0.03 sec. or less).

COMMENT.

The findings demonstrated shortening of the murmur in proportion to the relief of the stenosis, thus proving the direct relation between murmur length and severity of the stenosis when the ventricular septum is intact. The direct relation between width of splitting and the severity of stenosis was likewise demonstrated, confirming the observation of Leatham and Weitzman[5]. The findings also show that the auscultatory changes, especially the length of the murmur, give an early indication of the surgical result. Notable shortening of the murmur may be detected on the operating table after completion of the valvotomy. It can certainly be appreciated in the pulmonary area during the early post-operative period and readily recorded by PCG shortly thereafter, permitting a prediction of the post-operative severity of the stenosis long before this can be done by the electrocardiogram or X-Ray, both of which reflect the trend much more slowly and with less reliability. This stands to reason because the murmur and width of splitting reflect dynamic phenomena (duration and pressure of right ventricular systole) which quickly change after valvotomy, whereas the ECG and X-Ray take much longer to show signs of improvement since they reflect changes in the anatomical state of the right ventricle.

The auscultatory signs were of considerable value in the 7 earlier cases where blind transventricular valvotomies had been performed. In the 9 cases who had valvotomies under direct vision and pressures measured thereafter, there was less use for the auscultatory

signs. However, they did add important confirmatory evidence since post-operative pressures were not always reliable. It is believed that the signs will have considerable practical application in detecting whether or not regression of secondary infundibular stenosis is taking place in those cases where this complication is known to be present. For this reason, sound tracings will be routinely recorded at the same site and amplification during follow-up of all cases in order to study this phenomenon more carefully.

INFUNDIBULAR STENOSIS WITH INTACT VENTRICULAR SEPTUM.

Only two cases of this condition were submitted to infundibular resection. Both had very severe stenosis with proximal right ventricular pressures exceeding 200 mm.Hg. Open heart surgery under hypothermia was used in the first, and cardio-pulmonary by-pass in the second. Both cases had minute ventricular septal defects, but in one the defect was distal to the stenosis. The defects were so small as to render the ventricular septum functionally intact and their presence undetectable (see Chapter III).

In the first case the pre-operative auscultatory findings revealed very gross prolongation of right ventricular systole with a systolic murmur extending far beyond the aortic second sound, which it completely drowned. There was no recordable pulmonary component. As predicted, the stenosis was very severe (RVP 212/5 mm.Hg). Direct pressure recordings immediately following resection showed no fall in the right ventricular pressure. However, auscultation during the early post-operative period clearly revealed considerable shortening of the murmur with an audible aortic component and the phonocardiogram, 2 weeks after surgery, showed the emergence of a pulmonary component 0.05 sec. after the aortic sound (see Fig. 9, Chapter III). From the auscultatory findings, the right ventricular pressure was 70/6 mm.Hg.

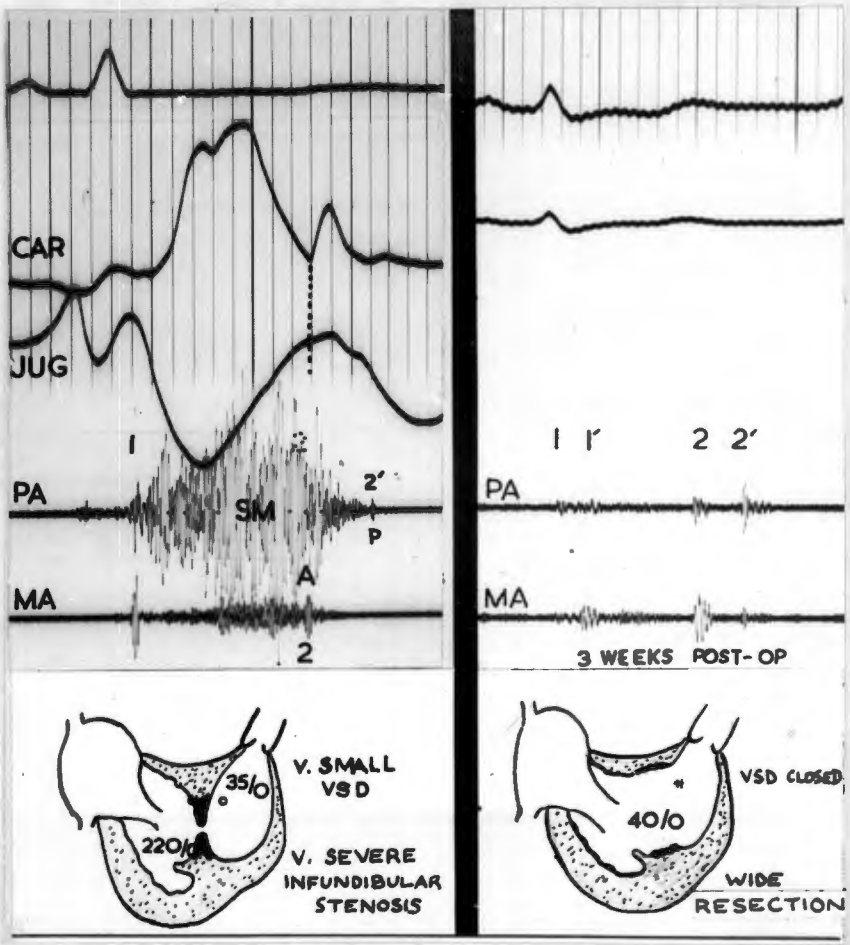

Fig. 5. Severe low infundibular stenosis before and after complete resection. The pre-operative murmur length and width of splitting was greatly increased suggesting very severe stenosis with intact septum, confirmed by pressure recordings at operation, as depicted in diagram. Since there was no additional valve stenosis and the minute septal defect distal to the stenosis was closed, there was no residual murmur after resection. Wide splitting persisted due to complete right bundle branch block (not well shown in ECG leads used) induced by the operation.

and a small left-to-right ventricular shunt was demonstrated. The observations in this case proved that in infundibular stenosis with functionally intact ventricular septum the duration and pressure of right ventricular systole are directly related to the severity of the stenosis, as in valve stenosis with intact ventricular septum. Thus the murmur shortened and softened after resection which was the

reverse of what would have happened had a large septal defect (Fallot's tetralogy) been present (see below).

The result in the second case was excellent because complete resection of the stenosis was possible using the heart-lung machine. Before operation, the murmur was extremely prolonged, extending well beyond the aortic second sound which it completely buried, and ended before a very soft pulmonary component, which was greatly delayed (0.14 sec.) (Fig. 5). These features denoted greatly prolonged right ventricular systole and hence very severe stenosis. This was confirmed at catheterisation, the proximal right ventricular pressure being 25/6 mm.Hg. He was an acyanotic, well-built man of 32 with mild dyspnoea. At ventriculotomy, severe infundibular stenosis was found. There was a small septal defect (2 mm. in diameter) in the infundibular chamber, the septum proximal to the stenosis being intact. The stenosis was widely excised and the septal defect closed. The right ventricular pressure dropped to 40/0 mm.Hg. Post-operatively, no murmurs could be heard, reflecting complete removal of the stenosis. However, wide splitting of both sounds was present due to complete right bundle branch block induced by the operation.

FALLOT'S TETRALOGY.

(1) PULMONARY VALVOTOMY AND INFUNDIBULAR RESECTION (BROCK OPERATION).

The effects of surgical relief of the stenosis (pulmonary valvotomy in 7 cases, infundibular resection in 3 cases and dilatation of the infundibulum in 3 cases) on the clinical condition and auscultatory signs was studied in 13 cases of Fallot's tetralogy.

Since only the stenosis was relieved by this operation, the change in murmur length could be used to predict the operative result. The auscultatory and PCG criteria used were those described above (see summary, Chapter IV) and summarised in Figure 1.

The assessment of the post-operative severity of the stenosis, based on the auscultatory signs, was correlated with the surgical result, as determined by the clinical method used in Chapter IV. Clinical assessment of the disability and degree of cyanosis had to be depended on, since most objective methods were unreliable in the tetralogy. Thus, the right ventricular pressure could not be used since it failed to alter whether a good or bad operation has been performed. This is because in the tetralogy, the right ventricular pressure is determined by the systemic resistance and not the stenotic resistance when the septal defect is large. Consequently, pressure data, whether obtained immediately after the operation or later by catheterisation, give no guide, except for a slight rise of the pulmonary artery pressure[13]. A much better guide is the degree to which the right-to-left shunt is reduced, since the less the stenosis the less the shunt and the greater the pulmonary blood flow. The most desirable end result obtainable by this type of operation, is the production of a milder grade of stenosis offering a resistance slightly less than the systemic resistance. This will permit a slight left-to right shunt through the ventricular septal defect (usually large in the tetralogy), so that central cyanosis disappears at rest while equal pressures persist in the right and left ventricles and the pulmonary artery pressure rises to normal level. Such a situation, though by no means ideal, is termed excellent for this operation. It results in the disappearance of cyanosis at rest, polycythemia, clubbing and squatting, with great improvement in effort tolerance and physical development[11, 12]. Slight cardiomegaly may occur.

Over-correction of the stenosis is undesirable because it produces a severe left-to-right shunt through the large ventricular septal defect[14-16]. Although there is temporary benefit from less

right-to-left shunt, all the serious haemodynamic consequences of a large ventricular septal defect with a severe left-to-right shunt will eventually emerge. The development of cardiomegaly both left and right sided, pulmonary plethora, enlarged pulmonary arteries and pulmonary hypertension, would all point to this undesirable result (see below).

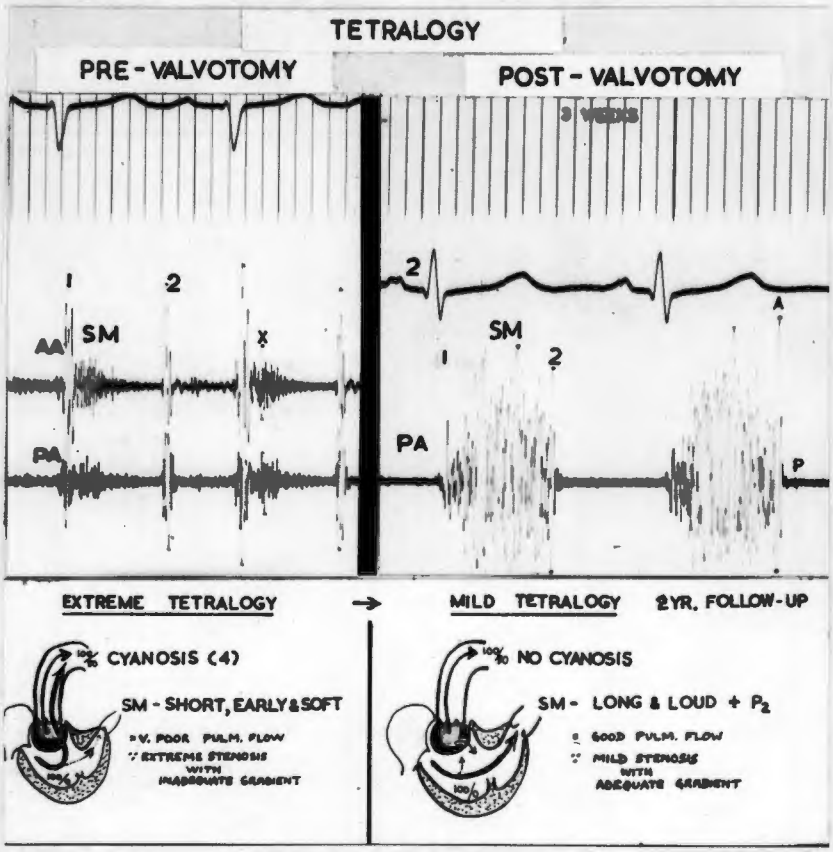

Fig. 6. Tetralogy before and after valvotomy. Conversion of an extreme case of tetralogy into a mild case was forecast in the early post-operative period, because of the development of a loud, prolonged systolic murmur extending into, but not beyond the aortic component and the recording of a soft pulmonary component. A two-year follow-up has confirmed this prediction.

A totally inadequate operation was revealed in time by persistence of unchanged central cyanosis, polycythemia and disability and such a result was naturally bad. Between a bad and excellent result were the grades of slight improvement and good result. If the grade of disability and cyanosis did not improve, the result was termed bad.

A slight or poor result was indicated by only slight improvement in the cyanosis and disability. A good result was the equivalent of producing a mild tetralogy with complete return to normal of the haemoglobin, disappearance of cyanosis at rest and ability to lead a normal life (except for strenuous exertion) and freedom from symptoms (11, 12). It was thus not difficult to grade the functional result on clinical criteria alone.

RESULTS.

Of the 13 cases, the result was bad in 3, slight in 1, good in 3, and excellent in 6 although in 1 of the latter, the later "over-correction" of the stenosis by subacute bacterial endocarditis converted the case into a large ventricular septal defect with marked left-to-right shunt. All 3 cases showing a bad result, showed no change in the length of the systolic murmur. All 6 cases with an excellent result developed a marked change in the murmur. Not only did it become much louder, but it now filled systole, extending into and slightly beyond the aortic second sound and frequently (4 cases) the pulmonary component became recordable or even audible (Figs. 6, 9). Such cases had the same auscultatory findings described in mild tetralogy. Pulmonary incompetence developed in 2 cases.

All 3 cases with a good result developed marked prolongation of the systolic murmur with the crescendo in the latter half of systole and a murmur extending into the aortic second sound, but a recordable pulmonary component did not emerge. The case showing slight improvement developed only slight prolongation of the systolic murmur, but it still remained in the unsatisfactory category of severe tetralogy since the crescendo occurred before midsystole followed by a rapid diminuendo with the murmur very soft at the aortic component (Fig. 9, middle row, second from the left).

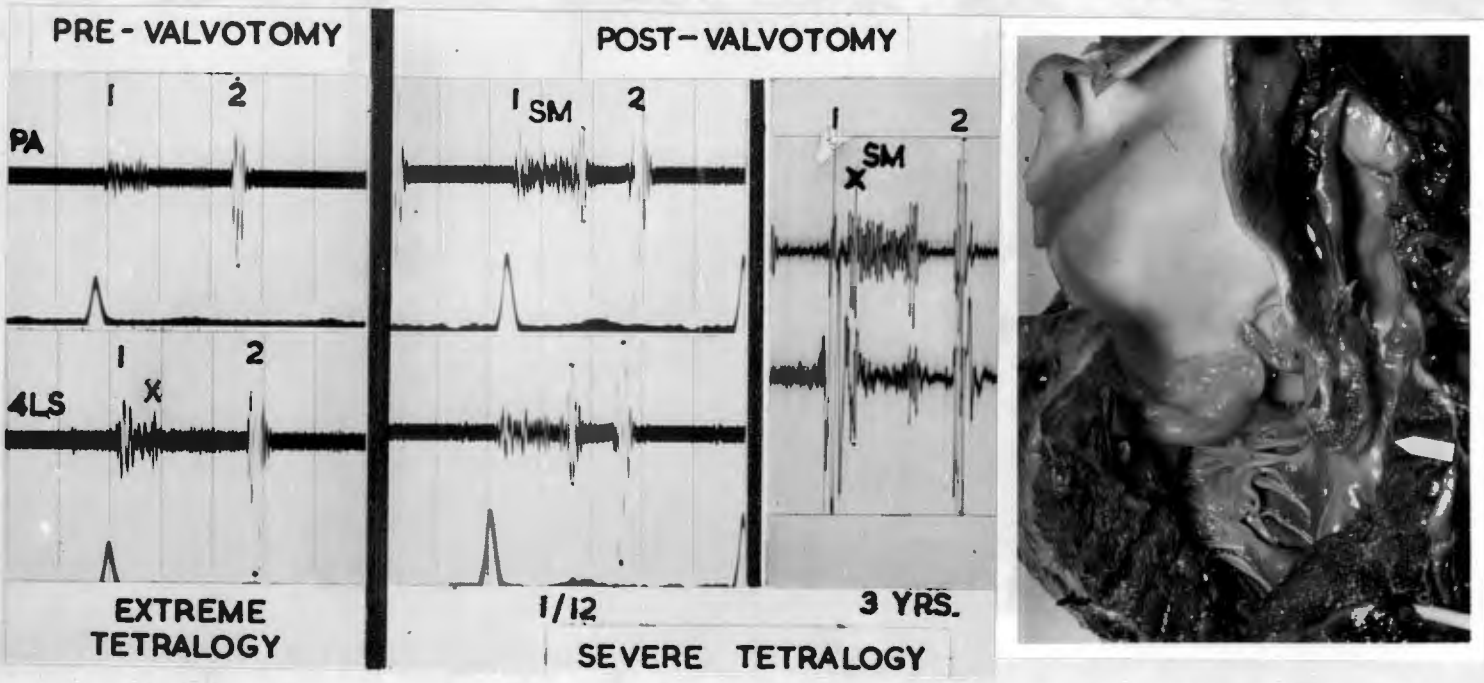

Fig. 7. Tetralogy before and after valvotomy. Before operation, the auscultatory features were those of extreme tetralogy. A bad result was predicted in the early post-operative period because the murmur was that of severe tetralogy; moreover it ended abruptly in mid-systole suggesting occlusion of the outflow tract during contraction of the infundibulum. 3 years later the auscultatory features were unchanged with persistence of the aortic ejection sound (X). The prediction of severe tetralogy was confirmed at necropsy. The specimen shows severe unrelieved infundibular stenosis (arrow) (and see enlargement on opposite page).

In 2 cases where a bad result had been predicted in the early post-operative period, the assessment was later proved correct at necropsy. Fig. 7 illustrates one of these cases. The pre-operative PCG showed an extremely short, soft, systolic murmur and an aortic ejection sound indicating extreme tetralogy. Immediately after a valvotomy the murmur became more obvious but it was soft and ended abruptly in mid-systole suggesting sudden occlusion of the outflow tract in mid-systole. The aortic ejection sound could still be heard. Since these were the auscultatory signs of severe tetralogy, a bad result was predicted. The child was lost sight of but when traced 3 years later, the murmur still showed the same features and the severe

disability and deep cyanosis confirmed the forecast made. She died following an attempt at infundibular resection and the necropsy specimen revealed a large septal defect with severe unrelieved infundibular stenosis in the tetralogy.

One case is worth citing since it proved that excessive removal of the stenosis carries the hazard of converting Fallot's tetralogy to the situation of a large ventricular septal defect with large left-to-right shunt. This patient had a pulmonary valvotomy with excellent result, the murmur becoming louder and longer with disappearance of symptoms and cyanosis. However, 16 months later, he developed bacterial endocarditis during which pulmonary incompetence emerged, suggesting that the pulmonary valve had been damaged. Following this illness, marked cardiomegaly developed and pulmonary plethora with "hilar dance" became a striking feature. There was now a very loud pan-systolic murmur maximal in the pulmonary area, followed by a blowing diastolic murmur of pulmonary incompetence. Cardiac catheterisation confirmed a gross left-to-right ventricular shunt of 7.9 litres/min., pulmonary blood flow being 13.5 and systemic flow 5.6 litres/min. Proximal right ventricular pressure was 130/10, the systolic pressure being similar to aortic pressure (140/75 mm.Hg.) Pressure in the outflow tract was 72/2 and in the pulmonary artery 35/10 mm.Hg. Pulmonary vascular resistance was low (0.3 units). At necropsy an unusually large septal defect (4 x 2 cms.) was found. There was no true infundibular stenosis and the pulmonary orifice admitted the index finger. The diameter of the pulmonary artery was nearly twice that of the aorta.

COMMENT.

The findings show that this operation increases both pulmonary blood flow and length of the systolic murmur by reducing the severity of the stenosis. This proves the inverse relation between murmur length, which reflects the volume rate of blood flow through the stenosis, and the severity of the stenosis. The findings also indicate that auscultation provides an accurate indication at a very early stage of the likely result from this type of operation. The development of a loud systolic murmur extending into the aortic second sound and a diminutive pulmonary second sound, guarantees an excellent result, provided relief of stenosis has been not excessive. In fact, if a loud pansystolic murmur is heard over the right ventricle immediately after completion of the operation, it at once indicates that adequate relief of the stenosis has been produced. Wood[3] found that the murmur often became explosive after the Brock operation.

Auscultation proved superior to other methods in the early prediction of the result, since the improvement in pulmonary blood flow was promptly revealed by the change in the murmur, whereas radiological methods required many months to demonstrate the change. Although lessening of the cyanosis was quite quickly shown time was needed to evaluate the result on this criterion alone. Regression of clubbing took many months, and improvement in effort tolerance could only be assessed after full convalescence. The E.C.G. was of no value since right ventricular hypertrophy persisted whatever the result.

(2) BLALOCK-TAUSSIG OPERATION.

To obtain further proof that the length of the systolic murmur is dependent on the severity of the stenosis, the effect of a Blalock-Taussig operation on the murmur was studied. The operation was performed in 7 cases and in all but one, the left subclavian artery

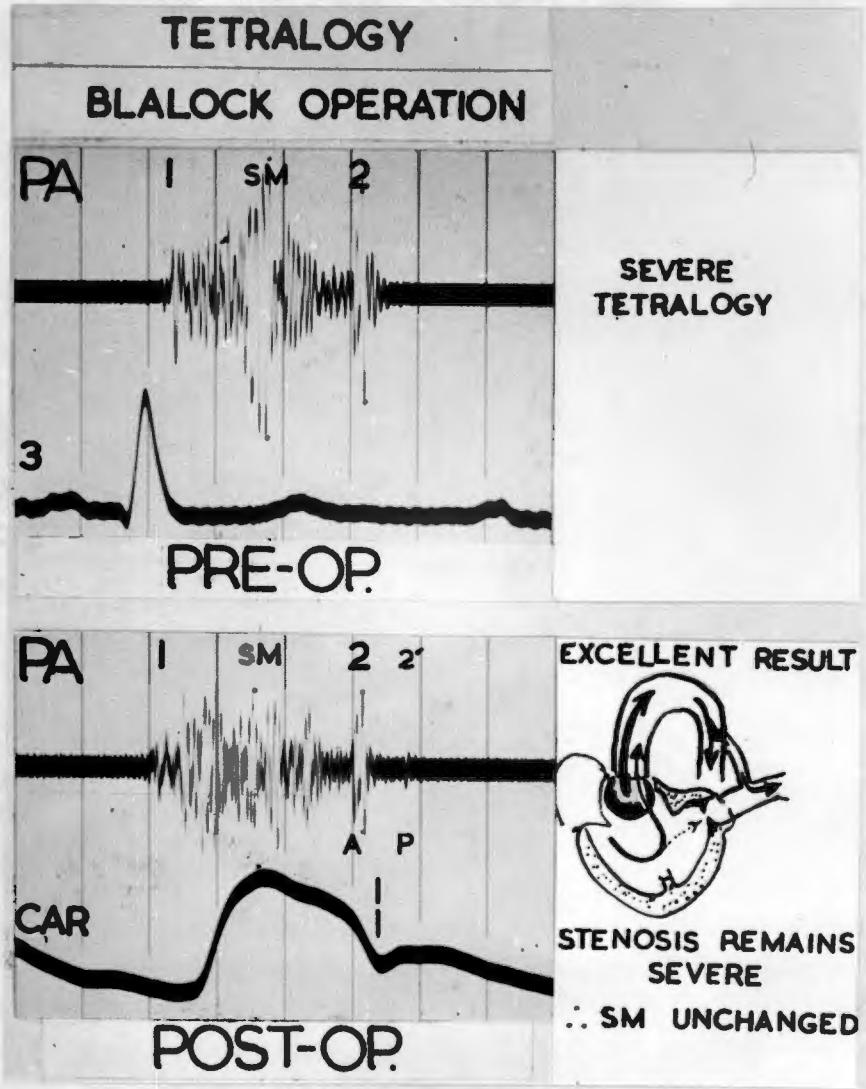

Fig. 8. Fallot's tetralogy before and after a Blalock-Taussig operation. Although the result was excellent and associated with a loud, continuous murmur and the emergence of a pulmonary component (P) suggesting a rise in pulmonary artery pressure, the crescendo and duration of the systolic murmur remained unchanged because the stenosis had not been relieved.

was anastomosed to the pulmonary artery. No case had a valvotomy or resection performed during the period of study, so that the operation achieved its effects quite independently of the stenosis. The result of operation, as determined by the same criteria used for the direct operation, was compared with auscultatory and PCG findings. Of the 7 cases, the result was bad in 1, slight in 1, good in 3 and excellent in 2. No correlation could be found between the length of the

systolic murmur and the surgical result (Fig. 9, third row). Moreover there was no increase in the length of the murmur after surgery in those cases showing as good a functional result as obtainable by the Brock operation (Fig. 9 and compare Figs. 6 and 8). These observations thus indirectly confirm the view that the murmur length is a function of the degree of stenosis in the tetralogy provided the systemic resistance remains constant.

Other auscultatory changes developed which were of value in predicting the result of this operation. A continuous murmur established the presence of a functioning anastomosis. This was always loud in good and excellent results. If, in addition to the continuous murmur, the pulmonary second sound, previously unrecordable, became recordable or even audible, it implied a significant rise in the pulmonary diastolic pressure (see Chapter IV) (Fig. 8). This occurred in 3 cases, all of whom were considered to have had good or excellent results. Conversely, a very soft continuous murmur usually suggested an indifferent result and the absence of a continuous murmur usually meant a non-functioning anastomosis, hence a bad result (Fig. 9).

(5) COMPLETE REPAIR.

While the above operative procedures are not ideal and will ultimately be replaced by the operation for complete repair of the defects, they have been of great interest and value in supporting the thesis of this paper. Furthermore, the auscultatory signs described should continue to be of value where the facilities for complete repair are not available or where a two-stage operation is planned. However, the ultimate objective must surely be repair of the septal defect and removal of the infundibular or valvular stenosis. Auscultation should also provide an early guide to the operative results, although the interpretation may be much more complex.

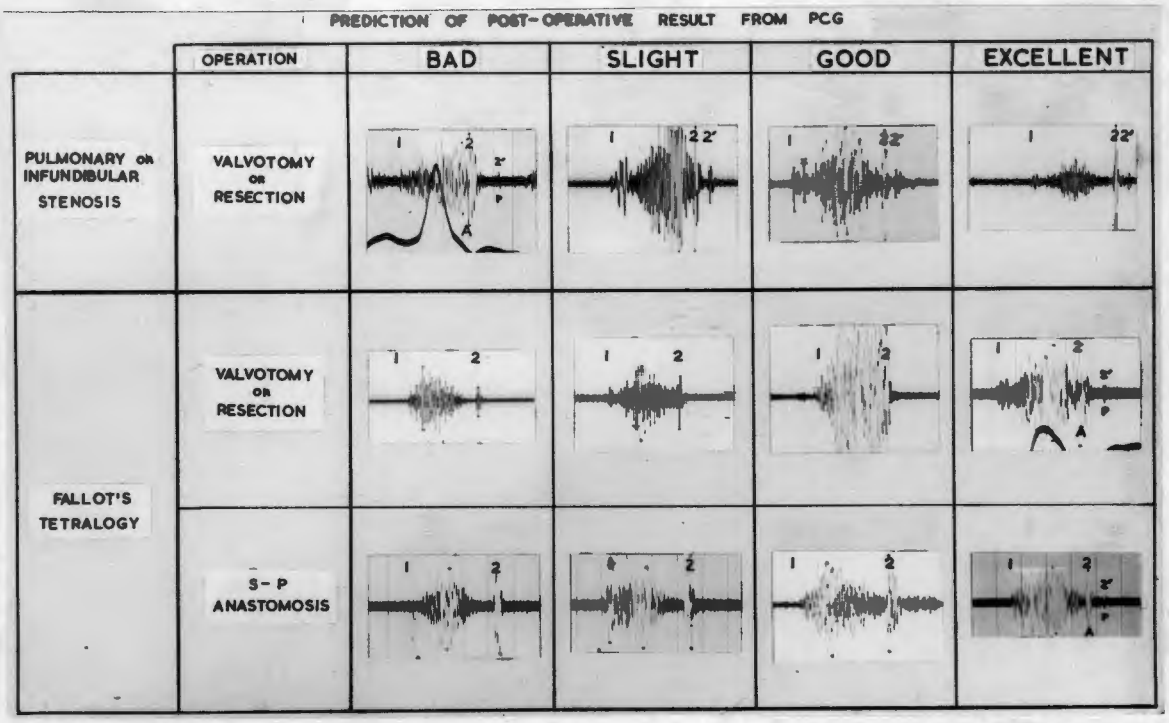

Fig. 9. Prediction of the post-operative result from the PCG. See text for details. Note the opposite effect induced on the intensity and duration of the systolic murmur by a successful valvotomy or resection in pulmonary stenosis and Fallot's tetralogy. A systemic-pulmonary anastomosis produced no lengthening of the pulmonary systolic murmur.

Complete closure of the ventricular septal defect creates an intact ventricular septum. Any remaining infundibular or valvular stenosis will then exert an effect on the duration and height of right ventricular systole proportionate to its severity as in stenosis with an intact ventricular septum. Thus, if the systolic murmur becomes or remains short and narrow splitting develops, an excellent result can be predicted since the short murmur reflects either mild residual stenosis or merely turbulent ejection of blood through a roughened outflow tract. Less adequate removal of the stenosis will result in a post-operative murmur of longer duration and wider splitting if a pulmonary component becomes recordable.

Fig. 10 shows the effect of complete repair on the murmur and heart sounds in a case of extreme tetralogy. The pre-operative

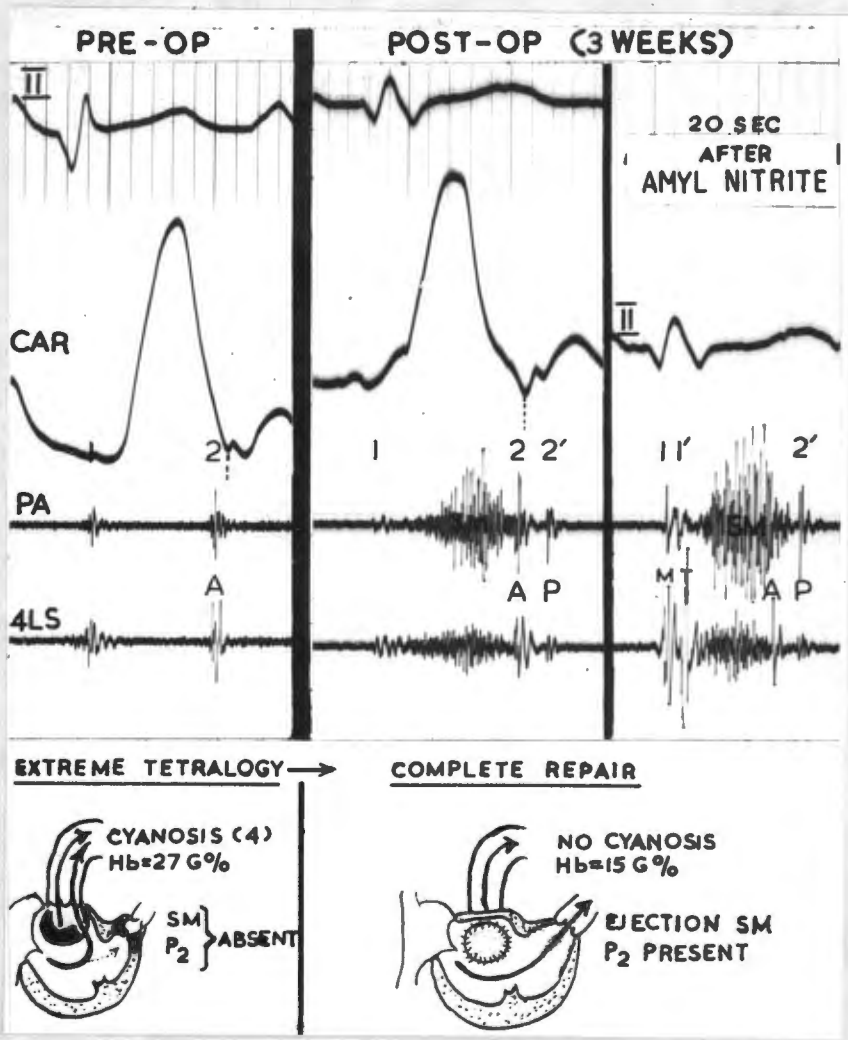

Fig. 10. Tetralogy before and after complete repair. He was an extreme case in whom a very soft, short, early murmur disappeared a few weeks before surgery. Severe infundibular stenosis was resected and ivalon patches were used to close the large septal defect and widen the outflow tract. Three weeks later a normal pulmonary component was recorded, denoting normal pulmonary arterial pressure and functioning of pulmonary valves, no pulmonary incompetence and a relatively short murmur. Amyl nitrite intensified the murmur, suggesting an ejection, rather than a V.S.D. regurgitant murmur. Delay in murmur and pulmonary second sound was due to complete right bundle branch block, shown also by split first sound after amyl nitrite.

PCG revealed an extremely soft and short murmur confined to early systole and an absent pulmonary second sound. These features were those of extreme tetralogy which was also shown by almost total disability and gross polycythaemia. At operation, a large septal defect was closed by a compressed ivalon patch and the severe infundibular stenosis resected and outflow tract widened using a patch

in the ventricular wall. The right ventricular pressure dropped from 81/-4 to 52/5 mm.Hg. and the pulmonary artery pressure rose from 22/15 to 47/12 mm.Hg. The post-operative result was excellent with rapid disappearance of clubbing and symptoms. The PCG recorded 3 weeks after the operation, showed a loud, delayed pulmonary component and a late systolic murmur of short duration. Since the operation had induced complete right bundle branch block, the delay in the murmur and pulmonary component was attributed to delayed activation of right ventricular systole rather than to prolongation of systole from persisting severe stenosis. That the murmur was not due to a small ventricular septal defect from incomplete closure of the defect was shown by the failure of the murmur to soften after amyl nitrite inhalation[17]. After the inhalation the murmur increased in loudness indicating that it was an ejection systolic murmur. However, the increase was not as great, or as sustained as in cases of pulmonary stenosis[3, 17], and it was assumed that the murmur merely reflected turbulent flow through a roughened but not stenosed outflow tract.

Incomplete closure of the ventricular septal defect with adequate relief of the stenosis will convert a large defect into a small one and will introduce the pansystolic murmur of a ventricular septal defect with a small left-to-right shunt. Such a murmur should be readily distinguished from a prolonged murmur of moderate stenosis and intact septum by using amyl nitrite. The murmur will soften in the former and greatly increase in the latter situation. Phenylephrine will also aid since it causes pronounced intensification of a septal defect murmur and very little effect in pulmonary stenosis with intact ventricular septum[18, 19]. When a small septal defect is combined with mild or moderate stenosis, a fusion of regurgitant and ejection systolic murmurs results. Recognition of this situation

is more complex but amyl nitrite and phenylephrene should prove helpful as discussed elsewhere[18].

Fig. 5 in Chapter VII illustrates the use of amyl nitrite and phenylephrene to determine the source of a residual systolic murmur after complete repair of the tetralogy. Before operation, he had severe tetralogy, the murmur being short, soft and early, with a prominant aortic ejection sound. Amyl nitrite softened the murmur while phenylephrene greatly intensified it, even bringing out a soft, delayed pulmonary second sound. Following surgery, he greatly improved in effort tolerance but had marked pulmonary incompetence and tricuspid regurgitation, both of which have persisted during the 5 month follow-up period. The pulmonary component of normal intensity emerged soon after surgery, the width of splitting being normal (0.03 sec.), thereby excluding moderate pulmonary stenosis with intact septum. The murmur in the pulmonary area had an ejection, rather than regurgitant configuration[6, 17], and the response to amyl nitrite and phenylephrene excluded a regurgitant murmur from incomplete closure of septal defect. Had a small septal defect been present, amyl nitrite would have softened and phenylephrene greatly intensified the murmur[18]. It is believed that the murmur in the pulmonary area was an ejection systolic murmur, possibly due to mild, residual stenosis, whereas in the fourth, left, intercostal space, a regurgitant tricuspid systolic murmur was present. Being a right-sided regurgitant murmur, amyl nitrite would intensify it[17] whereas phenylephrene would have no direct effect[19].

Fig. 11 illustrates the effect of complete repair on the murmur and width of splitting in a mild tetralogy. Amyl nitrite was valuable in assessing the origin of the residual murmur, since the post-operative murmur changed but little in configuration. The softening of murmur and disappearance of pulmonary second sound proved tetralogy, whereas intensification of the post-operative murmur and pulmonary component confirmed that the septum had been rendered intact. The delay in murmur and pulmonary second sound (split was reduced from 0.10 to 0.06 sec.) was attributed to complete right bundle branch block rather than to any significant residual stenosis with intact septum. At operation, following complete valvotomy and infundibular resection, and the use of an ivalon patch to close a VSD (2 cms in diam.) and to widen the outflow tract below the pulmonary valve, the right ventricular pressure dropped from 90/0 to 35/0 mm.Hg., while the pulmonary arterial pressure fell from 32/10 to 25/2 mm.Hg., proving that the murmur could not be attributed to any significant stenosis. Mild pulmonary incompetence was induced by the operation.

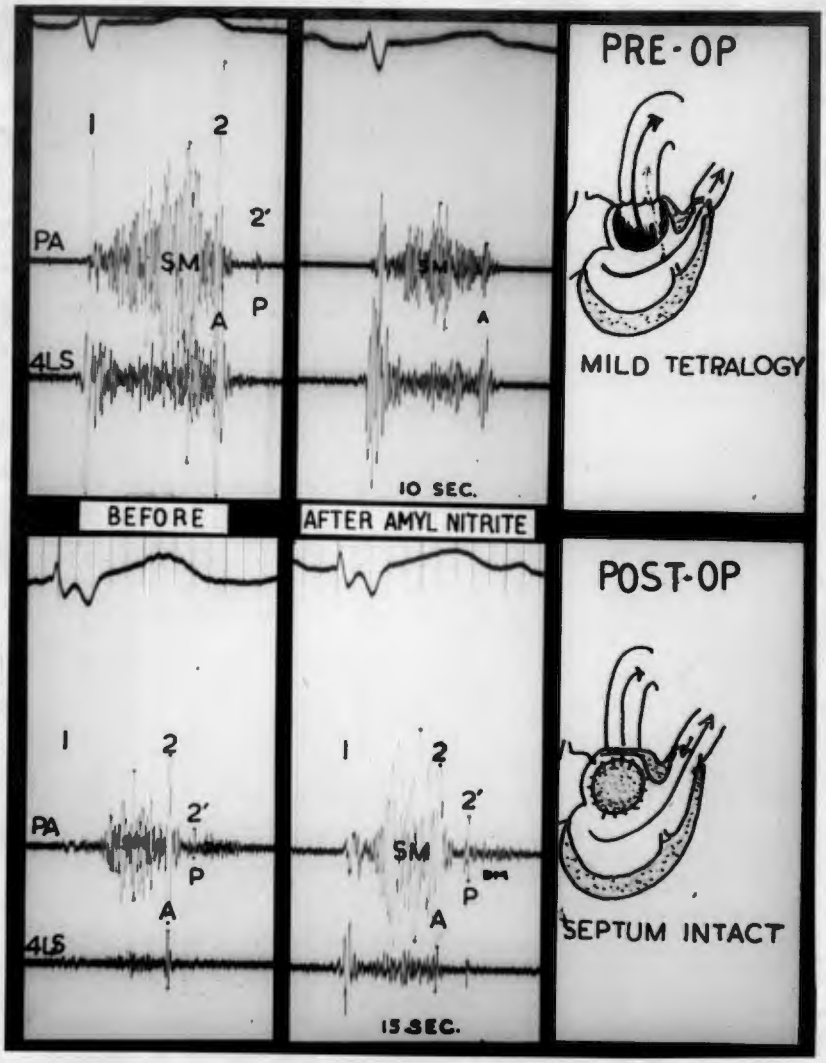

Fig. 11. Mild tetralogy before and after complete repair. Before surgery, there was a loud murmur with late systolic crescendo and a widely split second sound due to a soft, audible, delayed (0.10 sec.) pulmonary component. He was virtually asymptomatic, doubtfully cyanosed at rest and had minimal clubbing. Amyl nitrite softened the murmur and rendered P2 inaudible, proving Fallot's tetralogy. At surgery, a large septal defect was found together with relatively severe valve stenosis (diameter of orifice 4 mm.) and mild infundibular stenosis, illustrating that even in mild tetralogy the stenosis is severe. After valvotomy, infundibular resection and closure of the septal defect, the murmur softened but the configuration remained similar. However, amyl nitrite now intensified both murmur and pulmonary component proving that the septum was intact. Note narrowing of split second sound to 0.06 sec. and pulmonary incompetent murmur (DM). Delay (shift to the right) in murmur and pulmonary component presumably due to complete right bundle branch block, induced by surgery.

SUMMARY.

1. A study has been made to determine the value of auscultation and phonocardiography in assessing the result of surgery in pulmonary stenosis with intact ventricular septum and Fallot's tetralogy.

2. In pulmonary or infundibular stenosis with an intact ventricular septum, a successful valvotomy or infundibular resection resulted in marked shortening and softening of the murmur and reduction in width of splitting of the second sound. Less adequate relief of stenosis caused less shortening of the murmur and less reduction in the splitting. Criteria are given for grading the post-operative severity of the stenosis.

3. In Fallot's tetralogy, a successful valvotomy or infundibular resection (Brock operation) resulted in marked lengthening and intensification of the murmur and frequently the emergence of a very soft, audible pulmonary second sound, widely separated (av. 0.09 sec.) from the aortic second sound. These changes reflected increased volume rate of pulmonary flow through the stenosis and a rise in pulmonary artery pressure. Less adequate relief of stenosis caused less prolongation of the murmur and no emergence of a pulmonary second sound. Criteria are given for grading the post-operative result.

4. Auscultation was shown to be an excellent bedside method of predicting the surgical result of a valvotomy in the two conditions, since the change in murmur length and splitting developed rapidly and accurately reflected the degree to which the stenosis had been relieved. The opposite behavior of the murmur was attributed to the different dynamic situation in the two conditions. The observations proved that the length of murmur was directly related to the stenosis when the ventricular septum was intact, but inversely related in the tetralogy.

5. Following complete valvotomy under direct vision, the right ventricular pressure may fail to drop adequately because of severe subvalvular muscular hypertrophy. The resultant secondary infundibular stenosis may or may not regress over a period of time. The value of serial sound tracings in detecting the trend is emphasised. Gradual shortening of the initially prolonged murmur and narrowing of the split second sound indicates gradual reduction of right ventricular pressure and stenosis.

6. A successful Blalock-Taussig operation for the tetralogy did not lengthen the pulmonary systolic murmur, since the stenosis was not relieved by this operation. This indirectly confirmed the view that the length of murmur is a function of the degree of stenosis, provided the systemic resistance remains constant. However, auscultation was of value in other respects. The development of a loud continuous murmur, especially if associated with the emergence of a recordable pulmonary second sound, ensured a good result from this operation.

7. The use of auscultation in evaluating the result of the operation for complete repair of the septal defect and relief of the stenosis in the tetralogy is discussed. The ideal end result is either a short ejection systolic murmur and narrow splitting of the second sound or no murmur at all, with normal heart sounds. The use of amyl nitrite inhalation and phenylephrine in determining the origin of a residual systolic murmur is discussed.

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CHAPTER VI

THE USE OF AMYL NITRITE IN THE DIFFERENTIATION OF FALLOT'S TETRALOGY AND PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM

FOREWORD

In this chapter and in Chapter VII, the effects of decreasing and increasing the systemic resistance, respectively, on the murmur and heart sounds of the two conditions have been studied. Strikingly different responses occurred proving a valuable aid in differential diagnosis.

Clinical Communications

The Use of Amyl Nitrite in the Differentiation of Fallot's Tetralogy and Pulmonary Stenosis With Intact Ventricular Septum

L. Vogelpoel, M.B., M.R.C.P., V. Schrire, M.B., Ph.D., M.R.C.P., M. Nellen, M.D., M.R.C.P., and A. Swanepoel, M.B., M.R.C.P., Cape Town, South Africa

In previous communications concerning the differentiation of Fallot's tetralogy from severe pulmonary stenosis with intact ventricular septum and right-to-left interatrial shunt, attention was drawn to the striking difference in the duration of the systolic murmur.[1,2] In the tetralogy the murmur usually reaches a crescendo near mid-systole and ends either before or at the loud aortic second sound, which it does not obscure. In severe pulmonary stenosis with intact ventricular septum the murmur is much more prolonged, reaching a crescendo late in systole and extending well beyond the aortic second sound, which it often completely obscures. The murmur ends before a very soft pulmonary second sound which is very widely separated from the aortic component. This difference in behavior of the murmurs can be appreciated at the bedside and the diagnosis usually settled by auscultation.

In a subsequent publication[3] it was shown that the length of the systolic murmur closely reflects the severity of the stenosis. However, the murmur behaves in opposite fashion in the two conditions with increasingly severe stenosis. Thus, in pulmonary stenosis with intact ventricular septum the more severe the stenosis the longer and later the murmur. In Fallot's tetralogy the more severe the stenosis the shorter and earlier the murmur. A successful valvotomy or infundibular resection has an opposite effect on the murmur, shortening

From the Cardiac Clinic, Groote Schuur Hospital, and the Department of Medicine, University of Cape Town, Cape Town, South Africa.

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it in the former and lengthening it in the latter condition, so that accurate prediction of the operative result can be made from auscultation. These striking differences were shown to be due to the different dynamic situation in the two conditions.

Occasionally, however, it is difficult to distinguish between mild Fallot's tetralogy (cases often acyanotic at rest) and moderately severe pulmonary or infundibular stenosis with intact ventricular septum. In both conditions long systolic murmurs are found extending into the aortic second sound but not obscuring it. In both, wide splitting of the second sound with a delayed soft pulmonary component occurs.[3] Moreover, the similar clinical, electrocardiographic, and radiologic features, as well as the similar right ventricular and systemic systolic pressures found during cardiac catheterization, add to the diagnostic difficulties. Accurate diagnosis is essential in planning the surgical procedure.

The purpose of this paper is to show that inhalation of amyl nitrite induces an opposite effect on the length and loudness of the systolic murmur in the two conditions, and that this is dependent on the striking difference induced on the right ventricular pressure by this drug.[4] This harmless procedure may be used either at the bedside or during cardiac catheterization, and is of great value in establishing the diagnosis, particularly when the auscultatory and manometric findings of the two conditions overlap. Furthermore, it is of value in differentiating other acyanotic congenital cardiac conditions associated with a pansystolic parasternal murmur which occasionally closely simulate pulmonary or infundibular stenosis with intact ventricular septum.[14] Its use in differentiating aortic ejection from mitral regurgitant systolic murmurs has been shown by Barlow and Shillingford.[15]

MATERIAL AND METHODS

There were 22 cases of Fallot's tetralogy, 12 cases of pulmonary stenosis with intact ventricular septum, and 3 cases of infundibular stenosis with intact ventricular septum. The diagnosis was proved in all cases by cardiac catheterization, selective angiocardiography from the right ventricle, surgery, or necropsy, on the basis of criteria previously described.[1,2] Furthermore, the cases studied represented varying degrees of severity in each condition. No case was accepted if any doubt remained as to whether or not the ventricular septum was intact.

The effects of amyl nitrite on the systemic and right ventricular pressures were studied during cardiac catheterization in 10 cases of tetralogy, 8 cases of pulmonary stenosis with intact ventricular septum, and 2 cases of infundibular stenosis with intact ventricular septum. At the end of a routine diagnostic cardiac catheterization a control recording was made of the right ventricular and systemic pressures (brachial or femoral artery), together with a high-frequency phonocardiographic (PCG) tracing using the N.E.P. multichannel recording apparatus. Immediately consecutive right ventricular and systemic pressures were recorded through a two-way tap attached to the manometer head.[17] The PCG was recorded at the same attenuations throughout, and frequent recordings at fast paper speed (75 mm. per second) were made during held expiration throughout the study. Between the fast strips the recordings were made at slow paper speed (2.5 or 8 mm. per second). The patient was encouraged to take deep inhalations of amyl nitrite for approximately 15 seconds. The changes in the systemic and right ventricular pressures were monitored on an oscilloscope and recorded continuously at slow speed, interspersed with frequent short recordings at fast speed. Samples of blood were taken from the right ventricle and systemic artery before inhalation of amyl nitrite, and on several occasions during the peak action of the drug. This was of secondary importance in this study, inasmuch as the main purpose was to obtain pressure recordings and PCG tracings during the brief period of action by amyl nitrite.

After the pressures and pulse rate had returned to a constant level (usually by 4 minutes), the inhalation of amyl nitrite was repeated, the main object being to produce a significant drop in the systemic pressure. If the patient cooperated well, the tests were soon over, but in small infants and uncooperative patients several attempts were often required. If the patient strained, a Valsalva effect was produced, causing misleading results. During general anesthesia the effect of amyl nitrite is less marked, presumably because of vasodilatation induced by the anesthetic.

A parallel study was also made on outpatients attending the Cardiac Clinic, who were deliberately selected to show the effect of amyl nitrite on cases of different severity.[3] A control PCG tracing was recorded with one microphone at the site of maximum intensity of the murmur and one at a suitable site (usually at the fourth left intercostal space) to record the aortic second sound, together with an ECG lead. Ten deep inhalations of amyl nitrite usually produced the desired brisk fall in blood pressure, flush, and tachycardia. Phonocardiograms were recorded continuously during and after the inhalation, and frequent fast tracings (75 mm. per second) were made during held expiration throughout the study. Recordings with constant amplification were made during held expiration in order to assess accurately any change in the intensity of the murmur and heart sounds.

The duration of the inhalation was noted and a signal registered at intervals of 7.5 seconds after withdrawal of the ampule. Blood pressure readings (cuff method) were taken at very frequent intervals by one of us, while the other observed the changes in the murmur through the audiophone. Recordings were continued until the murmur had returned to its initial intensity and length, which usually required 3 to 4 minutes. The study was usually repeated at least once.

RESULTS

Fallot's Tetralogy.—

Effect on the systemic and right ventricular pressures: The effect of inhaled amyl nitrite on systemic and right ventricular pressures was studied in 10 cases of the tetralogy and is shown in Table I. In each case, during the first 15 to 30 seconds, there was a fall in both the systemic and right ventricular systolic pressures (Fig. 1). The fall in the systemic systolic pressure (average, 19 mm. Hg) was always slightly greater than the fall in right ventricular systolic pressure (average, 15 mm. Hg). In no case did the right ventricular systolic pressure rise during nor immediately after the maximal effect of the drug, provided the subject was not straining or crying. There were usually marked tachycardia and increased cyanosis immediately after inhalation. As the effect of the drug wore off, the systemic and right ventricular pressures gradually rose, while the tachycardia and cyanosis diminished, and the resting state was usually reached within 4 minutes.

During the inhalation, ear oximetry showed a sharp fall in the systemic arterial oxygen saturation, indicating an increase in right-to-left shunt (Fig. 1). As the effect wore off, so the arterial oxygen saturation gradually rose to the initial level. Ear oximetry was most useful in detecting slight transient cyanosis in mild cases in which there was acyanosis at rest.

Effect on the systolic murmur and heart sounds: During the first 30 seconds after the inhalation of amyl nitrite the pulmonary systolic murmur diminished in length and intensity in every case. This could be readily appreciated by the ear despite the marked tachycardia during the maximal effect of amyl nitrite. Thereafter, as the effect wore off, the systolic murmur increased in length and intensity and returned to its original state in about 3 minutes. The clinical observations were confirmed in each case by the PCG tracing, which also showed

TABLE I. THE EFFECT OF INHALATION OF AMYL NITRITE IN FALLOT'S TETRALOGY AND PULMONARY STENOSIS

NUMBER	CASE AGE, SEX	SEVERITY (1-4)	BEFORE AMYL NITRITE					MAXIMAL EFFECT OF AMYL NITRITE					AFTER AMYL NITRITE				
			SYSTEMIC B.P. (MM. Hg)	RVP (MM. Hg)	ART. O_2 (%)	R.V. O_2 (%)	RATE (PER MIN.)	SYSTEMIC B.P. (MM. Hg)	RVP (MM. Hg)	ART. O_2 (%)	R.V. O_2 (%)	RATE (PER MIN.)	SYSTEMIC B.P. (MM. Hg)	RVP (MM. Hg)	ART. O_2 (%)	R.V. O_2 (%)	RATE (PER MIN.)
								Fallot's Tetralogy									
1.	T.S. 18, M	1	120/80	117/5	93	57	95	100/69	100/0	—	—	110	125/82	117/0	—	—	100
2.	F.S. 24, F	2	95/65	105/5	61	40	80	80/58	90/5	—	—	83	105/68	112/5	67	45	80
3.	W.J. 4, M	2	90/50	100/5	—	—	160	82/45	82/2	—	—	155	—	110/5	—	—	165
4.	B.O. 6, M	2	95/70	95/0	65	57	95	60/42	82/-5	—	—	140	85/60	100/0	—	—	130
5.	A.P. 22, F	2	105/75	112/0	79	—	120	90/70	105/0	66	—	128	105/67	107/0	77	—	120
6.	M.J. 4, F	2	110/	105/0	75	55	98	90/	93/5	—	—	145	110/	102/0	—	—	125
7.	M.B. 8, M	3	95/60	108/0	48	36	130	75/50	75/0	—	—	150	86/50	100/0	26	18	140
8.	T.K. 6, M	3	82/50	95/0	13.9	—	125	67/38	80/0	13.3	—	135	82/52	100/0	12.3	—	130
9.	C.K. 3, F	3	—	57/-1	26	11	145	—	43/-1	—	—	150	—	70/1	—	7	130
10.	P.K. 3, M	4	75/50	75/0	—	—	90	—	68/0	—	—	100	—	70/5	—	—	100

Pulmonary Stenosis

1.	P.V. 16, F	1	135/80	25/3	92	72	98	100/50	53/3	—	—	125	140/90	30/3	93	72	105
2.	H.B. 17, M	1	137/100	60/2	96	66	95	80/56	100/2	—	—	110	115/70	55/2	95	73	76
3.	T.S. 8, M	1	95/60	52/5	86	66	84	72/35	100/–5	87	—	140	108/65	62/6	86	—	92
4.	B.V. 13, F	2	120/85	72/0	86	67	120	60/40	115/0	—	—	160	125/80	90/0	—	—	—
5.	D.D. 7, M	2	75/48	80/–5	90	65	140	45/20	135/–5	—	—	150	—	85/0	—	—	120
6.	A.S.* 6, F	2	120/75	92/10	94	64	105	70/42	155/15	—	—	160	135/95	100/20	89	60	130
7.	J.S.* 16, M	3	130/60	108/0	92	71	80	75/35	136/0	96	72	96	125/62	130/0	95	72	85
8.	K.T. 30, M	3	200/120	142/3	95	70	66	100/75	>200/3	—	—	105	195/120	160/5	—	—	74
9.	J.P. 16, F	3	120/72	124/8	91	62	118	63/42	185/10	91	71	160	142/92	160/0	91	—	135
10.	T.S. 8, M	3	120/65	125/10	80	55	78	90/48	182/5	82	58	98	113/65	136/8	77	58	85

*Infundibular stenosis.

that the first sound became loud, because of tachycardia, and the aortic second sound soft, because of the fall in systemic diastolic pressure.[5] A similar effect was noticed in all cases of tetralogy, whether extreme (1 case), severe (4 cases), moderate (5 cases), or mild (12 cases) (Figs. 4 and 5). The method of grading severity was based on criteria described elsewhere.[3] In the extreme case the murmur disappeared completely during the peak action of amyl nitrite, and a similar effect was recorded in 2 of the 4 severe cases studied. In one of these cases the initial short early systolic murmur buried an aortic ejection sound.

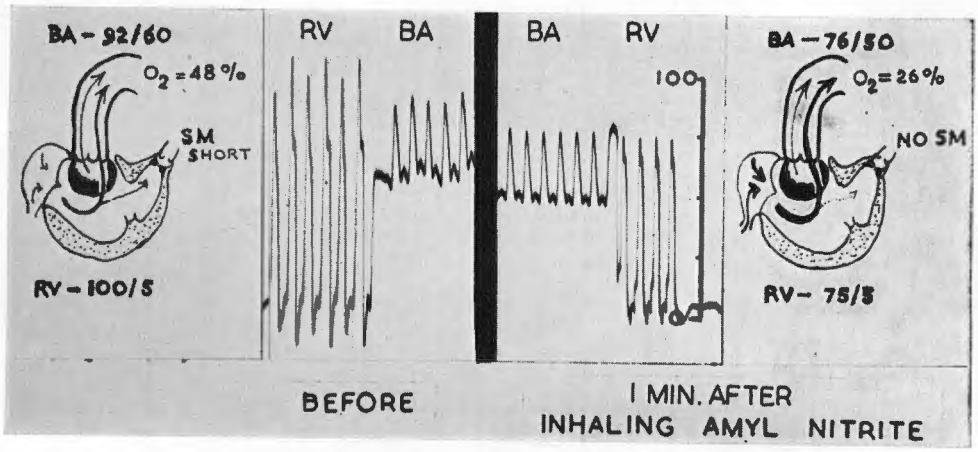

Fig. 1.—Severe tetralogy. Effect of amyl nitrite on immediately consecutive right ventricular (*RV*) and brachial artery (*BA*) pressures and arterial oxygen saturation. One minute after inhalation the BA and RV pressures dropped from 92/60 and 100/5 to 76/50 and 75/5 mm. Hg, respectively, and arterial oxygen saturation dropped from 48 to 26 per cent. The pulmonary systolic murmur temporarily disappeared, reflecting marked reduction in pulmonary blood flow.

However, when the murmur became much softer and earlier during the effect of amyl nitrite, the aortic ejection sound was clearly shown (Fig. 4). In the 5 moderately severe cases there was marked softening and shortening of the duration of the murmur during the peak action of the vapor. In one case sinus bradycardia persisted throughout, showing that in the tetralogy the shortening of the murmur is due to factors other than the sinus tachycardia induced by amyl nitrite.

In all 12 mild cases the systolic murmur was loud and long, extending into the aortic second sound but never completely obscuring it (Fig. 5). In 9 of these cases a soft pulmonary component could be recorded, causing wide splitting of the second sound (average, 0.08 second). The graphic appearance of the murmur in relation to the aortic second sound and the width of splitting was indistinguishable from that of moderately severe pulmonary stenosis with intact ventricular septum, wherein the right ventricular systolic pressure is between 60 and 120 mm. Hg.[3] The murmur was never as prolonged, even in the mildest tetralogy, as in severe pulmonary stenosis with intact ventricular septum.[3] In all these mild cases (including one case that had been converted from an extreme tetralogy into a mild acyanotic tetralogy by a successful valvotomy) the murmur became

much reduced in intensity, and shortened considerably. No case was encountered with a completely negative result, although the shortening of the systolic murmur was much more marked in some mild cases than in others. This must be related to the degree of cooperation of the patient, the lability of the vascular responses, and, possibly, the size of the ventricular septal defect.

In all 9 cases of mild tetralogy with a recordable pulmonary sound this sound disappeared during the maximal effect of amyl nitrite, and returned thereafter (Fig. 5). In one of these cases an incompetent pulmonary murmur followed the delayed sound and both disappeared during the maximal effect of amyl nitrite. These observations support the conjecture that pulmonary blood flow diminishes and pulmonary arterial pressure drops in association with the known drop in right ventricular systolic pressure. In fact, a drop in pulmonary arterial pressure during inhalation of amyl nitrite in cases of the tetralogy has been reported by Wood.[6]

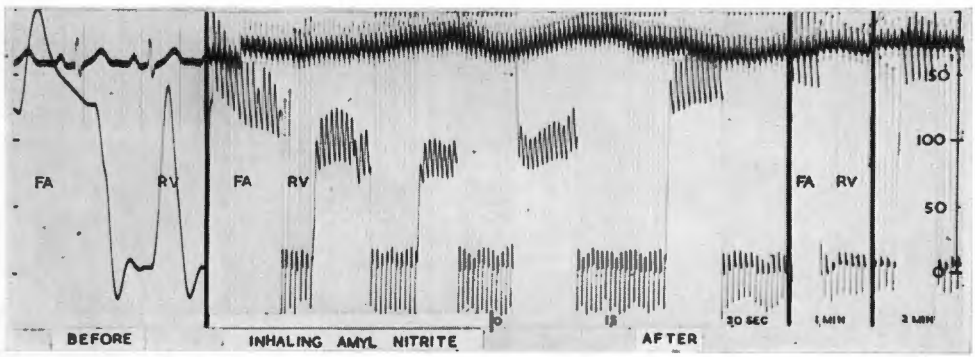

Fig. 2.—Severe pulmonary stenosis with intact ventricular septum. Effect of amyl nitrite on immediately consecutive femoral arterial (*FA*) and right ventricular (*RV*) pressures. Before amyl nitrite the FA and RV pressures were 200/120 and 142/0 mm. Hg, respectively. Cardiac rate was 68/min. During the 30 seconds of inhalation, FA pressure fell rapidly to 100/72 mm. Hg, while RV pressure rose steeply with each successive systole to reach a level exceeding 200 mm. Hg, the cardiac rate increasing to 100/min. After cessation of inhalation, FA pressure rose, reaching 175/135 after 30 seconds, 200/145 after 1 minute, and 195/146 mm. Hg after 2 minutes, while cardiac rate slowed to 78/min. RV pressure, however, remained much elevated throughout the 2 minutes, and although commencing to fall after 1 minute, it was still high (160/5 mm. Hg) at 2 minutes.

In a few cases, loud third and atrial sounds emerged for a short while and then quickly disappeared, even though the murmur remained short. The appearance of these sounds suggested rapid flow of blood into and through the right ventricle during the early phases of action of the drug.

Pulmonary and Infundibular Stenosis With Intact Ventricular Septum.—

Effect on the systemic and right ventricular pressures: The effect of inhaled amyl nitrite on the systemic and right ventricular pressures was studied in 8 cases of pulmonary valvular stenosis and 2 cases of infundibular stenosis, the cases being selected to cover a wide range of severity. There were 3 mild cases (right ventricular systolic pressure [RVP] under 60 mm. Hg), 3 moderately severe cases (RVP, 60 to 120 mm. Hg), one of whom had infundibular stenosis, and 4 severe cases (RVP, 120 to 180 mm. Hg), one of whom had infundibular

stenosis. The results are shown in Table I and indicate that whether the stenosis (valvular or infundibular) was mild, moderate, or severe the effect of amyl nitrite on the pressures was the same. In each case, during the first 15 seconds of inhalation of amyl nitrite, there was a quick fall in the systemic pressure and pulse pressure associated with a marked tachycardia. Within 10 seconds the pressure in the right ventricle began to rise rapidly with each successive beat (Fig. 2). After 20 or 30 seconds the systemic pressure was usually very low and the right ventricular pressure very high (Figs. 2 and 3). When the inhalation of amyl nitrite was stopped, the systemic pressure returned gradually to the basal level, but the right ventricular systolic pressure continued to rise and took much longer to return to normal than the systemic pressure (Fig. 3).

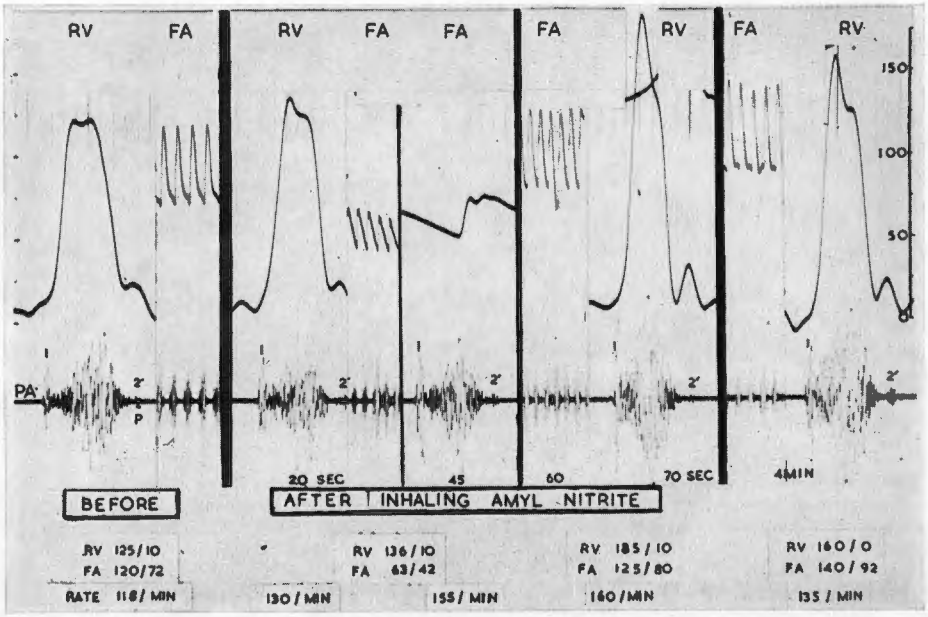

Fig. 3.—Severe pulmonary stenosis with intact ventricular septum. Before amyl nitrite the immediately consecutive RV and FA systolic pressures were almost equal, simulating Fallot's tetralogy. The systolic murmur at the pulmonary area (*PA*) was very prolonged, obscuring the aortic component, but ending before the very much delayed soft pulmonary component (*2,P*). After inhalation, the marked drop in systemic pressure followed by marked rise in RV pressure proved that the ventricular septum was intact. Note the much quicker return to normal of FA than RV pressure. The FA pressure reached resting level in 1 minute, after which there was an overshoot. The highest RV pressure was reached at 70 seconds, and even at 4 minutes it still exceeded the resting level. The systolic murmur increased in intensity with the rise in RV pressure, being loudest at 70 seconds and still increased at 4 minutes. The pulmonary component persisted throughout. Oxygen saturation of the RV blood rose from 62 to 71 per cent during the peak effect, while systemic oxygen saturation remained unchanged at 91 per cent.

Thus, the peak rise in right ventricular pressure usually occurred well after the peak fall in systemic pressure. In several cases the systemic pressure subsequently rose well above the basal level, with an increased pulse pressure, suggesting an overshoot phenomenon (Fig. 3). By 4 minutes the right ventricular pressure usually had returned to the initial level. The average fall in systemic

systolic pressure was 50 mm. Hg, while the average rise in the right ventricular pressure was 58 mm. Hg. These changes in pressure were therefore much more dramatic than those seen in the tetralogy. However, the most important diagnostic feature was the marked rise in right ventricular pressure, as opposed to its fall in the tetralogy. The divergent behavior of the pressures following inhalation of amyl nitrite readily distinguished those cases of pulmonary stenosis with intact ventricular septum in which equal systemic and right ventricular systolic pressures simulated the tetralogy (Fig. 3). Conversely, the response to amyl nitrite should also identify cases of tetralogy with discrepant right ventricular and systemic systolic pressures simulating stenosis with intact ventricular septum.[2,7-9]

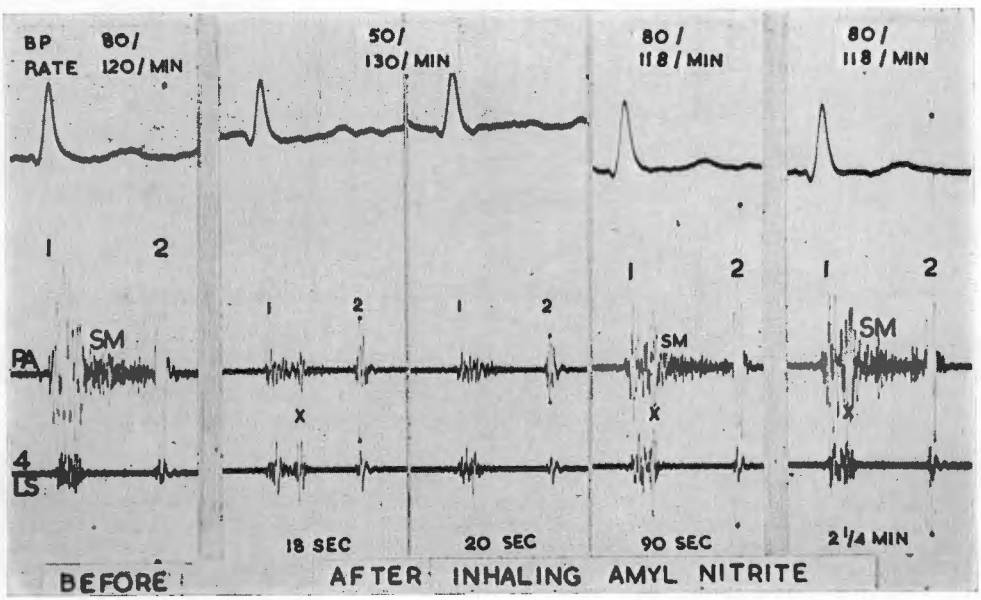

Fig. 4.—Severe tetralogy. Before amyl nitrite there was a soft systolic murmur which had an early crescendo and ended just before the very loud aortic second sound (*2*). Eighteen seconds after inhalation the murmur disappeared, exposing an aortic ejection sound (*X*). Two seconds later the ejection sound either disappeared or became much closer to the first heart sound. Gross diminution in intensity of the aortic second sound reflected the marked fall in systemic diastolic pressure. After 90 seconds, with the rise in blood pressure (and presumably in RV pressure), both murmur and ejection sound reappeared, and by 2¼ minutes the murmur had returned to the resting state. Each vertical line measures 0.04 sec. in this and subsequent phonocardiograms.

In cases without a right-to-left interatrial shunt there was no fall in systemic oxygen saturation, but this might be anticipated in cases with an atrial septal defect. Data on the change in oxygen saturation in the right ventricle were not adequate, and, in the main, were disappointing. A rise in oxygen saturation of the blood returning to the right heart would be anticipated following the sudden release of peripheral resistance. Those samples of blood taken during the peak action of amyl nitrite all showed a slight rise in oxygen saturation (Table I and Fig. 3). However, the technique used was too crude to detect

small evanescent changes in oxygen saturation. Moreover, this study was designed mainly to determine changes in pressure, which meant that sufficient samples could not be taken for oxygen estimation at the height of the circulatory changes. A catheter with double lumen was used on only one occasion, and by this means pressure and oxygen saturation data could be obtained simultaneously. This aspect is being investigated further.

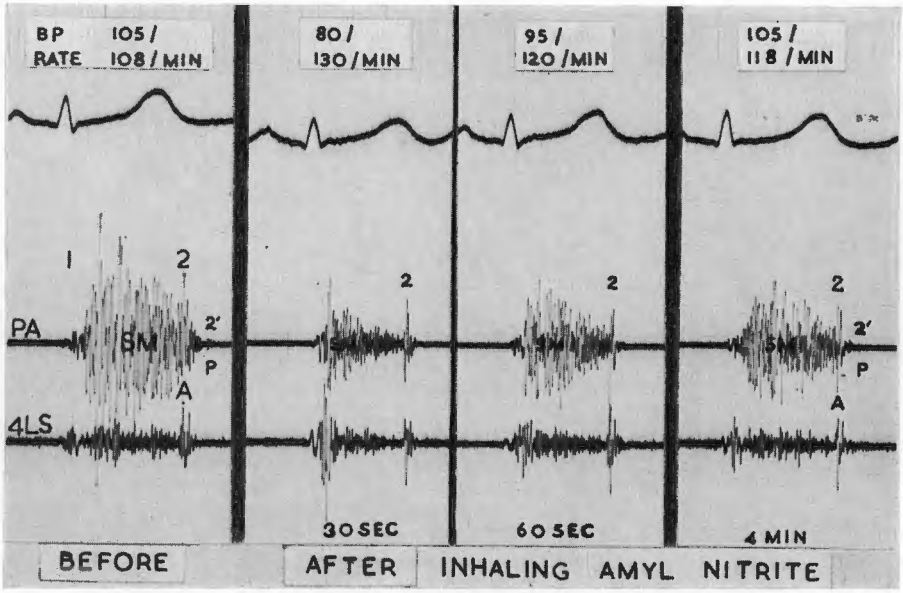

Fig. 5.—Mild (acyanotic) tetralogy. Before amyl nitrite the loud prolonged systolic murmur filled systole but did not obscure the aortic component (*2,A*). A very soft and delayed pulmonary component (*2,P*) was recorded 0.07 sec. after the aortic sound. These findings were indistinguishable from those of moderately severe pulmonary or infundibular stenosis. However, the marked temporary reduction in the intensity of the murmur with the disappearance of the pulmonary component following amyl nitrite proved Fallot's tetralogy. Compare with Fig. 6.

Effect on the systolic murmur and heart sounds: The effect of inhaled amyl nitrite on the auscultatory and PCG findings was studied in 5 mild cases, 6 moderately severe cases, 2 of whom had infundibular stenosis, and 4 severe cases, one of whom had infundibular stenosis. The changes induced during and after the inhalation were similar in all cases studied and quite different from those found in Fallot's tetralogy (compare Figs. 3 and 6 with Figs. 4 and 5). During the inhalation, while the systemic pressure was falling, the systolic murmur became much louder. This indicates that the reduced systemic pressure is accompanied by an increase in pulmonary flow unlike the response found in the tetralogy. During the period after inhalation, while the pulse rate was slowing, the murmur became even louder and more prolonged, reflecting the continued rise in right ventricular pressure, but usually after 4 minutes it had returned to its original intensity and duration.

The increase in loudness was invariably confirmed by the PCG tracing,

and the crescendo often appeared a little later in systole, suggesting prolongation of right ventricular systole in relation to left ventricular systole. Left ventricular systole might shorten while right ventricular systole lengthens during the peak action of the drug. This should result in a systolic murmur of increased duration in relation to the aortic second sound and a greater width of splitting.[3] However, it was difficult to compare the width of splitting before and during inhalation of amyl nitrite because of the marked difference in heart rate. The fact that the width of splitting, when measurable, remained virtually unchanged during the severe tachycardia must mean that there was either prolongation of right ventricular systole or shortening of left ventricular systole, or both (Figs. 3 and 6).

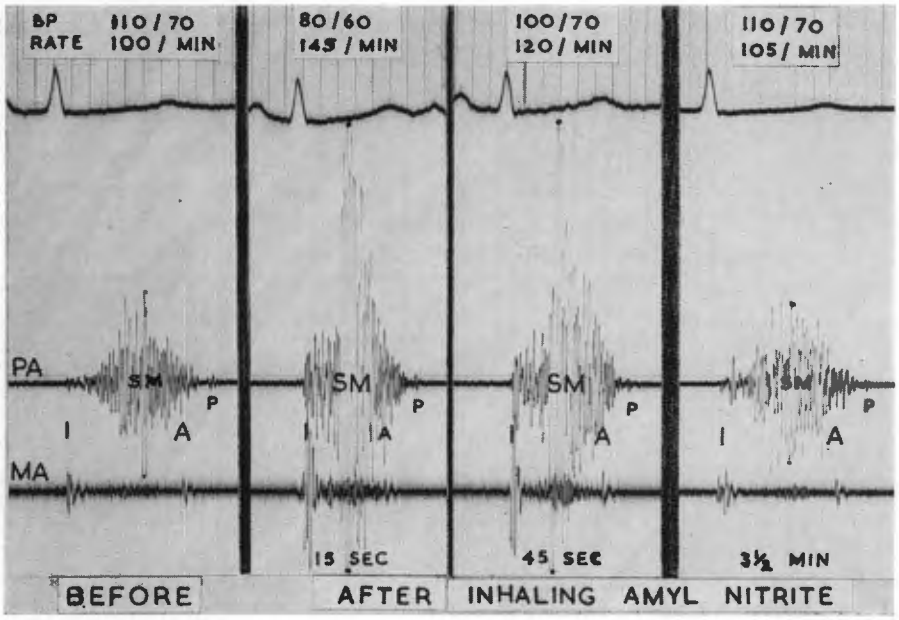

Fig. 6.—Moderately severe pulmonary stenosis with intact ventricular septum. The crescendo and duration of the murmur and wide splitting of the second sound could not be distinguished from those in mild acyanotic Fallot's tetralogy. However, the gross increase in loudness of the murmur with persistence of the pulmonary component (*P*) after amyl nitrite proved that the ventricular septum was intact.

The pulmonary component never disappeared, as occurred in all cases of mild tetralogy showing a recordable pulmonary component (compare Figs. 3 and 6 with Fig. 5). This suggests that the pulmonary blood flow and pressure were well maintained and probably moderately increased by the high right ventricular pressure. The fact that the pulmonary component never greatly increased in loudness may indicate that the pulmonary arterial pressure never rose much, despite the marked rise in right ventricular pressure. The effect of amyl nitrite on the pulmonary arterial pressure was measured in only one case. The pressure rose from 15/5 to 23/10 mm. Hg, remaining at this level for a minute after cessation of the inhalation. The RVP rose from 72/0 to 115/0 mm. Hg during a separate inhalation. The pulmonary component remained unchanged through-

out the synchronously recorded PCG tracing, while the murmur became greatly increased in intensity as well as prolonged in relation to the aortic second sound.

An atrial sound emerged in the occasional case during the inhalation but quickly disappeared as the cardiac rate slowed down.

COMMENT

The strikingly different response of the right ventricular pressure to overfilling with blood following the inhalation of amyl nitrite forms the basis of the different behavior of the systolic murmur in the two conditions. Amyl nitrite presumably acts by suddenly releasing the systemic peripheral resistance, resulting in a pronounced fall in systemic pressure and a marked tachycardia with an increased cardiac output. This must be associated with a sudden and marked increase in the venous return to the right side of the heart analogous to the tidal wave that follows the sudden opening of flood gates (Fig. 7).

In pulmonary or infundibular stenosis with intact ventricular septum the ventricle can discharge its contents only through the stenosed outlet, so that any increase in venous filling must be expelled by an appropriate increase in systolic pressure. The very steep rise in this pressure with each successive systole (Fig. 2), and the continued rise after the systemic pressure has returned to normal (Fig. 3), must imply a rapidly increasing venous return and indirectly reflect the profound extent to which amyl nitrite is capable of releasing the systemic resistance.

Similar changes in pressure occurred whether the stenosis was mild or severe, and the rise in the right ventricular pressure was invariably associated with a striking increase in the intensity of the systolic murmur, reflecting the marked increase in the speed and volume of blood ejected through the stenosis. The increase in the intensity of the murmur was always easy to appreciate on auscultation, thus permitting a confident diagnosis at the bedside.

In Fallot's tetralogy the dynamic situation is completely altered by the presence of a large ventricular septal defect, which offers to the right ventricle an escape route of much less resistance than its stenosed outflow tract, and hence the right ventricular pressure cannot significantly exceed the systemic pressure. Thus, the right ventricular pressure is determined not by the severity of the stenosis, as in the case of stenosis with an intact ventricular septum, but by the systemic resistance.* Pulmonary blood flow is therefore dependent on two main main factors, namely, the systemic resistance and the severity of the stenosis. For a constant systemic resistance, pulmonary blood flow is inversely proportional to the severity of the stenosis, as shown by the inverse relation between the length and loudness of the murmur and the severity of the stenosis, in contrast to the direct relation found in cases with an intact ventricular septum.[1,3] Conversely,

*This argument holds for the majority of cases of tetralogy in which the ventricular septal defect is large. It is appreciated that in the rare case of an exceptionally small septal defect,[3,7] or a large defect rendered functionally small by a tricuspid or endocardial flap valve,[10,18] the severity of the stenosis becomes the determining factor in the level of the right ventricular pressure. In fact, the smaller the defect the more closely will the behavior of the right ventricular pressure and murmur before and after amyl nitrite simulate stenosis with an intact ventricular septum.

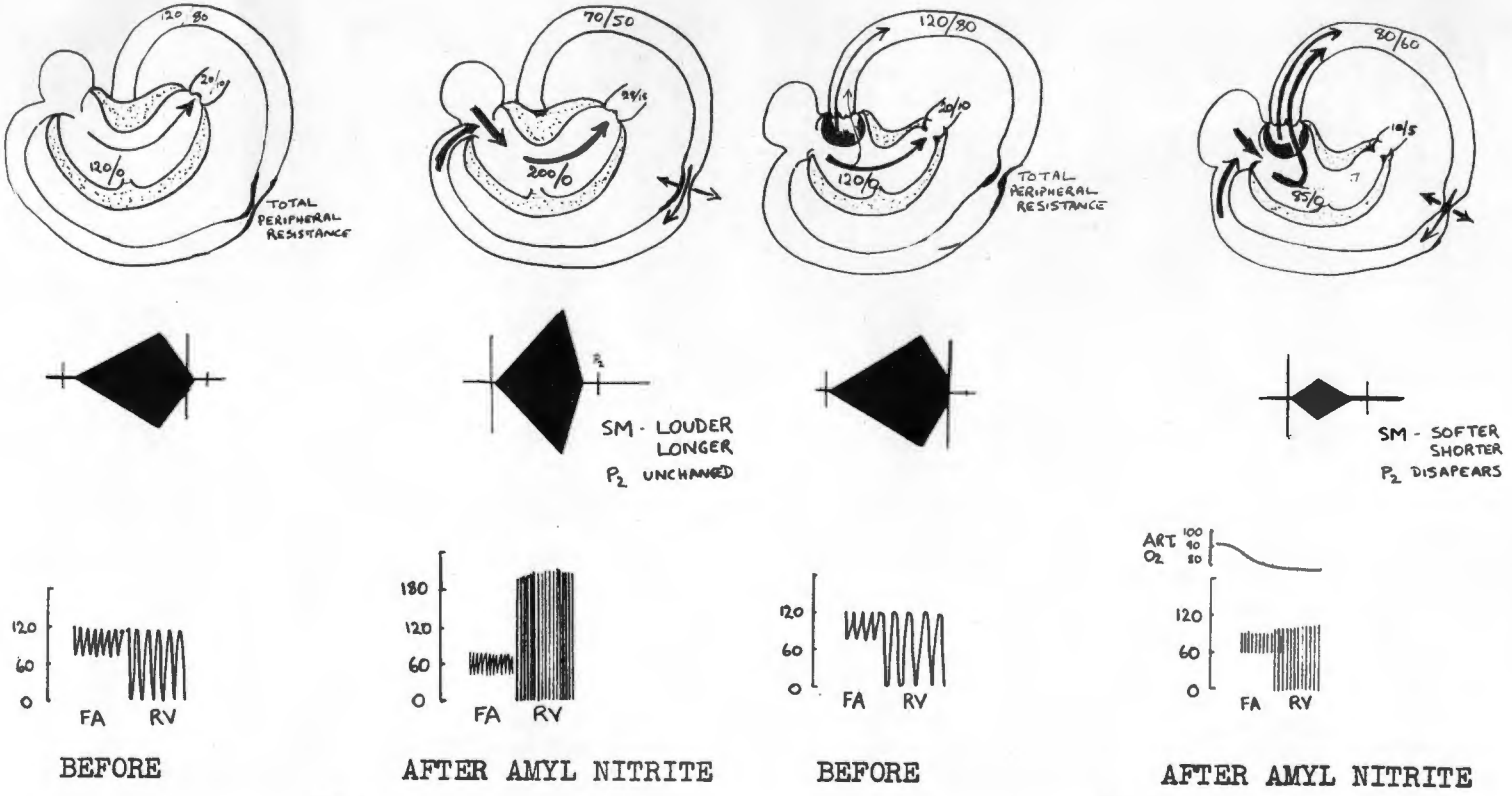

Fig. 7.

Fig. 8.

Fig. 7.—Moderate pulmonary stenosis. Before amyl nitrite, the length of murmur, width of splitting, and similar systemic and right ventricular systolic pressures are indistinguishable from those of mild Fallot's tetralogy. Amyl nitrite suddenly releases the peripheral resistance, causing a drop in systemic pressure and an increased venous return to the right heart. The marked increase in right ventricular pressure and loudness of murmur proves that the ventricular septum is intact.

Fig. 8.—Mild tetralogy. Pre-amyl nitrite phonocardiogram and pressure data are indistinguishable from those of moderate pulmonary or infundibular stenosis. However, amyl nitrite reduces both systemic and right ventricular pressures, proving the presence of a large ventricular septal defect. The drop in arterial oxygen saturation reflects the increased venoarterial shunt through the defect, while the softer and shorter murmur indicates the fall in pulmonary flow.

for a given degree of stenosis, pulmonary blood flow and, hence, the length and loudness of the murmur will be influenced by the systemic resistance. If the systemic resistance is high, the right ventricular systolic pressure rises, resulting in increased pulmonary flow, as shown by the favorable effect of systemic hypertension[16] and coarctation of the aorta[1,3] on the tetralogy. If systemic resistance falls, the right ventricular pressure should likewise fall, resulting in decreased

TABLE II. THE DIFFERENTIAL DIAGNOSIS BETWEEN MILD FALLOT'S TETRALOGY AND MODERATELY SEVERE PULMONARY OR INFUNDIBULAR STENOSIS

	MILD OR ACYANOTIC TETRALOGY	PULMONARY OR INFUNDIBULAR STENOSIS (MODERATELY SEVERE)
Symptoms	Nil or mild dyspnea (squatting usually absent)	Usually none
Cyanosis (ear oximetry)	May be absent at rest; brought out by effort, or amyl nitrite	Absent
Hemoglobin	Normal or slightly elevated	Normal
Clubbing	Absent or slight	Absent
"A" Wave	Normal	Often normal; may be dominant
Heart Size	Normal	Normal
RV Lift	Slight	Slight to moderate
Systolic Murmur		
Before	Loud; fills systole; A_2 not obscured	Loud; fills systole; A_2 partially obscured
After amyl nitrite	Softer and shorter	Louder and longer
Heart Sounds		
Before	Usually single; soft P_2 may be heard in PA; split always wide (average, 0.09 sec.)	P_2 soft in PA; split always wide (average, 0.08 sec.)
After amyl nitrite	Loud first; A_2 softer; P_2 disappears	Loud first; A_2 softer or hidden; P_2 remains
ECG	RV hypertrophy (moderate)	RV hypertrophy (moderate)
X-Ray	Lung fields normal or slightly oligemic Shape: sabot or normal Right aorta helpful	Lung fields normal or slightly oligemic Poststenotic dilatation if valvular stenosis, but absent if infundibular stenosis
Cardiac Catheterization		
Before	Pulmonary or infundibular stenosis Systemic systolic = RV systolic	Pulmonary or infundibular stenosis Systemic systolic = RV systolic
After amyl nitrite	Systemic and RV fall	Systemic falls ++; RV rises ++
Other Methods		
Aorta entered from RV	Conclusive if succeeds	Excludes
Selective angiocardiography from RV	Aorta filled	Aorta not filled
Dye Dilution	Aorta filled from RV	No filling of aorta from RV

pulmonary flow with shortening and softening of the murmur. Amyl nitrite was thus chosen as an agent which would selectively reduce the systemic resistance while subjecting the right ventricle to increased work. By such a circulatory manipulation the presence or absence of a ventricular septal defect can be readily detected.

The striking feature in the tetralogy was the fact that the right ventricular pressure fell despite the greatly increased venous return following the inhalation of amyl nitrite. This must imply the presence of a large ventricular septal defect capable of offering an effective escape route and permitting the right ventricular pressure to fall in response to the lowered systemic resistance (Fig. 8). It might be anticipated that cases of tetralogy with relatively small ventricular septal defects should show no fall, or even a rise in right ventricular pressure. So far no such case has been encountered. In the tetralogy the fall in systemic pressure was not so marked or so prolonged as in pulmonary stenosis with intact ventricular septum. This is attributed to the quicker adjustment of systemic arterial and venous blood volumes that must occur when there is a wide communication in the heart (Figs. 1 and 8). The increased venoarterial shunt during inhalation of amyl nitrite resulted in increased cyanosis, which was confirmed by oximetry. The fall in systemic resistance and, hence, in right ventricular pressure must reduce the gradient across the stenosis and result in a fall-off in pulmonary flow. In addition, pulmonary flow will also be handicapped by greater stroke volume lost down the aorta because of the fall in systemic diastolic pressure. This may account for the fact that marked shortening and softening of the systolic murmur sometimes occurred despite little fall in systemic systolic pressure.

It is believed that the transient reduction in blood flow through the stenosed outflow tract accounts for the reduction in the intensity and duration of the systolic murmur during the inhalation of amyl nitrite in all cases of tetralogy, whether extreme or mild (Figs. 4 and 5). In mild cases with the murmur loud at the aortic sound the murmur shortens so considerably that it ends before the sound, or obscures much less of it (Fig. 5). In severe cases the murmur shortens even more and not infrequently disappears, sometimes leaving only an aortic ejection sound[1-3,11,12] in its place (Fig. 4). The temporary disappearance of the pulmonary second sound in those mild cases in which it was recorded (Fig. 5) reflects the fall in pulmonary diastolic pressure that must accompany reduced pulmonary flow. As the systemic resistance rises with the wearing off of the effect of amyl nitrite, so the improving pressure gradient and pulmonary flow are revealed by a gradual increase in length and loudness of the murmur.

The chief application of these observations is in the diagnosis of mild or acyanotic cases of tetralogy from moderately severe cases of pulmonary stenosis. Both present many similar features (Table II). Thus, common to both are good effort tolerance, absence of squatting, absence of cyanosis at rest, a loud systolic murmur extending into the aortic component but not obscuring it and wide splitting of the second sound with a soft, delayed pulmonary component, right ventricular hypertrophy on electrocardiogram, similar radiologic appearances, and, at cardiac catheterization, similar systemic and right ventricular systolic pressures. Points favoring a mild tetralogy may be slight cyanosis during effort,

which if not visible is usually readily revealed by ear oximetry, and a mild polycythemia associated with minimal clubbing. Cyanosis due to a right-to-left interatrial shunt usually occurs only in severe cases of pulmonary stenosis in which the murmur is so prolonged as to render the diagnosis reasonably straightforward.[1] The diagnosis appears to depend on the awareness that cases of acyanotic tetralogy of Fallot may masquerade as pulmonary stenosis, and hitherto has often required specialized techniques such as selective angiocardiography from the right ventricle, a good prograde angiocardiogram, and selective dye dilution curves to show filling of the aorta from the right ventricle.[2] However, the use of amyl nitrite can quickly settle the problem either at the bedside or in the laboratory. The test can be repeated without harm to the patient, and phonocardiographic confirmation is useful but not essential. During cardiac catheterization the amyl nitrite test has proved more satisfactory and convenient than the exercise test which we used to employ whenever similar systolic pressures were encountered.

SUMMARY

The effect of the inhalation of amyl nitrite on the systemic and right ventricular pressures and on the systolic murmur and heart sounds has been studied in pulmonary stenosis with intact ventricular septum and Fallot's tetralogy.

In pulmonary or infundibular stenosis with intact ventricular septum the inhalation of amyl nitrite results in a pronounced fall in systemic pressure and a marked rise in right ventricular pressure. The increased right ventricular pressure results in a striking increase in the loudness of the systolic murmur. After cessation of the inhalation, pressures and murmur gradually return to their original state in about 4 minutes.

In Fallot's tetralogy the inhalation of amyl nitrite results in a moderate fall in both the systemic and right ventricular systolic pressures, with an increase in right-to-left shunt. The reduced right ventricular pressure results in a diminution in pulmonary flow, which is reflected by a decrease in the intensity and duration of the systolic murmur. As the effect of the vapor wears off, the pressures, murmur, and cyanosis return to the basal level, usually within 3 to 4 minutes.

The reasons for these striking differences are discussed fully. The effect was similar whether the case of pulmonary stenosis or Fallot's tetralogy was mild, moderate, or severe.

The amyl nitrite test is of value in settling the difficult and important diagnosis of mild (acyanotic) Fallot's tetralogy and moderately severe pulmonary or infundibular stenosis with intact ventricular septum, in cases in which the clinical, electrocardiographic, radiologic, and catheter findings may be identical. The different behavior of the systolic murmur at the bedside and of the pressures during cardiac catheterization readily distinguishes the two conditions.

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The Mean Ventricular Axis in Congenital Heart Disease: A Study Considering the Natural Incidence of the Malformations

Jorge Martins de Oliveira, M.D., Rodolfo Carballo, M.D.,* Elias S. Imperial M.D.,* João Tranchesi, M.D.,** and Henry A. Zimmerman, M.D.****
Cleveland, Ohio

Recently, Sodi-Pallares and collaborators[1] have stressed the importance of the mean manifest electrical axis of the ventricular activation process (ÂQRS) in the differential diagnosis of congenital heart diseases. They divided the frontal plane into 6 parts, according to Bayley's triaxial system, thus analyzing the distribution of 16 congenital malformations from 60 to 60 degrees.

The importance of such a study is beyond any discussion, and the value of the determination of ÂQRS in the diagnosis of congenital heart diseases has been extensively proved by our daily experience. However, it called our attention to the fact that the incidence of the lesions observed in their series does not correspond to the approximate "natural incidence"† of the different types of malformations in the whole group of congenital heart diseases. For instance, they found a high incidence of tetralogy of Fallot and tricuspid atresia as compared to a relatively low incidence of ventricular septal defect and pure pulmonic stenosis. Thus, we feel that the results obtained by Sodi-Pallares and co-workers are biased, since their study was based only on cases in which electrocardiograms were available.

In order to appreciate the results that would be obtained if the approximate natural incidence was considered, we performed a careful analysis of the findings in the paper referred to above, and carried out a study of our own on the distribution of the mean ventricular axis in patients with congenital cardiac anomalies.

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*Fellow, Marie L. Coakley Cardiovascular Laboratory, St. Vincent Charity Hospital, Cleveland, Ohio.

**Chief, Department of Electrocardiography, Hospital das Clinicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil.

***Director, Marie L. Coakley Cardiovascular Laboratory, St. Vincent Charity Hospital, Cleveland, Ohio.

†We call "natural incidence" that which could be obtained from the statistical studies of different authors, based on confirmed anatomic diagnosis (by surgery or autopsy).

ADDENDUM

(1) The findings in this Chapter have been neatly confirmed by the different response of the systolic murmur and pulmonary second sound before and after complete repair of the tetralogy. Before closure of the large septal defect, the murmur softened and shortened and P2 (if present) disappeared, whereas after creating an intact septum, the murmur and pulmonary component intensified after amyl nitrite (see Figs. 10 and 11 (Chapter V) and Fig. 5, Chapter VII). These observations prove the important role of the septal defect in determining the different behavior of the systolic murmur in the two conditions.

(2) Since this publication, many more cases have been studied. Tape recordings are now used in conjunction with the PCG and by this means, an excellent opportunity has been obtained for accurate and continuous study of the effect of amyl nitrite.

(3) It is now appreciated that in pulmonary stenosis with intact septum the degree of murmur intensification after amyl nitrite may on occasion, be much less striking in severe cases and absent when right ventricular failure is present. The most striking intensification occurs in mild and moderate cases.

CHAPTER VII

THE USE OF PHENYLEPHRINE IN THE DIFFERENTIATION OF FALLOT'S TETRALOGY FROM PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM

The previous chapters have adequately proven that when severe pulmonary stenosis is combined with a large ventricular septal defect (Fallot's tetralogy) the length and intensity of the systolic murmur is determined both by the severity of the stenosis and the systemic resistance*. When the septum is intact, however, the murmur length and intensity is determined by the severity of the stenosis and not directly by the systemic resistance. Thus abrupt fall in systemic resistance by amyl nitrite reduced right ventricular pressure, pulmonary flow and murmur in the tetralogy, but had no such direct influence when the septum was intact. Here the right ventricular pressure and murmur increased in response to the increased volume rate of venous return induced by sudden reduction in peripheral resistance (Chapter VI). These observations proved the important role of the septal defect in explaining the different behavior of the systolic murmur in the two conditions.

* Footnote. The actual resistance was not measured but reasonably inferred from the demonstrated gross changes in systemic blood pressure.

It remains to study the effect of increasing the systemic resistance in the two conditions. A rise in systemic resistance should increase right ventricular pressure, pulmonary flow and murmur in the tetralogy, but have no such effect when the septum is intact. In this chapter, phenylephrine was used to test these suppositions. This drug was selected as a suitable pressor agent since Bestermann[1] had described its useful effect in eliciting difficult aortic and mitral murmurs in cases of acute rheumatic fever. The drug aids auscultation by provoking marked bradycardia with an increased stroke volume during its hypertensive effect. It was shown to be safe, provided the maximal dose was not exceeded and this has been confirmed.

The beneficial effect of systemic hypertension on pulmonary blood flow in Fallot's tetralogy was previously shown by Hamilton et al[2], while Vogelpoel and Schrire[3](see Chapter I, page 14) independently reported the favourable combination of coarctation of the aorta and Fallot's tetralogy. This case had severe hypertension and a greatly elevated right ventricular systolic pressure to which was attributed the absence of right-to-left shunt, good pulmonary flow, as judged by a harsh systolic murmur extending beyond aortic valve closure and a soft, very delayed (0.12 sec.), easily audible, pulmonary second sound. When given amyl nitrite the systolic pressure dropped from 200 to 110 mm.Hg. with consequent softening and shortening of the murmur and disappearance of the pulmonary second sound. These observations were the first to draw my attention to the paramount importance of the systemic resistance in controlling pulmonary blood flow and murmur in the tetralogy. Furthermore, they suggested that pressor agents might be a useful tool in the study of the pulmonary second sound in the tetralogy. It will be shown that the increased pulmonary flow and

pressure following phenylephrine is capable of eliciting a previously unrecordable pulmonary second sound even in severe cases of tetralogy.

MATERIAL AND METHODS

There were 7 cases of Fallot's tetralogy and 4 cases of pulmonary stenosis with intact ventricular septum. The diagnosis was proved in all cases by methods described in previous chapters. It was confirmed at operation in 5 cases of tetralogy and all 4 cases of pulmonary stenosis.

The effects of phenylephrine on the systemic and right ventricular pressures were studied in 6 of the 7 cases of tetralogy and 3 of the 4 cases of pulmonary stenosis. In the two cases not studied at catheterisation the injection was given intravenously and the effect on the blood-pressure (cuff method) and PCG was studied. At the end of a routine diagnostic cardiac catheterisation, a control recording was made of the right ventricular and systemic pressures (brachial and femoral artery), together with a high-frequency PCG tracing using the M.R.P. multichannel recording apparatus. Immediately consecutive right ventricular and systemic pressures were recorded through a two-way tap attached to a manometer head. More recently, the pressure tracings were recorded synchronously using 2 manometers adjusted to give identical base-line and sensitivity. The PCG was recorded at the same attenuation throughout, and frequent recordings at fast paper speed (80 mm. per sec.) were made during held expiration. Between the fast strips, the recordings were made at slow paper speed (2.5 or 8 mm. per sec.). After obtaining a control recording, phenylephrine* was injected slowly via the catheter into the right ventricle. The change in systemic pressure and pulse rate was monitored on an oscilloscope and recorded continuously at slow speed, interspersed with frequent short recordings at fast speed. A response was usually noticeable about 15 seconds after 0.25 mg. had been injected and if only slight, another 0.25 mg. was given slowly. Usually, 0.5 mg. was well tolerated, adequate and effective. The dose was purposely exceeded in 2 cases to produce a maximal presser response. 1.5 mg. was given to one case of tetralogy without ill effect or production of ectopic rhythm.

The peak rise in blood-pressure occurred within the first minute; thereafter gradually returned to the initial level in about 6 - 8 minutes, depending on the dose used and the individual response. Arterial blood samples were taken before and during the peak action of the drug in several cyanosed subjects. The injection was occasionally repeated after 15 or more minutes with the catheter in the pulmonary artery, to study the effect on the pulmonary arterial pressure. The duration of injection was noted and a signal registered at 7.5 second intervals thereafter.

* Footnote. Phenylephrine hydrochloride (Boots) had to be carefully diluted since the ampoules contain 10 mg. in 1 ml. and usually only 0.5 mg. was required. A dilution of 1 ml. phenylephrine in 9 ml. of sterile water or saline was first made in a syringe. 9 ml. were discarded, leaving 1 ml. (i.e. 1 mg.) behind which was then diluted in 9 ml. sterile water. Of the 10 ml. (containing 1 mg. phenylephrine), usually 5 ml. (i.e. 0.5 mg.) was required.

In most cases amyl nitrite was administered several minutes after the injection, while the pressures were subsiding, but still high. The technique used was the same as described in Chapter VI.

RESULTS

(1) FALLOT'S TETRALOGY

Effect on the systemic and right ventricular pressures: Data were obtained in 6 cases as shown in Table I and Figs. 1 and 2. There were 3 acyanotic and 3 severe cases. In each subject phenylephrine caused a similar rise in systemic and right ventricular systolic pressures. In 3 cases the systolic pressures before phenylephrine were discrepant (systemic exceeding RV by 18 mm.Hg. and RV exceeding systemic by 22 and 25 mm.Hg. respectively in 2), but during the hypertensive and bradycardic response, the pressures became virtually identical. The average rise in systemic systolic pressure was 51 mm.Hg. (range 20 - 98 mm.Hg.). While the average rise in right ventricular systolic pressure was 49 mm.Hg. (range 25 - 117 mm.Hg.), the change in systemic pulse wave contour was always striking in that two peaks emerged, the first being a striking anacrotic notch or shoulder, followed by a prolonged "tidal"wave[4]. Even more striking was the change in the dicrotic notch which progressively ascended up the descending limb of the pulse wave while the dicrotic wave diminished in amplitude and sometimes disappeared. (Figs. 1 - 3). As the presser effect were off, so the anacrotic and tidal wave shoulders became less pronounced, while the dicrotic notch level descended again. The changes presumably resulted from a marked increase in systemic peripheral resistance[5]. There was usually a marked rise in right ventricular end-diastolic pressure.

TABLE I

THE EFFECT OF PHENYLEPHRINE IN FALLOT'S TETRALOGY

Case ge. Sex	Sevor-ity (1-4)	BEFORE PHENYLEPHRINE					AFTER PHENYLEPHRINE						COMMENT
		Systemic B.P. (mm.Hg)	RVP (mm.Hg)	PAP (mm.Hg)	ART.O2 (%)	PCG	Systemic B.P. (mm.Hg)	RVP (mm.Hg)	PAP (mm.Hg)	ART.O2 (%)	PCG	Dose P.E. (mg)	
B.P. 13 M.	1	160/75 150/75	132/10	30/10	95	75/min. Loud pan SM. Goes beyond A2. Soft P2 0.09" split.	180/105 170/105	170/15	40/15		65/min. SM much louder reaches P2. P2 little louder, 0.08" after A2.	0.4 0.5	Acyanotic LR shunt 2 L/min. Infundib. stenosis Amyl nitrite dropped BP, RVP, SM softened and shortened, P2 disappeared
M.K. 26 F.	1	100/60	122/5	15/5	97	75/min. Loud SM. Crescendo midsyst Goes beyond A2 V. soft P2 0.10" after A2.	170/95	160/15			56/min. SM and P2 much louder, reaches P2. Split remains 0.10".	0.5	Acyanotic LR shunt 2 L/min. Infundib. stenosis. Amyl nitrite caused reverse effect as above (See Fig. 2).
V.S. 13 F.	1	100/65	95/5	29/6	94	78/min. Loud SM. Partially buries A2. No P2; mild P1.	130/110	138/20			55/min. SM much louder, goes beyond A2. P1 murmur much louder. No P2.	0.75	Post-Inf. resection, now acyanotic. LR shunt 2 L/min. Amyl nitrite caused reverse effect as above, and P1 murmur disappeared.
F.S. 24 F.	2	110/70 (cuff)				68/min. Loud SM. cresc. before midsystole, ends before A2. No P2 Slight aortic incompetence.	160/120 (cuff)				46/min. SM louder, but cresc. and duration same A1 murmur louder. No P2.	0.4	Moderate case. Amyl nitrite had reverse effect.
P.K. 16 M.	3	117/75	117/0	I.C 20/0	69	80/min. V. soft, short, early SM. Loud aortic ejn. sound. No P2.	215/120	220/20	I.C. 60/10	81	38/min. Loud SM. Cresc. well before midsystole, but reaches A2. Ejn. sound buried. Soft P2 0.12" after A2	1.5	Severe case. Infundib. stenosis. No side effects to large dose. Amyl nitrite caused reverse effect, as above.
S.vZ. F.	3	80/70	85/5	12/7	53	100/min. Soft, short, early SM Aortic ejn. sound.	120/96	120/15		73	88/min. SM louder cresc. still early but reaches A2. No P2. Aortic ejn. sound buried.	0.5	Severe case. Amyl nitrite caused reverse effect and Art. O2 dropped to 69%.
I.vN. F.	3	100/70	125/5		56	V. soft, short early SM, ends in midsytole. Aortic ejn. sound. No P2	150/105	150/10		85	SM much louder, cresc. midsytole, extends slightly beyond A2. P2 emerged 0.08" after A2.	0.5	Severe case. Amyl nitrite caused reverse effect and dropped Art. O2 (See Fig. 1).

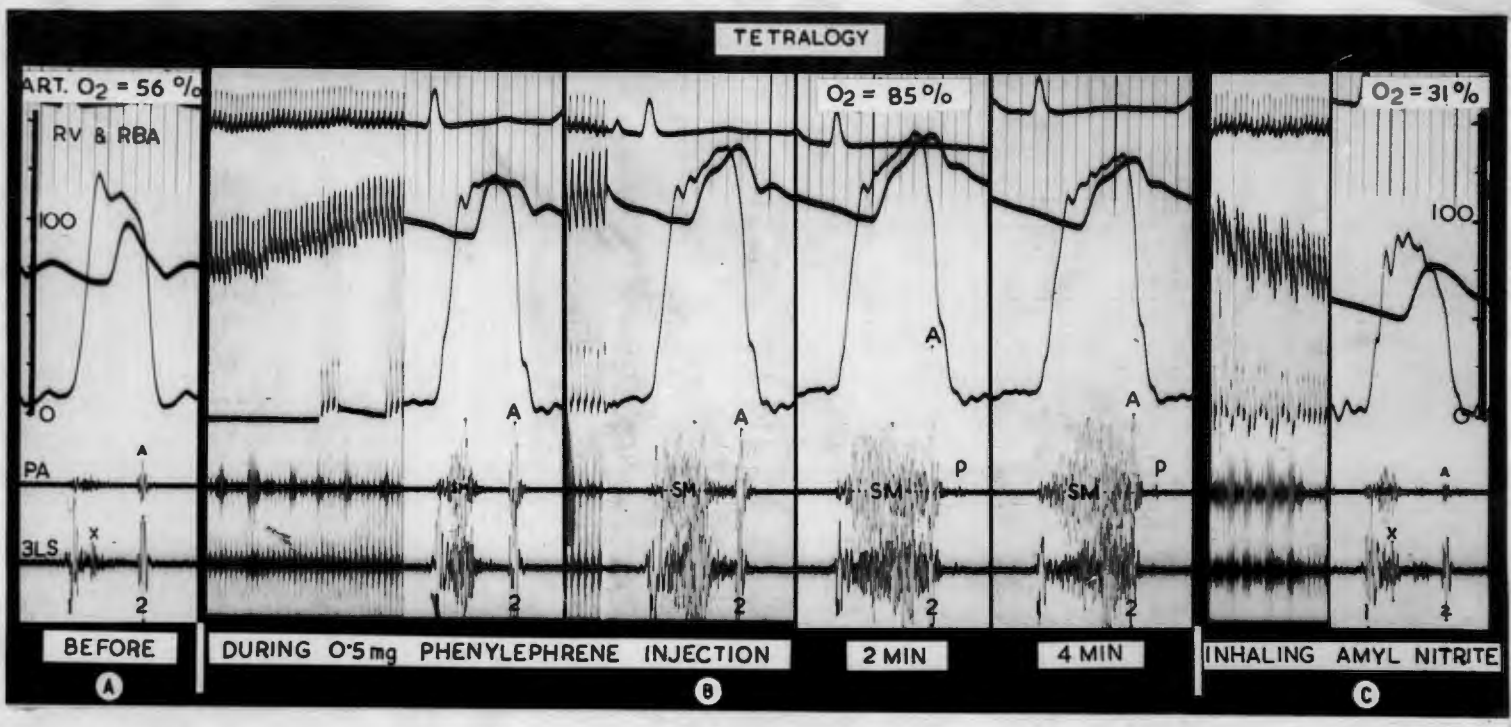

Fig. 1. Severe tetralogy. The effect of increasing and decreasing systemic resistance on the arterial O2 saturation, right ventricular and systemic pressures and PCG. (A) Before phenylephrine, the very soft, short, early systolic murmur, with aortic ejection sound (X) and absent pulmonary component indicated severe tetralogy with poor pulmonary blood flow. Arterial O2 saturation was 56%, RV 125/5 and RBA 100/70 mm.Hg. (B) During P.E. injection, the systemic and RV systolic pressures became identical, both rising steadily together, reaching a peak at 2 minutes (RV 150/105,RBA 150/105 mm.Hg.). The rise in RV pressure caused progressive improvement in pulmonary blood flow as shown by the striking change in the murmur. The first response was increased loudness, the murmur remaining very early and short. Thereafter it progressively lengthened and by 4 mins., extended slightly beyond A2. A soft, delayed (0.08 sec.) pulmonary component (P2) emerged at 2 minutes but only after the murmur lengthening, had indicated increased pulmonary flow and arterial O2 saturation risen to 85%. (C) At 4 minutes, when RV and RBA pressures were still high and PCG showed good flow, the systemic resistance was abruptly reduced by amyl nitrite. The rapid fall in RV and RBA pressures to 95/2 and 80/52 mm.Hg. was shown. Note the pronounced softening and shortening of the murmur and disappearance of P2 indicating a marked drop in pulmonary flow and pressure. Arterial O2 saturation fell to 31%.

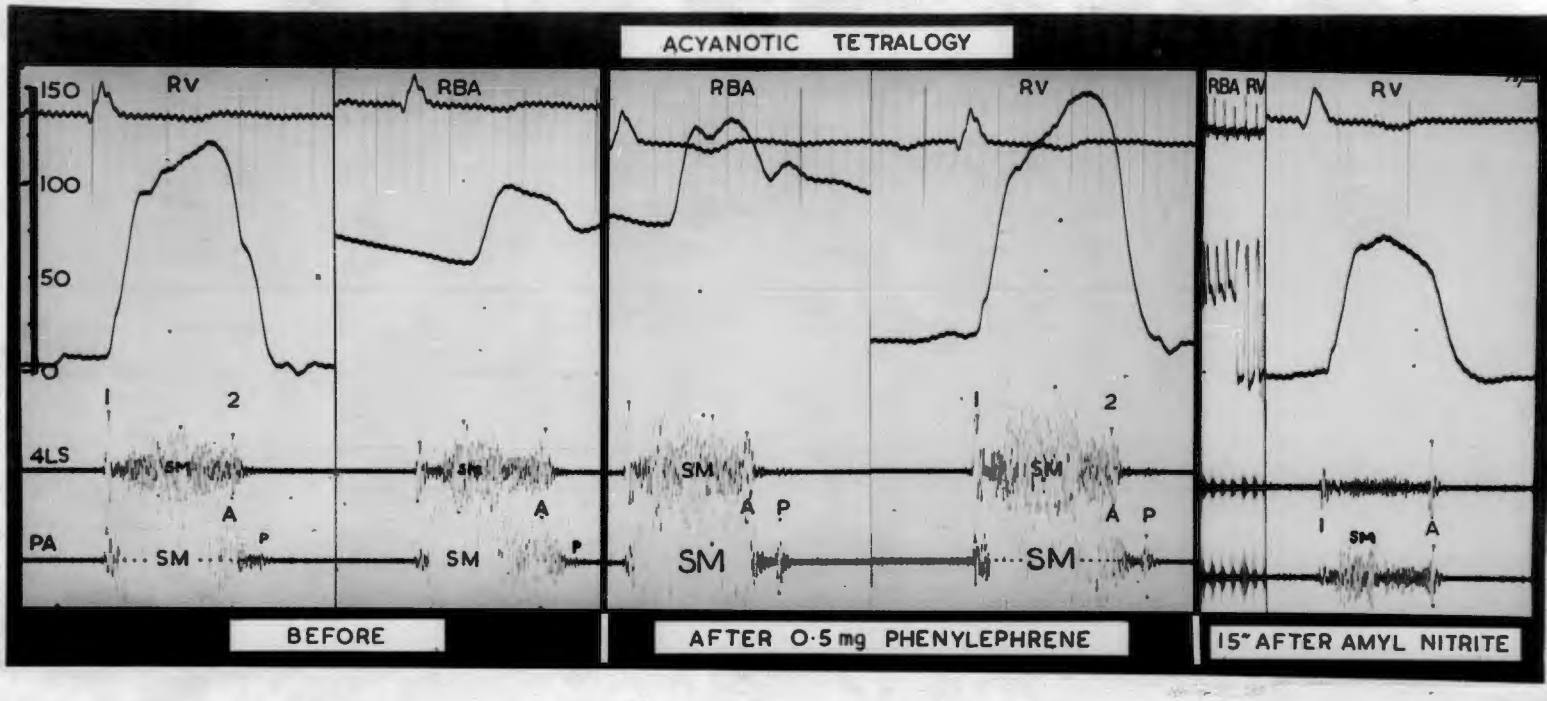

Fig. 2. Acyanotic tetralogy. Effect of increasing and decreasing systemic resistance on the murmur and pulmonary second sound. Note the similar increase in systemic and RV systolic pressures after phenylephrine and decrease after amyl nitrite, thereby proving Fallot's tetralogy. The change in intensity of the murmur and pulmonary component (P) with increase and decrease in systemic resistance likewise proved Fallot's tetralogy. The intensification of the very soft and delayed (0.10 sec.) P2 was striking after P.E., when RVP had risen from 125/5 to 155/10 mm.Hg. and systemic from 100/60 to 130/80 mm.Hg. Splitting remained very wide at 0.11 sec., showing no selective delay in aortic valve closure as seen in stenosis with intact septum. 15 sec. after amyl nitrite, RV and RBA pressures dropped to 70/0 and 70/30 mm.Hg. respectively, with marked softening of the murmur and disappearance of P2, suggesting drop in pulmonary flow and pressure.

Bradycardia was always produced, although the degree varied and was not directly proportionate to the level of blood pressure induced. Transient nodal rhythm not infrequently occurred. In some subjects, pre-existing premature beats were abolished while in others, phenylephrine caused extra-systoles.

Effect on pulmonary arterial and infundibular chamber pressure.

In one case the pulmonary arterial pressure rose from 30/10 to 40/15 mm.Hg., and in another the pressure in the infundibular chamber rose from 20/0 to 60/10 mm.Hg., during the peak action of phenylephrine.

Effect on the arterial oxygen saturation.

This was studied in 3 severe cases who were deeply cyanosed. In all there was a striking increase in oxygen saturation during the peak action of phenylephrine (see Table I and Fig. 1).

Effect on the systolic murmur and heart sounds.

Striking intensification of the murmur was shown in all 7 cases. The change in murmur was more dramatic in the severe cases where the murmur was initially soft, short and early. Following phenylephrine, it became much louder and more prolonged. The progressive intensification and lengthening of the murmur with progressive rise in right ventricular and systemic blood-pressure is shown in Fig. 1. In this case the arterial oxygen saturation rose from 56% to 85% proving that the change in murmur did, in fact, accurately reflect the increased pulmonary blood flow from increased systemic resistance. The emergence of a soft pulmonary second sound 0.08 sec. after the aortic sound in a tetralogy of this severity was of great interest (see below).

Although the murmur became much louder and longer in the severe cases, the site of the crescendo in systole changed much less.

In the three acyanotic subjects the murmur was initially very loud and prolonged. Nevertheless, phenylephrine caused marked

intensification and slight, but maximal prolongation in that the murmur reached the delayed pulmonary component (Fig. 2).

Phenylephrine intensified both the aortic and pulmonary components of the second sound. In 2 acyanotic cases the drug greatly intensified the initially very soft and delayed pulmonary component. The aortic and pulmonary components remained widely separated throughout the hypertensive effect of phenylephrine suggesting that left ventricular systole had not become selectively delayed as in some cases of pulmonary stenosis with intact ventricular septum (see below and compare Figs. 2 and 4). Presumably, prolongation of systole from sudden hypertension affects both ventricles equally in the presence of a large ventricular septal defect. Of special interest was the emergence of a soft, delayed pulmonary component in 2 severe cases, in whom this sound was previously unrecordable (Table I and Figs. 1 and 5). In both, this sound emerged only after the murmur had first become greatly intensified and lengthened, indicating increased pulmonary flow. This sequence suggested that an increase in pulmonary flow preceded the rise in pulmonary arterial pressure necessary to induce recordable pulmonary valve closure. It is also possible that phenylephrine increased the pulmonary pressure by increasing the pulmonary vascular resistance. In one of the cases the infundibular pressure and systemic arterial oxygen saturation had risen from 20/0 to 60/10 mm.Hg. and 69 to 81%, respectively, when the pulmonary sound emerged.

The aortic ejection sound recorded in all 3 severe cases became engulfed by the intensified systolic murmur following phenylephrine (Fig. 1 and 5). Since ejection into the pulmonary artery precedes ejection into the aorta, the systolic murmur commences before the

aortic ejection sound hence, when loud, the murmur completely buries the sound. This evolution of events is well shown in Figure 1, supporting the views previously expressed in Chapter IV.

Effect of Amyl nitrite given after phenylephrine.

In all 7 cases, amyl nitrite was administered to abruptly reduce the systemic resistance still elevated by phenylephrine. In all cases there was a progressive drop in systemic and right ventricular pressures the systolic pressures both falling together (Fig. 1), during, and for some 30 seconds after the inhalation. The murmur softened and shortened, reflecting a pronounced drop in pulmonary flow and the pulmonary component disappeared indicating a drop in pulmonary arterial pressure. The arterial oxygen saturation dropped sharply in 2 severe cases where this effect was studied. (Table I and Fig. 1).

Amyl nitrite also caused a rapid obliteration of the anacrotic and tidal wave shoulders induced by phenylephrine as well as a rapid descent in the dicrotic notch and disappearance of the dicrotic wave. These pulse contour changes presumably indicate a lowered systemic resistance.

(2) PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM.

Effect on the systemic and right ventricular pressures:

Data were obtained in 2 cases as shown in Table II. Both had severe stenosis. Phenylephrine caused a rise in systemic pressure which behaved quite independently of the right ventricular pressure. In the first case the systemic pressure rose from 107/65 to 148/100, while the right ventricular pressure dropped from 152/0 to 143/0 mm.Hg. In the first case, although the systolic pressures became nearly equal by coincidence during the peak hypertensive effect, the unrelated behavior was shown during right ventricular alternans which followed after ventricular premature beats (Fig. 3). The systolic pressure of the weaker right ventricular systole fell well below the systemic pressure which showed no evidence of left ventricular alternans.

TABLE II

THE EFFECT OF PHENYLEPHRINE IN PULMONARY STENOSIS WITH INTACT SEPTUM

No.	Case Age. Sex	Severity (1-4)	BEFORE PHENYLEPHRINE					AFTER PHENYLEPHRINE						COMMENT
			Systemic B.P. (mm.Hg)	RVP (mm.Hg)	PAP (mm.Hg)	ART.O2 (%)	PCG	Systemic B.P. (mm.Hg)	RVP (mm.Hg)	PAP (mm.Hg)	ART.O2 (%)	PCG	Dose P.E. (mg)	
1	J.P. 17 F.	1	108/50	40/0	17/5	96	105/min. Short SM. Cresc. before mid-syst. Ends at A2 - Split 0.06.	150/75		27/9		52/min. Slight increase in loudness but not length. Split closed due to delay in A2.	0.5	Mild stenosis. Slight increase in murmur probably due to bradycardia. Amyl nitrite caused gross intensification.
2	F.W. 10 M.	3	107/65	130/12	16/6	97	108/min. Loud SM v. late cresc. A2 buried. V. soft P2 0.08" after A2. Loud pulm. click.	148/100	142/10		94	82/min. SM slightly softer. Split remains 0.08". Pulm. click little softer.	0.5	Severe PS. No significant change in SM or split. (See Fig. 3.)
3	M.M. 7 M.	3	98/65	152/0	25/10	96	105/min. Loud SM, late cresc. A2 buried. V. soft P2 0.08. Loud pulm. click.	135/90	143/0		95	60/min. SM unchanged. Click disappeared. Split narrowed to 0.06".	0.75	Severe PS. During nodal rhythm after P.E. SM much softer and shorter despite high RVP.
4	W.vD 10 M.	4	140/70 (cuff)	(195/0)			95/min. Loud long SM. A2 buried. Split 0.11".	200/130 (cuff)				50/min. SM virtually unchanged. A2 v. delayed, closing split completely. P2 slightly increased.	0.5	V. severe PS. Severe BP response may explain grossly delayed A2 closure. (See Fig. 4).

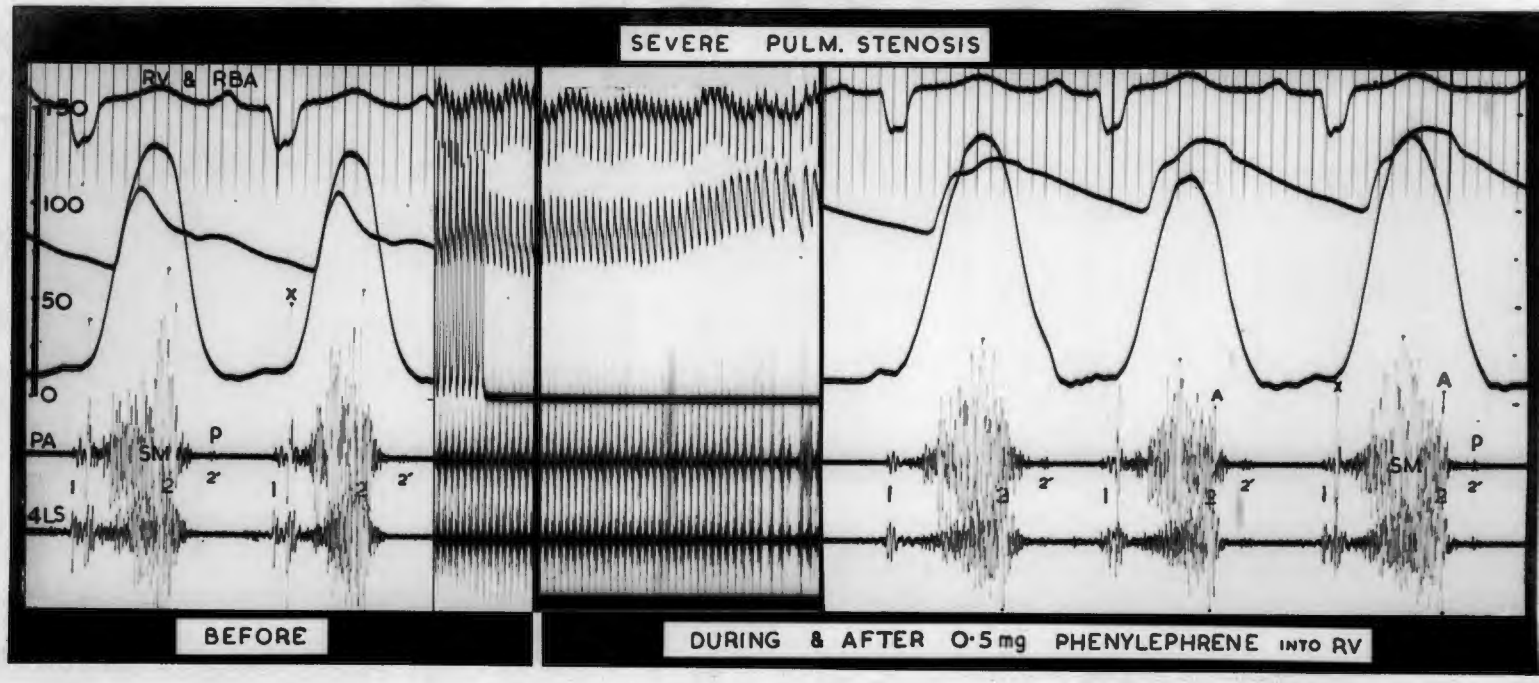

Fig. 3. Severe pulmonary stenosis. The effect of phenylephrine on the PCG and synchronously recorded right ventricular and brachial arterial pressure tracings. Before the injection the loud, kite-shaped murmur completely engulfed A2 but ended before the very delayed and soft P2 indicating severe stenosis with intact septum. The right ventricular pressure (132/12 mm.Hg.) exceeded the systemic pressure (110/68 mm.Hg.), suggesting, but not proving an intact septum. During and after the injection, the systemic pressure rose progressively, with marked change in pulse contour, to 142/100 mm.Hg., behaving independently of the RV pressure which increased slightly to 140/12 mm.Hg.) The three cycles recorded at fast speed followed a ventricular premature beat (not shown) and showed right, but not left ventricular alternans, during which the systemic and RV systolic pressures were discrepant suggesting an intact ventricular septum. The murmur softened slightly and the pulmonary component remained soft, while the aortic component seemed to shift slightly to the right with each successive systole. The pulmonary ejection sound (E) softened slightly. The behavior of the PCG favoured an intact septum (compare with Fig. 2).

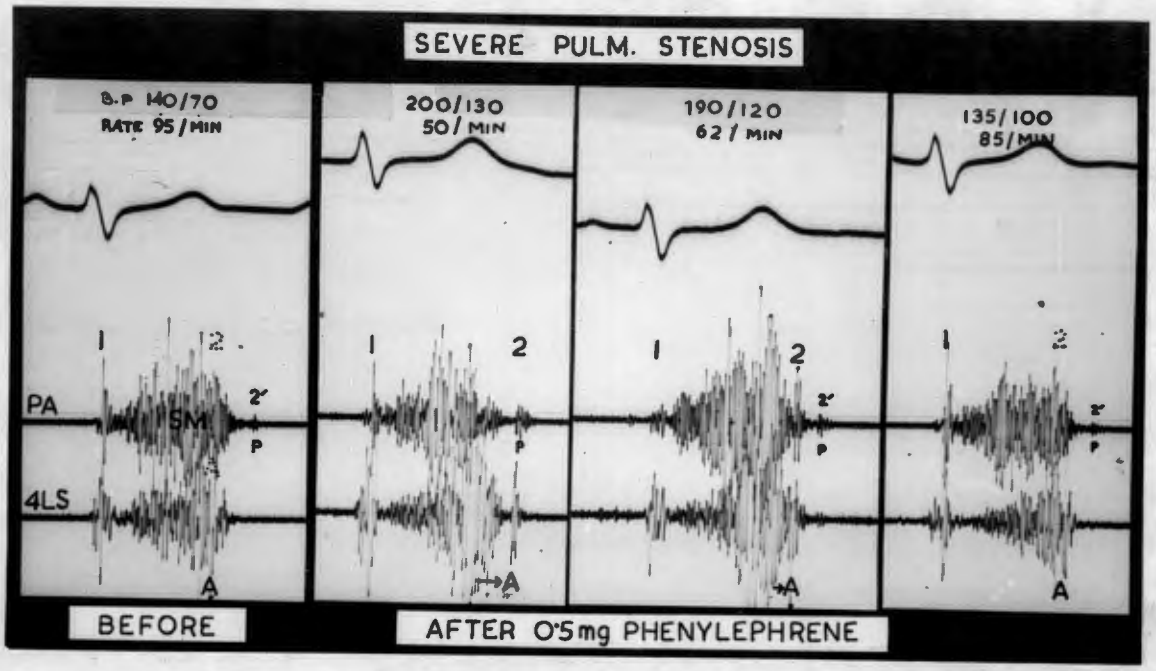

Fig. 4. Severe pulmonary stenosis. Before phenylephrine the PCG was that of very severe stenosis, the murmur extending well beyond and burying the aortic component and ending before the very delayed (0.11 sec.) and soft, pulmonary component (2,P) (RVP was 195/0 mm.Hg.). Despite the profound hypertensive and bradycardic response to 0.5 mg. phenylephrine I.V., there was little change in the murmur and pulmonary component, proving that the ventricular septum was intact (compare with Figs. 2 and 5). A striking feature was the marked shift to the right of the aortic second sound from prolongation of L.V. systole during the rise and peak action of the drug, and its gradual return thereafter. By 6 minutes the sound had nearly returned to its former position within the murmur.

In the very severe case not catheterised, the systemic pressure rose from 140/70 to 200/130 mm.Hg.

The effect of phenylephrine on the systemic pulse wave contour was the same as described above.

Effect on the pulmonary arterial pressure.

Data were obtained in only 1 patient who had mild stenosis following a valvotomy done 1 year previously. The systemic pressure rose from 108/50 to 150/75 while the pulmonary arterial pressure rose from 17/5 to 27/9 mm.Hg.

Effect on the arterial oxygen saturation.

This was studied in the 2 severe cases; the saturation dropped from 97 to 94% in one, and from 96 to 95% in the other. The change was clearly of no significance.

Effect on the systolic murmur and heart sounds.

Four patients were studied; the stenosis was mild in 1, severe in 2 and very severe in 1 (Table II). The change in intensity and length of the murmur was insignificant, bearing in mind the marked bradycardia produced. The increased stroke volume caused by bradycardia probably accounted for the slightly increased intensity of the murmur in 3. In 1 case the murmur actually became a little softer, probably due to the slight drop in right ventricular pressure.

Comparison of figures 1 and 2 with 3 and 4 at once illustrates that a rise in systemic resistance does not significantly change a pulmonary stenotic murmur when the ventricular septum is intact. This is conclusively proven in a study on a patient with tetralogy before and after closure of the septal defect. Before surgery, phenylephrine greatly intensified and prolonged the murmur and elicited a pulmonary second sound. That this effect was due to the large septal defect

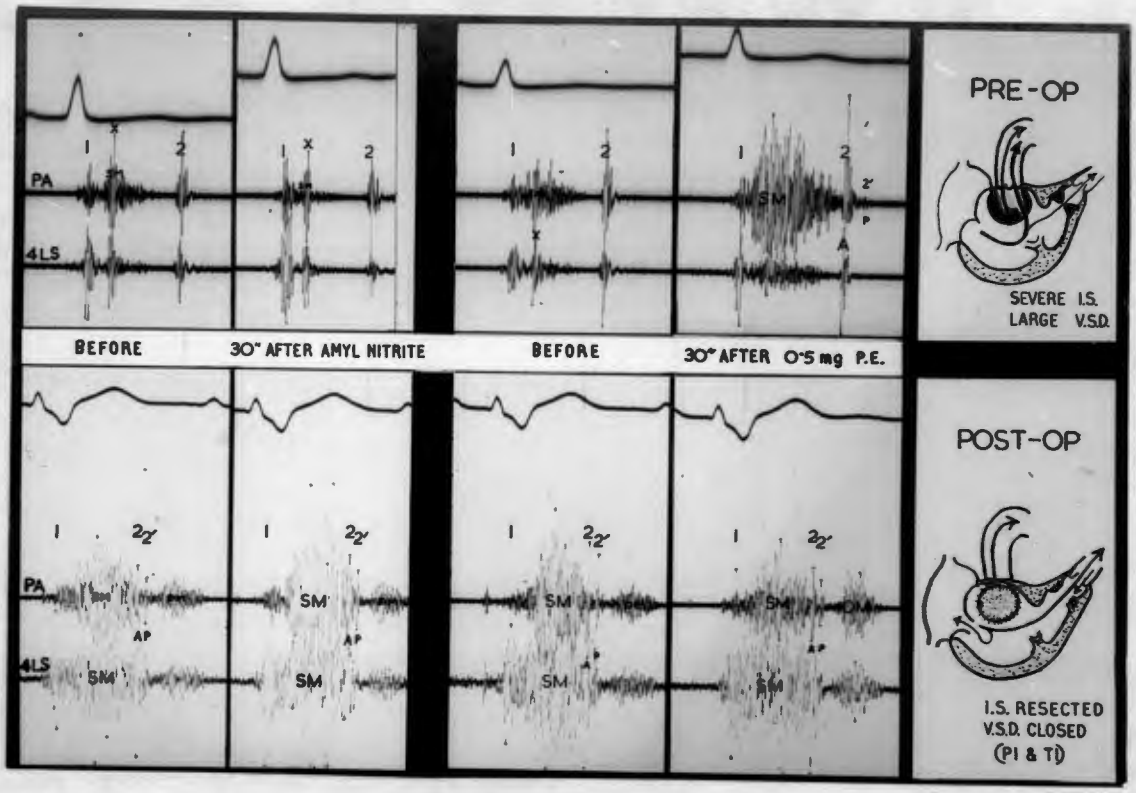

Fig. 5. Severe tetralogy before and after repair of large septal defect and infundibular resection. The study proves that the systemic resistance directly controls pulmonary blood flow and murmur in the tetralogy due to the presence of a large septal defect. Before surgery, decrease and increase of systemic resistance with amyl nitrite and phenylephrine respectively, caused pronounced decrease and increase in pulmonary flow and murmur. Note emergence of soft, delayed (0.07 sec.) P2 and loud murmur engulfing aortic ejection sound (X) after phenylephrine (B.P. rose from 130/90 to 140/120 mm.Hg. Following surgery which created an intact ventricular septum, similar manipulation of systemic resistance with amyl nitrite and phenylephrine failed to provoke the same change in murmur. The systolic murmur (SM) (pulmonary ejection systolic murmur in PA and probably tricuspid regurgitant systolic murmur in 4LS), increased after amyl nitrite but did not change after phenylephrine. Note appearance of normal P2 and close splitting after surgery, suggesting rise of pulmonary arterial pressure to normal and adequate relief of stenosis respectively. The diastolic murmur (DM) following P2 was due to pulmonary incompetence.

was shown by failure of phenylephrine to cause a change in the murmur when the defect was closed and the stenosis resected. Similarly, the decrease in murmur after amyl nitrite was also shown to be dependent on the presence of a large septal defect.

The effect on the second heart sound differed from that in the tetralogy. In 2 cases during the early hypertensive effect of phenylephrine, splitting of the second sound disappeared due to marked delay (shift to the right) in aortic valve closure, presumably from prolongation of left ventricular systole. In the first case with mild stenosis, the split was 0.06 sec. before phenylephrine, but during the rising systemic pressure, the second sound became single and remained thus for 3 minutes; thereafter, the aortic sound gradually returned to its former position with gradual increase in the width of splitting. In the second case with very severe stenosis, pulmonary valve closure was delayed 0.11 sec. due to grossly prolonged right ventricular systole. During the severe hypertensive response to phenylephrine (B.P. rose from 140/70 to 200/130 mm.Hg.) the aortic sound appeared to shift grossly to the right; thereafter slowly moved back to its former position within the crescendo of the murmur (Fig. 4). In the remaining 2 cases, splitting narrowed slightly in one but not in the other.

There was little change in the intensity of the pulmonary second sound in comparison to the relatively marked increase in the tetralogy, suggesting that pulmonary blood flow and pressure is much less influenced by the systemic resistance when the ventricular septum is intact.

In 2 severe cases with loud pulmonary ejection sounds, this sound became softer in one and disappeared in the other after phenylephrine.

Effect of amyl nitrite given after phenylephrine.

In all 4 cases, amyl nitrite resulted in a prompt fall in systemic pressure which occurred independently of the right ventricular pressure. The right ventricular pressure and murmur steadily increased 30 to 45 seconds after withdrawing amyl nitrite, reflecting the dynamics of pulmonary stenosis with intact ventricular septum (see Chapter VI).

DISCUSSION

The strikingly different response of the right ventricular pressure and systolic murmur to increasing systemic peripheral resistance in the two conditions is attributed to the presence of a large ventricular septal defect in the tetralogy. The observations proved that in the tetralogy, pulmonary blood flow, and hence murmur, is determined both by the severity of the stenosis and the systemic resistance. Increase of the latter resulted in elevation of both systemic and right ventricular pressures. The improved pressure gradient across the pulmonary or infundibular stenosis resulted in a greater volume of blood ejected through the stenosis, as reflected by the intensification and lengthening of the murmur and increase in arterial oxygen saturation. The greater the right ventricular pressure rise, the greater the improvement in pulmonary blood flow. Even in severe cases, marked transformation of the murmur could be produced with emergence of a previously unrecordable pulmonary second sound.

The important role of the systemic resistance in governing pulmonary blood flow in the tetralogy was conclusively shown by the abrupt reversal of the beneficial effects of raised systemic

resistance when the resistance was suddenly reduced by amyl nitrite. Thus, the systemic and right ventricular pressures, arterial oxygen saturation, murmur length and intensity, rapidly diminished with disappearance of the pulmonary second sound, suggesting marked fall-off in pulmonary blood flow and pressure (Fig. 1). When the septal defect was closed in the tetralogy, increase and decrease in systemic resistance no longer produced the same effect (Fig. 5).

In pulmonary stenosis with intact ventricular septum, increase in systemic resistance caused a rise in systemic blood pressure independently of the right ventricle, hence there was no significant change in the murmur and pulmonary second sound. Selective prolongation of left ventricular systole during marked hypertensive responses greatly shortened or closed the previously widely split second sound. Narrowing of the split did not occur in the tetralogy presumably because systemic hypertension would delay systole in both ventricles equally.

The observations on the pulmonary second sound in the tetralogy were of great interest. Phenylephrine elicited soft pulmonary components in 2 severe cases by increasing pulmonary blood flow and pressure sufficiently to make a silent sound recordable. The sound thus rendered recordable was as delayed (0.08 and 0.12 sec.) as in mild cases, supporting the view that splitting of the second sound is always wide in the tetralogy (see Chapter IV).

Phenylephrine proved usefal in identifying a doubtful,delayed, very soft sound as the pulmonary component. In mild cases of tetralogy, when the pulmonary component is just recordable it is often fleeting due to variation with respiration. However, phenylephrine intensifies the sound making its recognition much more certain.

COMMENT.

The diagnostic value of phenylephrine is obvious although as a test it is much less attractive than amyl nitrite.

Preparation of a solution requiring careful dilution and need for an intravenous injection, are major drawbacks. However, during cardiac catheterisation, it is very simple to use and a useful means of deciding whether or not a large septal defect is present in a case of pulmonary stenosis. This is especially true in cases where the right ventricular and systemic systolic pressures are unequal. Manipulation of the systemic resistance by first increasing it with phenylephrine and then abruptly reducing it with amyl nitrite should provide valuable information about the state of the ventricular septum in the difficult case.

SUMMARY

1. The effect of phenylephrine on the systemic, right ventricular, pulmonary arterial pressures and on the systolic murmur and heart sounds has been studied in Fallot's tetralogy and pulmonary stenosis with intact ventricular septum.

2. In both conditions, phenylephrine caused a pronounced elevation in systemic blood-pressure and bradycardia, depending on the dose given and individual response. The progressive change in pulse wave contour suggested a marked increase in peripheral systemic resistance.

3. In Fallot's tetralogy, whether severe or acyanotic, the systemic and right ventricular systolic pressures behaved in identical fashion, both rising and falling together. Increased pulmonary blood flow and pressure, as reflected by marked intensification and lengthening of the murmur, and intensification of the pulmonary second sound, respectively, resulted from the rise in right ventricular pressure which improved the pressure gradient across the stenosis. The arterial oxygen saturation greatly improved in the cyanosed cases. Amyl nitrite reversed the beneficial effects by abruptly reducing the high systemic resistance.

4. In pulmonary stenosis with intact ventricular septum, whether mild or severe, the systemic and right ventricular pressures behaved quite independently of one another. The right ventricular pressure change was insignificant as reflected by insignificant change in murmur intensity and length, allowing for the increased stroke volume from bradycardia. When the hypertensive response was marked, left ventricular systole appeared to be selectively delayed as judged by marked delay in aortic valve closure, closing a previously widely split second sound.

5. The different behavior of the right ventricular pressure and systolic murmur was attributed to the presence of a large ventricular septal defect. This was proven conclusively in a case of tetralogy studied before and after complete repair of the septal defect.

6. The observations prove the thesis that pulmonary blood flow, and hence murmur length and intensity, in the tetralogy is determined both by the systemic resistance and the severity of the stenosis.

7. Phenylephrine was shown to be a useful tool in studying the pulmonary second sound in the tetralogy. By increasing pulmonary blood flow and pressure, this drug greatly intensified the very soft, fleeting, pulmonary component in mild tetralogy, thereby assisting in its recognition. It was also capable of eliciting a pulmonary component in severe cases of tetralogy.

8. The diagnostic value of phenylephrine is discussed.

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APPENDIX

It was found impossible to include the protocols of all cases studied; however, complete clinical, PCG, ECG, radiological, cardiac catheterisation, angiocardiographic data, including operative and necropsy findings where applicable, are available in the Cardiac Clinic, Groote Schuur Hospital, Cape Town.

A final summary of the thesis will not be presented since the conclusions have been adequately stated in the Introduction and at the end of each chapter.
