The Pathologic Anatomy of Tetralogy of Fallot and Its Variations*

MAURICE LEV, M.D., F.C.C.P. AND FRIEDRICH A. O. ECKNER, M.D.
Chicago, Illinois

Tetralogy of Fallot, from the physiologic point of view, consists fundamentally of ventricular septal defect with pulmonary tract stenosis and may be divided into cyanotic and acyanotic types. From the anatomic and surgical point of view one must include overriding aorta. Traditionally, however, right ventricular hypertrophy was added to make up the tetralogy.

At the Congenital Heart Disease Research and Training Center, we have examined 1519 hearts since September 1, 1957 to the present. Of these, 158 were specimens of tetralogy of Fallot of which 11 were acyanotic. The present report is an analysis of the variations of the three basic components in tetralogy of Fallot, and a study of the various complexes found in this entity.

Basic Components of Cyanotic Tetralogy of Fallot

Ventricular Septal Defect

The usual defect is situated in the anterior portion of the muscular septum, anterior to the pars membranacea (Fig. 1A). It involves the inter-ventricular portion of the pars membranacea to a varying degree. However, it spares the atroventricular part of the latter. The defect is confluent with the mouth of the aorta, and lies beneath the posterior part of the right and the anterior part of the posterior aortic cusp.

It enters the right ventricle in the lower part of the conus beneath the arch (crista), between the latter and the anterior leaflet

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of the tricuspid valve and the adjacent part of the medial leaflet (Fig. 1B).

In a lesser number of cases, the defect is situated more anteriorly, lying beneath the right aortic cusp, and only slightly beneath the posterior aortic cusp (Fig. 2A). It then enters the right ventricle in the lower and middle third of the conus (Fig. 2B). Such a defect may be large enough to extend posteriorly and also involve the inter-ventricular part of the pars membranacea. In still a lesser number of cases, the defect lies within the region of the pars membranacea, both its inter-ventricular portion and its atrioventricular portion (Fig. 3). In tetralogy, such a defect also involves a considerable amount of the anterior portion of the muscular septum in front of it, and in some cases the posterior portion of the septum behind it as well. This defect thus lies beneath the posterior aortic cusp and to a varying degree the right aortic cusp. In this position, it is likewise confluent with the mouth of the aorta. It enters the right ventricle in the lower part of the conus beneath the arch, and in some cases in the upper part of the sinus as well. It is in intimate relationship with the anterior and anterior part of the medial leaflet of the tricuspid valve. The mitral and tricuspid valves are in intimate contact through the defect, and may even share a common leaflet.

Uncommonly, a defect is found in the anterior septum not involving the pars membranacea at all (Fig. 4A), and lying beneath the right and sometimes the adjacent part of the left aortic cusp. Such a defect enters into the upper as well as in some cases the lower part of the conus (Fig. 4B). The higher (with respect to the pulmonary trunk and conus) the defect is in the anterior portion of the ventricular septum, the more likely is it for the defect to perforate the arch, rather than to deviate it. In general, in most cases of tetralogy, the arch is deviated, as described below.

However, the position of the defect on the left side, does not always predicate its position on the right, because of the extent of obliquity of the defect (Fig. 5A and B).

Overriding Aorta (Fig. 6)

In all tetralogies, the aorta overrides the septum, emerging either mostly from the left or mostly from the right, or straddling more or less evenly. In this series, where the amount of overriding was distinctly indicated, in 48 cases it emerged about 75 per cent from the left ventricle, in 35 cases about 50 per cent from each chamber and in 24 cases mostly from the right ventricle. This must not be construed to indicate that these figures necessarily represent the amount of overriding in the average population of tetralogies. It may so indicate, or it may indicate that the greater the overriding, the worse the prognosis surgically.
Pulmonary Tract Stenosis

The architecture of the conus or infundibular area, and its muscle bundle arrangement is intimately tied up with the position of the defect, and the amount of overriding of the aorta. It must be stressed that in the vast majority of instances, the arrangement present produces a narrowing of the pulmonary conus region.

The usual case of tetralogy in this series showed the following arrangement of musculature (Fig. 7). The septal band consisted of two to three or more bands. The uppermost band proceeded to the base of the pulmonary trunk. One or more of the lower bands combined with a displaced parietal band to form the arch (or crista). This parietal band was displaced away from the tricuspid valve on to the anterior wall of the right ventricle, making way for the entry of the defect. A second parietal band filled in the gap between the above mentioned parietal band and the anterior leaflet of the tricuspid valve. The deviation of the parietal band thus narrowed the conus of the pulmonary trunk, while making way for what might be called a conus or passageway for part of the aorta. The narrowing of the conus of the pulmonary trunk was thus in the usual case diffuse. At the same time, in some of these cases, there was a shortening of the pulmonary conus as well.

In a lesser number of cases, the arch was partially or completely perforated rather than deviated by the defect (Fig. 8). This reached its acme in occasional cases where there was very little or no muscular separation between the outflow tracts of the pulmonary trunk and aorta. This was especially seen in marked overriding of the aorta or in a high (with respect to the pulmonary trunk) defect of the ventricular septum.

A lesser number of cases of tetralogy, however, have different architectures in the conus area. In some of these, the septal band protrudes more into the lumen accounting for some of the narrowing (Fig. 9). There may be several parietal bands the centers of which hang down free in the conus region instead of hugging the wall, thus dividing off the conus region into parts (Fig. 10). In some, the mouth of the conus is narrowed and the latter structure pursues a circuitous route to the base.
FIGURE 4: One type of ventricular septal defect in tetralogy of Fallot. See text. (A) Left ventricular view; (B) Right ventricular view; S—Septal band; P—Parietal band; A—Arch.

of the aorta. Where the narrowing is at the mouth, a separate conus chamber may be set up.

From the above it may be gleaned that the conus is either diffusely narrowed, or narrowed in any one region in its course. This narrowing may be reinforced by focal or diffuse fibroelastic thickening. In one case (Fig. 10) in this series, sharp spurs of thickening produced a secondary stenosis in the center of the conus. Thus, conus stenosis is the usual finding in tetralogy of Fallot. However, a few cases were present in this series in which there was no narrowing of the conus, there being a true stenosis of the pulmonary valve only. In this series, it was difficult to decide in which cases there might be a secondary stenosis of the pulmonary valve in addition to the infundibular stenosis, since we were dealing with fixed material.

THE COMPLEX—CYANOTIC
TETRALOGY OF FALLOT
External Anatomy (Fig. 11)
The heart is either normal in size or somewhat enlarged. In the vast majority of cases, the apex is formed by both ventricles. The apex is blunt, and in some cases, frankly snub-nosed. The anterior descending coronary artery in some cases takes an S shaped course. In only a rare case, in this series, in uncomplicated tetralogy was the apex formed exclusively by the right or left ventricle. The aorta and

FIGURE 5: One type of ventricular septal defect in tetralogy of Fallot. See text. (A) Left ventricular view; (B) Right ventricular view; S—Septal band; P—Parietal band; A—Arch. Arrow points to the entry of the defect into the right ventricle.
aorta to the right, the pulmonary to the left. The aorta is larger than the pulmonary trunk. The proximal border of the right ventricle in some cases is concave upward and to the right. An absolutely typical boot is uncommonly seen.

Internal Anatomy

The right atrium is always hypertrophied and in some cases is dilated, with focal or diffuse endocardial hypertrophy. Occasional architectural abnormalities in the atrial septum in general, or in the remnants of the venous valves are noted. The tricuspid orifice is normal in size. The tricuspid valve has a tendency to be mitralized—that is, the medial leaflet may be combined with the inferior, or the anterior leaflet may be greatly enlarged taking in part of the medial. The fused medial and inferior leaflets may be connected to abnormal papillary muscles on the septum instead of to the inferior papillary muscle. This valve shows generalized increased hemodynamic change, with focal hemodynamic change adjacent to the defect.
The valve uncommonly may be perforated or rarely have an aneurysmal dilatation near the defect. The right ventricle is hypertrophied and usually not enlarged, with focal endocardial hypertrophy in the sinus region, in addition to the endocardial changes in the conus described above. The pulmonary orifice is smaller than normal, but it is rarely normal or enlarged. The pulmonary valve is in most cases bicuspid, rarely unicuspid, or in some cases tricuspid but abnormal. Under all circumstances it is thickened. The pulmonary trunk and the two pulmonary arteries are small. The pulmonary veins rarely showed stenosis in this series. This is probably more frequent than indicated here, but this could not be substantiated in the fixed material. The

**Figure 8** (upper): Pulmonary valvular stenosis with absent arch in tetralogy of Fallot. S—Septal band; P—Parietal band; AV—Aortic valve; PT—Pulmonary trunk. **Figure 9** (center): Septal band contributing considerably to the infundibular stenosis in tetralogy of Fallot. S—Septal band; P—Parietal band; A—Arch. Arrow points to the defect entering the right ventricle. **Figure 10** (lower): Free parietal band (cut across) dividing off lower infundibulum, with endocardial ridges narrowing the mid-infundibulum in tetralogy. S—Septal band; P—Parietal band; R—Endocardial ridges. Arrows point to parietal band dividing off lower infundibulum.
left atrium is either normal or small, with a normal endocardium in most cases, but occasionally with endocardial hypertrophy.

The mitral orifice and its valve are normal in most cases, but the valve occasionally shows focal or diffusely increased hemodynamic change. The left ventricle is either normal in size or smaller than normal with a wall of average thickness, and with focal or rarely diffuse endocardial hypertrophy. This is especially marked proximal to the defect where there may be actual ridge formation. The aortic orifice is enlarged; the aortic valve is normally formed, but with considerably increased hemodynamic change. Rarely a bicuspid aortic valve may accompany a bicuspid pulmonic valve. Uncommonly, the coronary ostia emerge high or above the sinuses of Valsalva. In one case in this series, the right coronary artery emerged from the pulmonary trunk. A right aortic arch is common, as is a left superior vena cava entering the coronary sinus. Rarely, under these circumstances the coronary sinus may straddle entering both atria. A patent foramen ovale is very common, and an aneurysm of the fossa ovalis is sometimes seen. Less common than a foramen ovale is a small ductus arteriosus. A narrowing of the ostium of the right or left pulmonary artery may accompany the complex. The position of the coronary ostia and the coronary artery distribution are discussed in a separate communication.

THE COMPLEX—ACYANOTIC TETRALOGY OF FALLOT

There is no specific morphologic type which distinguishes acyanotic from cyanotic tetralogy. The lack of cyanosis is related to the relatively mild extent of the infundibular stenosis.

External Anatomy (Fig. 12)

The heart may be normal or enlarged. The apex is formed by the left ventricle or both ventricles. The vessels at the base have a tendency to be of more equal size than in cyanotic tetralogy, with either the aorta or the pulmonary trunk somewhat larger than the opposite vessel.

**Figure 11** (upper): Characteristic shape of heart in cyanotic tetralogy of Fallot. **Figure 12** (center): External and right ventricular view of a heart of acyanotic tetralogy. Note the apex formed by the left ventricle and the mild infundibular stenosis. **Figure 13** (lower): Tetralogy of Fallot with pulmonary atresia. S—Septal band; P—Parietal band. Arrow points to entry of ventricular septal defect into right ventricle.
**Internal Anatomy**

The basic features of the ventricular septal defect in the acyanotic type are the same as in the cyanotic. However, the amount of overriding of the aorta appears to be less in this group. Correspondingly, the amount of deviation of the parietal band is less, and hence a mild form of infundibular stenosis is present. In one case in our series, no infundibular but a valvular stenosis was present. In contrast to cyanotic tetralogy, the left atrium and ventricle are frequently hypertrophied and enlarged with in some cases diffuse endocardial hypertrophy of the chambers, enlargement of the mitral orifice and increased diffuse hemodynamic changes of its valve.

**Variations in the Complex of Tetralogy of Fallot**

The complexes aside from the simple type seen in our series were classified as follows:

1. With pulmonary atresia
2. With common A-V orifice or persistent ostium primum
3. With absence of the pulmonary valve
4. With tricuspid stenosis
5. With mitral stenosis
6. With atrial septal defect
7. With aortic regurgitation
8. With widely patent ductus arteriosus

**A. With Pulmonary Atresia (Extreme Tetralogy of Taussig) (Fig. 13)**

**External Anatomy of the Complex**

The heart is normal in size or slightly enlarged. Although the apex is usually formed by both ventricles or by the left ventricle, it is more common to find the right ventricle forming the apex in this complex than in ordinary tetralogy. From the base the huge aorta is seen to lie to the right of the minute pulmonary trunk, or the aorta is to the right and anterior, and less commonly the aorta is to the right and posterior.

**Internal Anatomy of the Complex**

The ventricular septal defect is situated more anteriorly than in most cases of tetralogy, as the aorta in general is found to be more in a straddling position, or coming off mostly from the right ventricle. Accordingly, the muscle bundles of the right ventricle present a somewhat different picture than in ordinary tetralogy. The septal band proceeds to the base in the usual manner and may terminate there not forming an arch with a parietal band, or an arch may be formed with a parietal band which is
deviated far to the left almost touching the ventricular septum to the left. Thus a minute blind pulmonary conus is formed, or no conus at all. An accessory parietal band proceeds from the base of the aorta on to the anterior wall of the right ventricle adjacent to the anterior leaflet of the tricuspid valve. The right atrium and right ventricle are more relatively hypertrophied and enlarged than in tetralogy and the left atrium and ventricle are more atrophied. In a few cases, however, the left ventricle is dilated, raising the question of obstruction to outflow from this chamber. A patent foramen ovale is common, and a patent ductus arteriosus was consistently present in our series.

We prefer the nomenclature of pseudo-truncus for these cases of tetralogy of Fallot with pulmonary atresia. The former category also includes partial or complete transposition with pulmonary atresia.

B. WITH COMMON A-V ORIFICE OR PERSISTENT OSTIUM PRIMUM (FIG. 14)

This combination alters both the complexes tetralogy and common A-V orifice.

External Anatomy of the Complex

The heart is enlarged. The apex is formed either by the left ventricle or both ventricles. The aorta and pulmonary trunk have varying positions dependent upon the amount of overriding of the aorta. The aorta is larger than the pulmonary trunk, but the difference in their size is not as marked as in tetralogy alone.

Internal Anatomy of the Complex

The common A-V orifice takes the place of the ordinary ventricular septal defect of tetralogy. There is a distinct tendency for the right atrium to be more greatly enlarged than in ordinary tetralogy and for the left ventricle to be hypertrophied and enlarged. However, the left ventricle is as variable in size as in ordinary common

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A-V orifice, and as in the latter the right ventricle may be smaller than normal. The aortic orifice has a tendency to be normal in size, rather than enlarged, while the pulmonary orifice is usually smaller than normal. Occasionally a true pulmonary valvular stenosis is superimposed on the infundibular stenosis.

C. With Absence of the Pulmonary Valve (Fig. 15)

In these cases, instead of a formed pulmonary valve there are only nubbins of valvular tissue in this region. The pulmonary trunk and the two pulmonary arteries are greatly enlarged, often aneurysmally, and the right ventricle has a tendency to be larger than in the ordinary tetralogy.

D. With Tricuspid Stenosis

The tricuspid stenosis as seen morphologically is rather mild. It did not appear to be of physiologic importance in most cases in our series, in the form of an increase in size of the left and smallness of the right ventricle.

E. With Mitral Stenosis (Fig. 16)

Here the mitral orifice was distinctly, but slightly smaller than normal. In one case, this was related to a posteriorly located ventricular septal defect with a component which was left atrial-right ventricular (Fig. 16). In this latter case it had produced a hypertrophy of the left atrium.

F. With Atrial Septal Defect (Pentology)

A small patent foramen ovale is found in about half the cases of tetralogy. These are not included in the present discussion, although they may have produced right to left shunt at the atrial level. Only cases with true atrial septal defect of the fossa ovalis type were separated as a group.

In this group, the complex is not altered appreciably from ordinary tetralogy. The left atrium and left ventricle are not appreciably enlarged to warrant any evidence of a large sized right to left shunt. Likewise, the amount of right atrial hypertrophy and enlargement is not more than in other cases of tetralogy to represent evidence of left to right shunt at the atrial level. This, of course, does not deny the catheterization evidence of such small scale shunting in either direction at this level.

G. With Aortic Regurgitation

In these cases, the right aortic cusp is redundant, and herniated into the right ventricle. The apex is then formed by the left ventricle, which is greatly hypertrophied and enlarged.

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FIGURE 16: Tetralogy of Fallot with mild mitral stenosis. (A) Left atrial view; (B) Left ventricular view; LA—Left atrium. Rod is inserted in the opening between the left atrium and right ventricle.
H. WITH WIDELY PATENT DUCTUS ARTERIOSUS

A small patent ductus is found in about one-third of the cases of tetralogy. However, most of these are insufficient to yield an acyanotic patient. In only two cases in this group was the ductus of large size, producing an acyanotic type. In one case there was calcification of the pulmonic valve (the only instance of this in this series).

SUMMARY

1. The complex tetralogy of Fallot shows marked variation in the position of the defect, the amount of overriding of the aorta, and the type and extent of infundibular stenosis.

2. In addition, there are various types of complexes which have tetralogy as their base. There are: tetralogy associated with (1) pulmonary atresia; (2) common A-V orifice; (3) absence of the pulmonary valve; (4) tricuspid stenosis; (5) mitral stenosis; (6) atrial septal defect; (7) aortic regurgitation, and (8) widely patent ductus arteriosus.

RESUMEN

1. El complejo de la tetralogía de Fallot muestra una variación marcada en la posición del defecto, el grado en que éste es sobremontado por la aorta y el tipo y extensión de la estenosis infundibular.

2. Además, hay varios tipos de complejos que tienen como base la tetralogía de Fallot. Tales son: la tetralogía asociada a: (1) atresia pulmonar; (2) orificio común A-V; (3) ausencia de válvula pulmonar; (4) estenosis de la tricúspide; (5) estenosis mitral; (6) defecto de tabique auricular; (7) regurgitación aórtica, y (8) ductus arteriosus muy abierto.

ZUSAMMENFASSUNG

1. Die komplexe Fallot'sche Tetralogie zeigt ausgesprochene Varianten in der Position des Defektes, dem Ausmaß der Trichterstenose.

2. Außerdem waren verschiedene Komplextypen vorhanden, die die Tetralogie zur Grundlage hatten. Diese sind: Tetralogie verknüpft mit (1) pulmonaler Atresie; (2) gemeinsamer Atrio-Ventrikularklappenöffnung; (3) Fehlen der Pulmonalklappen; (4) Tricuspidal-Stenose; (5) Mitralstenose; (6) Vorhofseptumdefekt; (7) aortalen Rückstrom und (8) weit offenem ductus arteriosus.

For reprints, please write Dr. Lev, 637 South Wood Street, Chicago 12.

DIABETES MELLITUS AND MYOCARDIAL INFARCTION

Forty-three cases of myocardial infarction associated with diabetes mellitus are presented. This is of uncommon occurrence (in about 4.5 per cent of cases of myocardial infarction). An acute diabetic syndrome—an exceedingly high hyperglycemia (400-1400 mg. per cent), glycosuria and acidosis occurred in several severe cases of myocardial infarction. In some cases with lethal outcome, various forms and stages of acute pancreatitis, particularly the acute severe pancreatitis were revealed. The clinical course of myocardial infarction associated with diabetes mellitus was more severe than that of non-associated cases. The severity was most often expressed by the presence of thrombosis and embolism.

A carbohydrate deficient diet was sufficient in treating diabetes mellitus in 20 cases. Insulin was administered in 23 cases. One should be careful in estimating the insulin dosage, as severe hypoglycemic state occurs more easily than usual in these cases. It is best to choose low and fractionated doses. The same caution is necessary in administering anticoagulants.