FALLOT'S TETRALOGY—NATURAL HISTORY

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Fallot's tetralogy is the commonest cyanotic congenital cardiac malformation and the third commonest of all congenital heart diseases in Singapore chi dren (Loh, 1969)[5]. Like all congenital malformations, it has a genetic basis and the mode of inheritance in the majority of cases is probably multi-factorial. The risk of inheriting tetralogy of Fallot among the population at large is approximately 1 per 2,000 livebirths. However, the risk for the first degree relatives of patients with tetralogy increases to 1 in 33 (Wong, 1972)[8].

DEFINITION

The primary disorder lies in the underdevelopment of the subpulmonary conus with the inevitable consequences of associated anomalies, e.g. a large V.S.D., pulmonary stenosis, overriding aorta and right ventricular hypertrophy. The overriding aorta is functional rather than anatomical as the fibrous continuity between the anterior leaflet of mitral valve and aortic valve is maintained.

Taussig (1971)[7] included pulmonary atresia in the definition, but Kirklin (1970)[4] defined tetralogy of Fallot from a surgeon's viewpoint as that in which the ventricular septal defect is as large as the aortic orifice, situated immediately beneath the aortic valve and slightly more anterior than the usual isolated high defect. The pulmonary stenosis is in part or wholly infundibular, but sufficiently severe to cause systemic pressure in the right ventricle. The former includes the extreme form in which the obstruction is complete, and the latter the mild form i.e. the so-called acyanotic Fallot's tetralogy.

The present series of 213 patients of Fallot's tetralogy comprises the mild form as well as the severe, but the complete obstruction as in pulmonary atresia is excluded.

INCIDENCE

Over a period of 10 years, i.e. 1962-1971, the total number of cases of tetralogy followed-up at the Cardiac Clinic is as follows:

Year Before 1962	C.H.D.	Fallot's tetralogy 36	Percentage
1962	78	10	12.8%
1963	132	12	9.1%
1964	189	22	11.6%
1965	225	24	10.6%
1966	171	14	8.2%
1967	187	15	8.1%
1968	203	16	7.9%
1969	207	22	10.9%
1970	223	23	10.3%
1971	210	19	9.0%
Total	1,824	177	9.7%

Therefore, the incidence of this disorder among children is 9.7%. The incidence varies from 6% at infancy (Venables, 1969) to as much as 18.2% (Aryanpur, 1972) as shown below, depending on the age at which patients were detected and the source of the material:

Incidence of Fallot's Tetralogy

Australia	—	6%	(Venables, 1969) at infancy
New Zealand	—	9%	(Neutze, 1971) at infancy
Taiwan	—	12.5%	(Shann, 1969) at all ages
Philippines	—	15%	(Imperial, 1963) at autopsy
Ceylon	—	8.5%	(Walloppillai, 1972) at all ages at cardiac catheterisation
Iran	—	18.2%	(Aryanpur, 1972) in children
Nigeria	—	12.3%	(Antia, 1972) in children
Singapore	—	9.7%	

AGE, SEX & RACE

The mean age of the present series of 213 cases is 6.1 years. There were 139 males and 74 females, giving a sex ratio of male to female as 1.9:1. The male predominance has been consistently reported as 1.5 in much larger series of 728 cases (Taussig et al, 1971)[7], of 202 cases at Mayo Clinic (Hawe et al, 1969)[2] and of 380 cases (Campbell & Polani, 1955)[6].

Severe congenital cardiac defects seem to be more common among the male patients and the less severe forms among the females shown as follows:

All types of congenital heart disease seen at the Cardiac Clinic: Male—Female = 1.0—1.0
Ventricular septal defect: Male—Female = 1.0—1.0
Patent Ductus Arteriosus: Male—Female = 1.0—2.6
Atrial Septal Defect (secundum): Male—Female = 1.0—1.4
Fallot's Tetralogy: Male—Female = 1.9—1.0
Transposition of great arteries Male—Female = 1.5—1.0

The racial distribution of tetralogy is compared with that of the population in Singapore with the following results:

Ethnic Groups	S'pore Population (June 1972)	%	Fallot's Tetralogy Cardiac Clinic (1962-71)	%	Tetralogy of all ages investigated at Cardiovascular Lab. (1964-71)	%
Chinese	1,634,600	76%	165	77.5%	104	74.9%
Malays	323,200	15%	31	14.5%	22	15.8%
Indians	149,600	7%	12	5.5%	11	7.9%
Others	40,000	2%	5	2.5%	2	1.4%
	2,147,400		213		139	

All races seem to be equally affected by this disorder as shown above in the group of patients at the Paediatric Department as well as those of all ages investigated at the Cardiovascular Laboratory.

CLINICAL MANIFESTATIONS

The main clinical features are briefly summarised as follows:

1. Cyanosis at birth (severe tetralogy) = 12%
2. Cyanosis from 3 months to 1 year = 73%
3. Cyanosis after infancy = 15%
4. Hypoxic spells at one time or other = 45%
5. History of squatting = 50%
6. Convulsions = 18%
7. Cerebrovascular accidents = 6.6%

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8. Brain abscess = 3.8%
9. Subacute endocarditis = 2.8%
10. Cardiac failure = 2.3%

As hypoxic spells and squatting are characteristic of tetralogy, it is interesting to note that these features are equally common among the less cyanosed patients. As nutritional iron deficiency anaemia is common, some of the severe tetralogy may appear less cyanosed in the presence of anaemia. Hypoxic spells could be relieved or even aborted by a simple blood transfusion.

On auscultation, an early ejection systolic murmur along the left sternal edge, caused by the obstruction of right ventricular outflow tract is the most consistent finding. The intensity of the murmur depends on the severity of obstruction—the softer the murmur, the more severe is the obstruction.

On analysing the chest X-rays, 74% show a normal-sized heart on the basis of measuring the cardio-thoracic ratio. 30% show the so-called "boot-shaped" heart, and 15% a right-sided aortic arch.

The electrocardiographic findings show more than 80% with a right axis deviation of QRS complex in the frontal leads and evidence of right ventricular hypertrophy in the precordial leads.

Pulmonary stenosis:

It is not easy to be absolutely sure of the anatomical types of obstruction at the right ventricular outflow tract even from cardiac catheterisation or angiocardiography. The results of the autopsy findings at one extreme were combined with those of the surgeon at open heart surgery as follows:

Stenosis	Valvular	Infundibular	Combined lesions
Surgical	3%	51%	46%
Autopsy	9%	30%	29%
	5.6%	39.8%	54.6%

Bicuspid pulmonary valve = 17%

NATURAL SURVIVAL

In Singapore, by 1971 only about 12% of 213 patients underwent surgical treatment—palliative as well as definitive correction and the remaining 186 cases form the basis of the study of natural survival.

There were 108 deaths over a period of 10 years, giving a mortality rate of 58% and the mean age of death is 5.2 years. The percentage of death according to age by medical management is 10% by 1 year, 33% by 5 years and 55% by 10 years, shown as follows:

Age: below 1yr. 1yr. 2yrs. 3yrs. 4yrs. 5yrs 6yrs. 7yrs. 8yrs. 9yrs 10yrs.

Death: 5% 10% 16% 23% 29% 33% 38% 42% 46% 51% 55%

The percentage of death in this series runs almost parallel to that reported by Campbell (1972)[1] for the first ten years, and would undoubtedly take the same course in the subsequent years if the remaining surviving patients were to be deprived of the benefit of surgical therapy for the rest of their lives. Fortunately, this would not be the case in Singapore.

In Campbell's series, 50% of his patients succumbed by the first decade, 84% by second decade and 96% by the third decade. Only 4% of his 296 cases were alive after the age of 30 years.

Similarly, among the cases of tetralogy of all ages investigated at the Cardiovascular Laboratory, Outram Road General Hospital, 55% were below 5 years of age, 69% below 10 years, 83% below 15 years and 90% below 20 years, and less than 1% was above 30 years. From the above data, it could be inferred that natural survival after the age of 30 years would be extremely rare.

CAUSES OF DEATH

The major causes of death in tetralogy are hypoxic spells (62%), cerebrovascular accidents (17%) and brain abscesses (13%). 81% of the deaths caused by hypoxaemia occurred during the first 3 years of life. Cerebrovascular accidents, commonly a combination of cerebral thrombosis, infarction and haemorrhage, seem to occur in the first 5 years of age and brain abscesses thereafter.

There were 4 non-fatal cases of cerebrovascular accidents out of 14, but all the cases of brain abscesses died despite surgical drainage carried out in 3 out of 8 patients. Brain abscesses tend to be multiple and recurrent. Taussig et al (1971)[7] reported an incidence of 5.5% with 40% mortality in spite of surgical treatment in a group of 728 patients who had had Blalock-Taussig anastomoses and had been followed up for a period of 20 years.

Cardiac failure is rare in paediatric age group, i.e. 2.3% in the present series, but it is apparently common in adult patients. An incidence as high as 42% among the cyanotic group of tetralogy has been reported (Higgins & Mulder, 1972)[3].

So far the mortality pattern has been confined to Hospital patients. However, it would not be too different from the true picture as all the patients with tetralogy are symptomatic and would have to be referred to the Hospital for further management eventually.

Of 108 deaths, 29 patients were discovered to have died at home. From the history, 25 of them died after a bout of hypoxic spells and 4 of them after an attack of convulsion. Therefore, hypoxaemia is undoubtedly the most common cause of death in tetralogy. It is not uncommon to see patients with tetralogy brought in dead after a series of hypoxic attacks at home.

COMPARISON WITH OTHER CYANOTIC C.H.D.

The cyanotic group comprises about one-third of all congenital heart disease, i.e. 631 out of 1,824, and tetralogy forms one-third of all cyanotic lesions, i.e. 33.7%. To compare the natural survival with those of other major cyanotic cardiac defects, tetralogy seems to have the best prospects (Fig. 1).

Among the other major defects, e.g. transposition of great arteries, total anomalous pulmonary venous drainage, persistent truncus arteriosus, tricuspid atresia, and pulmonary atresia, mortality is very high during infancy and early childhood whereas the mortality rate in tetralogy takes a more gradual ascent as shown in Fig. 1. The survival of pulmonary atresia with or without intact ventricular septum depends largely on the persistent patent ductus and the adequacy of aorto-pulmonary anastomoses. After the initial high death rate at 6 months of age, the prospect of subsequent survival approximates to that of tetralogy at the end of 10 years solely because of associated P.D.A. and adequate aorto-pulmonary anastomoses.

SUMMARY

The study of natural history of tetralogy of Fallot based on 213 cases over a period of 10 years is summarised in Fig. 2.

12% of the patients with the severe type of lesions presented with cyanosis at birth. In 73%, cyanosis was noted from the age of 3 months to a year, and in 15% after infancy.

Hypoxic spells occurred in 45% of the patients, carrying the highest mortality during the first 3 years of life and accounting for 62% of all deaths.

Cerebrovascular accidents occurring in 6.6% of the patients seemed to appear from the age of 1 to 8 years.

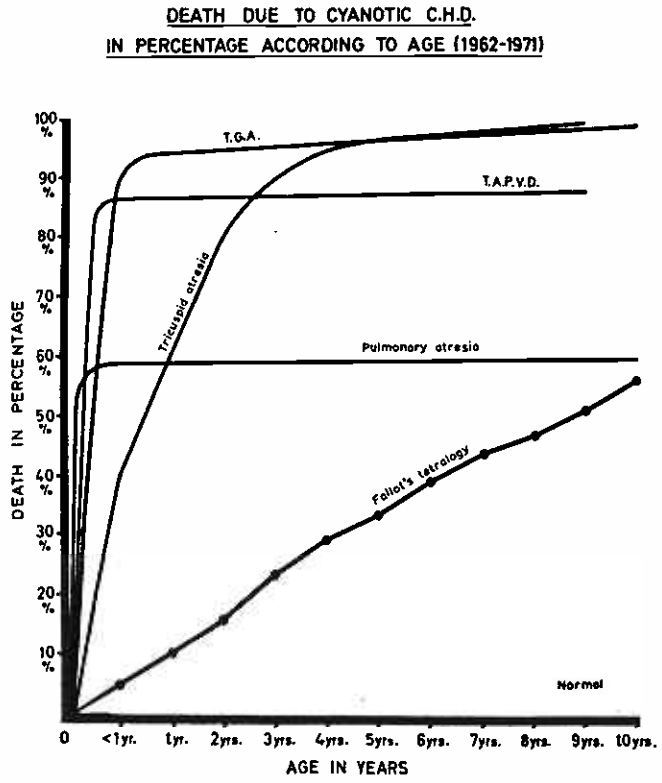

Fig. 1. This diagram shows the comparative death rate of five major cyanotic congenital heart defects over a period of 10 years.

The majority of them were fatal and were responsible for 17% of the total deaths.

Brain abscesses occurred in 3.8% of the patients from the age of 5 to 11 years. All were fatal and thus accounted for 13% of all deaths. Incidentaly, these were the commonest cause of death in children after the age of 5 years.

Natural survival was 44% at 10 years, 10% at 20 years, and less than 1% after the age of 30 years.

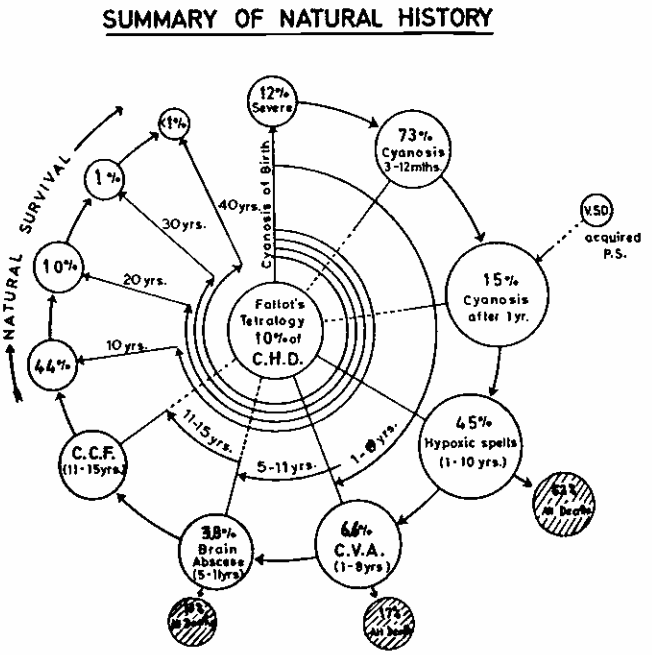

Fig. 2. This diagram summarises the natural history of Fallot's tetralogy.

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