EISENMENGER—V.S.D.—A STUDY OF CONGENITAL AND ACQUIRED PULMONARY VASCULAR DISEASE

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In large ventricular septal defects with high pulmonary vascular resistance, reversal of the shunt occurs if the pulmonary vascular resistance exceeds that of the systemic. The term Eisenmenger's syndrome has been applied to this haemodynamic situation. However, since the terms Eisenmenger's complex and syndrome are often loosely used to denote any situation characterised by severe pulmonary hypertension with a right-to-left shunt, it is best to abandon these non-specific terms in favour of the term Eisenmenger—V.S.D. in case of ventricular septal defect.

There has been disagreement as to whether increased pulmonary vascular resistance represents an abnormality dating from birth due to persistence of the foetal vascular pattern or whether increasing pulmonary arteriolar resistance develops later, as a sequel to the ventricular septal shunt and high flow in the pulmonary circulation.

There appears to be two schools of thought regarding the aetiology of Eisenmenger—V.S.D. Evans and Short (1958)[4] suggested that the pulmonary arteries of patients with ventricular septal defect with severe pulmonary hypertension are congenitally determined and that the pulmonary vascular disease progresses even after surgical closure of the defect. In this group, it follows that reversal of shunt, giving rise to cyanosis occurs very early in life.

In the other school, the pulmonary hypertension is considered to be secondary to a large defect and left-to-right shunt. The small pulmonary arteries and arterioles become progressively narrower due to medial muscular hypertrophy and intimal sclerosis, over an interval of many years. Eventually when the pulmonary vascular resistance equalises or exceeds that of the systemic, reversal of shunt occurs and the status of Eisenmenger's situation is achieved. Kidd *et al* (1965)[6] in their study on the haemodynamics in ventricular septal defect in childhood, concluded that progressive pulmonary vascular obstruction developed gradually from increased pulmonary blood flow and no case of congenital Eisenmenger—V.S.D. was found.

Probably, both these situations exist and the present clinical and haemodynamic study of nine cases substantiates both views.

CASE REPORTS

Case No. 1. S.C.K. $2\frac{1}{2}$ years. Chinese male. P. No. 110053

He was the youngest of seven siblings. He had a normal birth history, and a birth weight of 8 lbs. 2 oz. Apparently, he was perfectly well until $2\frac{1}{2}$ years of age when he was referred by the Orthopaedic Department to the Paediatric Department for acute cervical adenitis. A cardiac lesion was suspected on routine examination. He was small for his age, weighing only 20 lbs. 4 oz. No cyanosis was detected at rest but after crying, slight cyanosis was noticed at the extremities. His pulse was regular and of normal volume, BP = 95/55 mm. Hg. A prominent 'a' wave was seen at the jugular venous pulsation. There was no precordial bulge and the heart was not clinically enlarged. No thrill was palpable but a diastolic shock was felt over the pulmonary area. There was a soft systolic murmur Grade 1/6 with an ejection click and a loud closely split second sound at the 2nd and 3rd left intercostal spaces at the sternal edge. No diastolic rumble was heard at the apex but a third sound was easily audible (Hb. = 13.9 gm.%, PCV = 41%).

Chest X-ray showed a slightly enlarged heart with a cardio-theracic ratio of 0.52, a prominent pulmonary artery and branches, and slight pulmonary plethora as shown in Fig. 1.

His electrocardiogram showed a mean QRS axis of + 135° and an isolated right ventricular overload pattern (Fig. 2).

Cardiac catheterisation was performed and it confirmed the diagnosis of a large ventricular septal defect with reversal of shunt (Table I).

Comment: Right heart study revealed a two-way shunt at the ventricular level and the catheter entered the descending aorta via a V.S.D. Aortic blood was desaturated even at rest. Severe pulmonary vascular disease was already present and this must have been present since

TABLE I

Haemodynamic Data **Catheter No. 787 (9-6-67)**

Pressure mm. Hg.	Oxygen	Saturation %	Content Vol.%
Pulmonary wedged mean 11 mm. Hg.	PA	78%	13.5 Vol.%
PA 93/56 (70) mm. Hg.	RV	78%	13.5 Vol.%
RV 99/0-6 mm. Hg.	RA	65%	10.5 Vol.%
RA mean 4 mm. Hg.	IVC	65%	10.5 Vol.%
Aorta 105/60 (81) mm. Hg.	R.BA	90%	15.5 Vol.%
BP 95/55 mm. Hg.	Abd. Aorta	90%	15.0 Vol.%
	Capacity	100%	17.0 Vol.%

	Systemic	Pulmonary
Cardiac Output	1.8 L/min.	2.8 L/min.
Cardiac Index	3.4 L/min./m.^{2}	5.4 L/min./m.^{2}
L-R shunt 1.3 L/min.	R-L shunt 1.0 L/min.	Net L-R shunt 0.3 L/min.

Pulmonary vascular resistance = 10.9 units
Systemic vascular resistance = 16.9 units

TABLE II

Haemodynamic Data **Catheter No. 722 (10-3-67)**

Pressure mm. Hg.	Oxygen	Saturation%	Content Vol.%
Pulmonary wedged mean 8 mm. Hg.	PA	89%	17.0 Vol.%
PA 100/68 (81) mm. Hg.	RV	89%	17.0 Vol.%
RV 103/0-8 mm. Hg.	RA	69%	13.0 Vol.%
RA mean 6 mm. Hg.	SVC	69%	13.0 Vol.%
BA 100/68 (77) mm. Hg.	IVC	65%	12.5 Vol.%
	BA	95%	19.5 Vol.%
	Capacity		21.5 Vol.%

	Systemic	Pulmonary
Cardiac Output	1.8 L/min.	3.2 L/min.
Cardiac Index	3.0 L/min./m.^{2}	4.2 L/min./m.^{2}

L-R shunt 1.52 L/min. R-L shunt 0.43 L/min. Net L-R shunt 1.1 L/min.
Pulmonary vascular resistance 17.5 units
Systemic vascular resistance 24.0 units

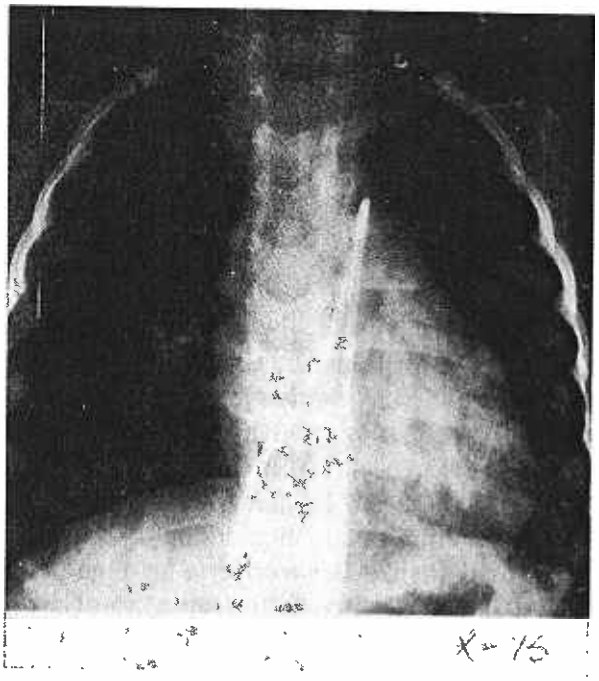

Fig. 1. This chest X-ray of Case 1 shows a slightly enlarged heart, a prominent main and right pulmonary arteries and very mild pulmonary plethora. The catheter enters the aorta through the ventricular septal defect from the right ventricle.

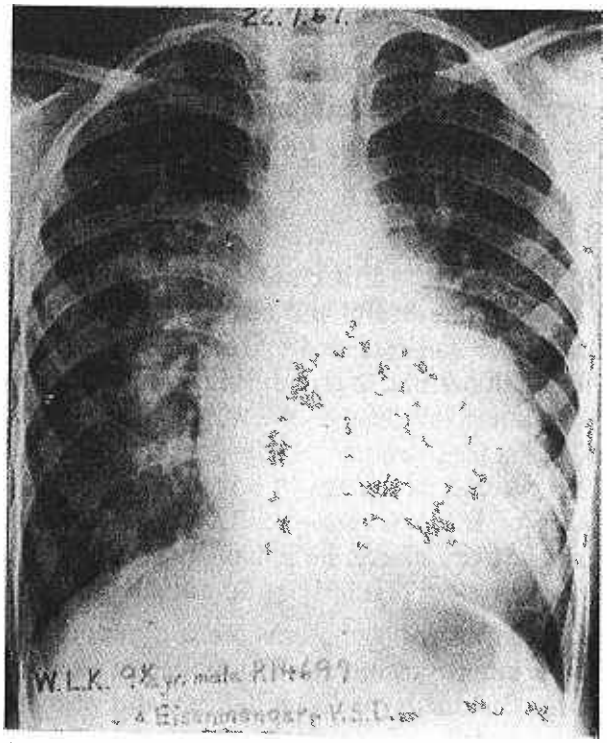

Fig. 3. The chest X-ray of Case 2 shows an enlarged heart, prominent pulmonary arteries and ischaemic peripheral lung fields.

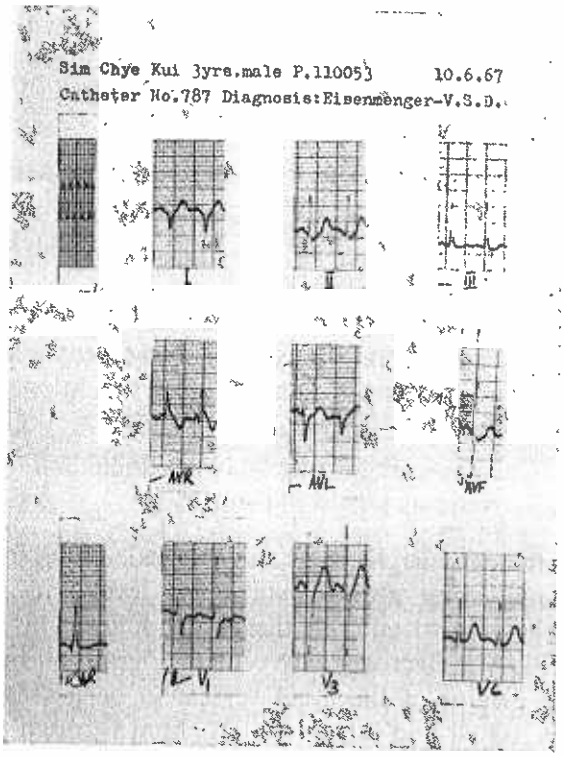

Fig. 2. The electrocardiogram of Case 1 shows mean QRS axis of +135° and an isolated right ventricular hypertrophy.

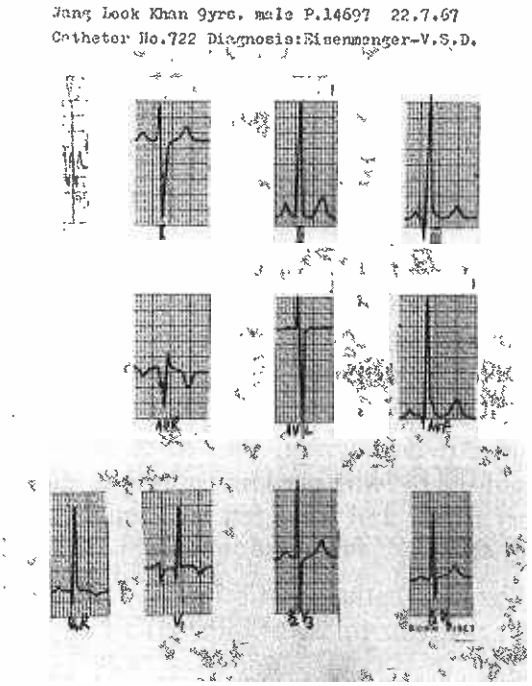

Fig. 4. The electrocardiogram of Case 2 shows a mean QRS axis of +114°, severe right ventricular hypertrophy as well as left ventricular hypertrophy. Note V_6 is taken at half voltage.

birth because there was no history of recurrent chest infection with cardiac failure so characteristic of a large left-to-right shunt before the onset of Eisenmenger—V.S.D. allowing him an apparently normal infancy with his cardiac lesion discovered only incidentally.

Case No. 2. W.L.K. 9½ years. Chinese male. P. No. 14697

He was the fifth child of six siblings. His birth was uneventful and birth weight was 7 lbs. 15 oz. He had repeated episodes of chest infection with cardiac failure during infancy and was hospitalised at the ages of 7 weeks, 8 months and 10 months. Cyanosis was first recorded (by Dr. H.B. Wong) at the age of 8 months and a diagnosis of Eisenmenger—V.S.D. was made clinically. After infancy, he remained quite well and was follow-up regularly as an outpatient.

The present symptoms were dyspnoea and more intense cyanosis after moderate exertion. He occasionally had palpitations and also had one attack of paroxysmal supraventricular tachycardia which was well-controlled by digitalis. On examination, he was stunted in stature. He had slight cyanosis and clubbing. His pulse was regular but of small volume, BP=100/70 mm. Hg. There was a prominent 'a' wave in the jugular pulsation. He had a marked precordial bulge and had clinical evidence of biventricular hypertrophy. There was no thrill but a diastolic shock was felt at the pulmonary area. On auscultation, there was an ejection click and a loud single second sound followed by an early diastolic murmur over the pulmonary area. A mid-diastolic rumble with a marked third sound was heard at the apex (Hb. = 15.2 gm.%, PCV = 45%).

Chest X-ray showed enlargement of both ventricles with a cardio-thoracic ratio of 0.60, a prominent pulmonary artery and branches and ischaemic peripheral lung fields, giving a 'pruning' appearance as shown in Fig. 3.

Electrocardiogram showed a mean QRS axis of +114° with predominent right ventricular hypertrophy and some left ventricular overload (Fig. 4).

Cardiac catheterisation was done and the findings are as follows (Table II).

Comment: Right heart study showed a two-way shunt at the ventricular level with severe pulmonary vascular obstruction. The systemic blood was desaturated and the pulmonary vascular resistance was 17.5 units. The presence of cyanosis was noted by a reliable clinician at the age of 8 months. He has been followed-up regularly as an outpatient. The cyanosis has persisted for almost 9 years with relatively few symptoms. Therefore, it is most likely that his severe pulmonary vascular disease was present at birth or early infancy and that he, in fact, has congenital Eisenmenger—V.S.D.

Case No. 3. L.M.W. 8 years. Chinese male. P. No. 59372

This patient was the youngest of seven siblings. The birth history was normal. His birth weight was 9½ lb. His only symptom was cyanosis after crying, first noticed by his mother at the age of one year. Apart from this, he was perfectly well until he was 4 years old when he was admitted with bronchopneumonia. Cyanosis was also noted then. After recovery, he remained so well that he defaulted follow-up at the Cardiac Clinic until he was 7¾ years old, when he was admitted for investigation. His effort tolerance was said to be quite good and he took part in the normal school activities. On examination, he appeared well. He had cyanosis and clubbing. His pulse was regular but of small volume, BP=100/60 mm. Hg. There was a prominent 'a' wave in the jugular venous pulsation. There was no precordial bulge and clinically the heart was not enlarged. There was no thrill but a diastolic shock was palpable. On auscultation there was an ejection systolic murmur Grade 1/6 with a loud second sound and an early diastolic murmur at the pulmonary area (Hb. = 15.3 gm.%, PCV = 51%).

Chest X-ray showed an enlarged heart with a cardio-thoracic ratio of 0.55, a prominent pulmonary artery and branches, and an ischaemic peripheral lung field (Fig. 5).

Electrocardiogram showed a mean QRS axis of +98° and an isolated right ventricular overload pattern as denoted by the 'q' wave in V_1 (Fig. 6).

Cardiac catheterisation was done and the findings are as follows (Table III).

Comments: Right heart study revealed a bidirectional shunt at the ventricular level and the catheter also entered the descending aorta via a PDA. Selective right ventriculogram showed the origins of the great vessels to be normally orientated and a right-to-left shunt through the V.S.D.

The pulmonary and systemic vascular resistances were almost equal and the predominent shunt at the ventricular level was right-to-left. This patient was apparently very well in spite of

TABLE III

Haemodynamic Data **Catheter No. 680 (23-12-66)**

Height = 3′ 7¾″ Wt. = 32¾ lb. Chest = 10.5 cm. BSA = 0.67 m.²
Oxygen consumption = 127 c.c./min.

Pressure mm. Hg.			Oxygen	Saturation %	Content Vol.%
Pulmonary wedged mean 10 mm. Hg.			PA	78%	15.0 Vol.%
PA	92/64 (75)	mm. Hg.	RV	77%	15.5 Vol.%
RV	93/0-5	mm. Hg.	RA	70%	13.0 Vol.%
RA	mean 5	mm. Hg.	SVC	70%	12.5 Vol.%
Aorta	106/64 (80)	mm. Hg.	IVC	67%	12.5 Vol.%
			Aorta	85%	18.5 Vol.%
			Capacity		21.0 Vol.%

	Systemic	Pulmonary
Cardiac Output	2.3 L/min.	2.1 L/min.
Cardiac Index	3.4 L/min./m.²	3.1 L/min.

L-R shunt 0.52 L/min. R-L shunt 0.71 L/min. Net R-L shunt 0.2 L/min.
Pulmonary vascular resistance 21.0 units
Systemic vascular resistance 22.0 units

TABLE IV

Haemodynamic Data **Catheter No. 341 (28-7-65)**

Height = 2′ 3½″ Weight = 15 lb. Chest = 10 cm. BSA = 0.36 m.²
Oxygen consumption = 72 c.c./min.

Pressure mm. Hg.			Oxygen	Saturation %	Content Vol.%
Pulmonary wedged mean 10 mm. Hg.			PA	86%	13.5 Vol.%
PA	76/46 (57)	mm. Hg.	RV	84%	13.5 Vol.%
RV	75/0-3	mm. Hg.	RA	60%	10.0 Vol.%
RA	mean 2	mm. Hg.	SVC	64%	9.5 Vol.%
BP	80/60	mm. Hg.	FA	94%	15.0 Vol.%
			Capacity	100%	16.5 Vol.%

	Systemic	Pulmonary
Cardiac Output	1.4 L/min.	2.4 L/min.
Cardiac Index	4.0 L/min./m.²	6.6 L/min./m.²

L-R shunt 1.3 L/min. R-L shunt 0.9 L/min. Net L-R shunt 0.4 L/min.
Pulmonary vascular resistance 7.1 units

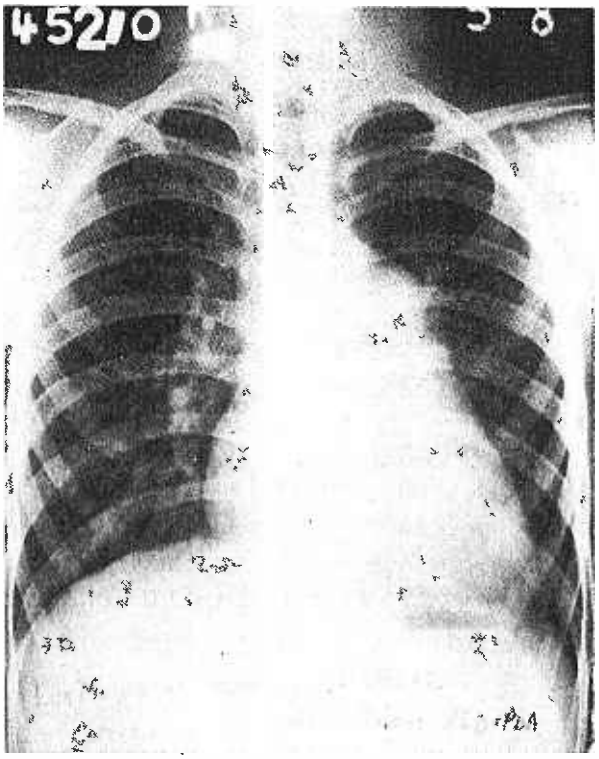

Fig. 5. Shows the chest X-ray of Case 3. The heart is slightly enlarged. The pulmonary conus and the right pulmonary artery are prominent. The lung fields are ischaemic.

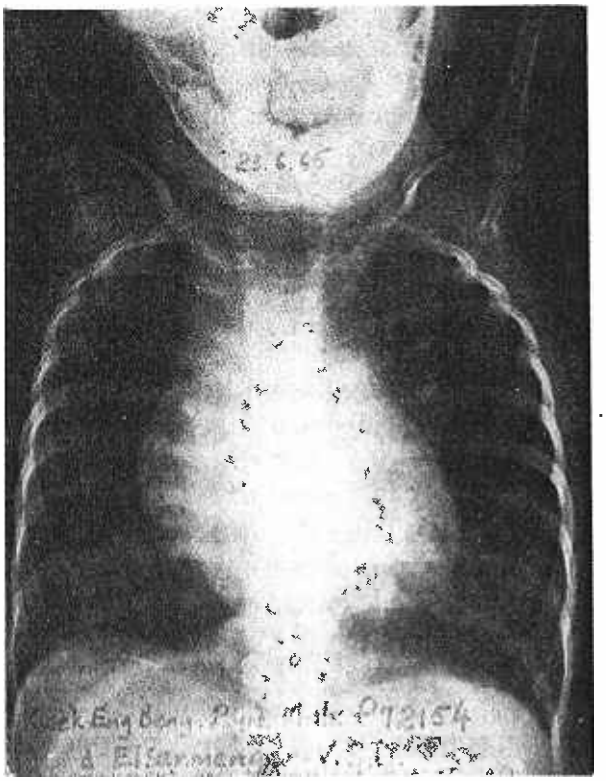

Fig. 7. The chest X-ray of Case 4 shows a moderately enlarged heart with reduced pulmonary blood flow.

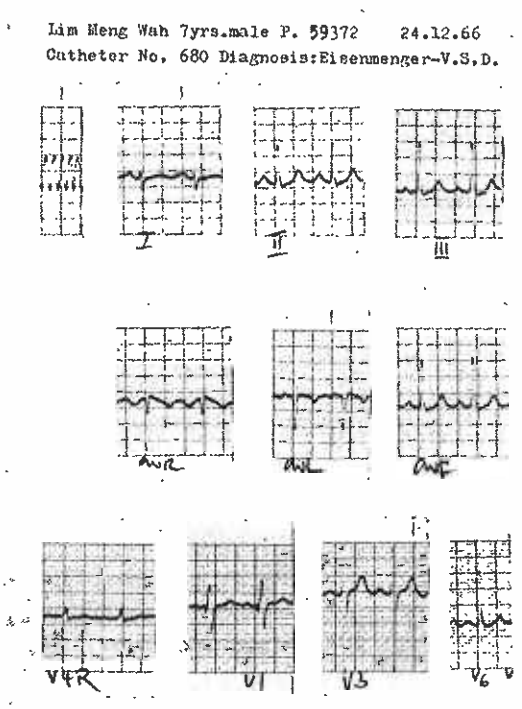

Fig. 6. The electrocardiogram of Case 3 shows a mean QRS axis of +98° and right ventricular hypertrophy as evidenced by the presence of a 'q' wave and an upright 't' wave in V_1.

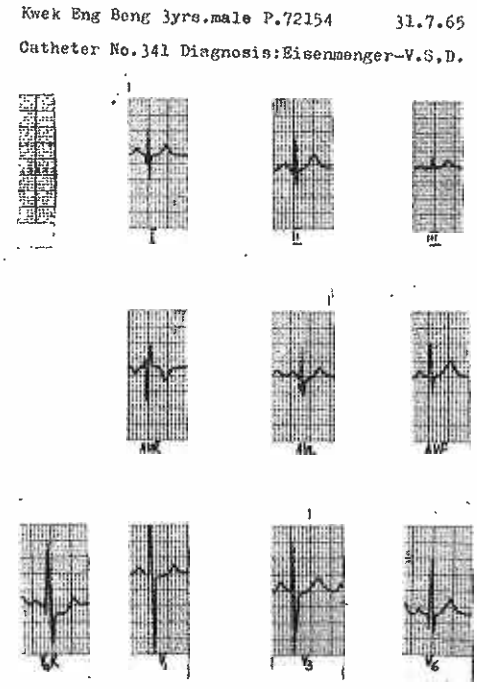

Fig. 8. The electrocardiogram of Case 4 shows severe right ventricular hypertrophy by the presence of a 'q' wave and an upright 'T' wave in V_4R and probably some left ventricular overload.

his cardiac lesion and, with the history of the onset of cyanosis at 1 year of age and with very little in the way of symptoms he must have had his Eisenmenger's state since birth.

Diagnosis: Congenital Eisenmenger—V.S.D.

Case No. 4. K.E.B. 2 years. Chinese male. P. No. 72154

He was the youngest of five siblings. He was a premature baby weighing 5 lb. 14 oz. at birth. He was first admitted for chest infection with cardiac failure at 5 months of age and a cardiac lesion was detected. Intermittent cyanosis was noted. His milestones were delayed and he had generalised hypotonia due to amyotonia congenita.

He was investigated at the age of 2 years. On examination, he was small and underdeveloped. He was pale but had no obvious cyanosis. His pulse was regular and of good volume, BP=105/65 mm. Hg. He had a marked precordial bulge and right ventricular hypertrophy. Both a systolic thrill and a diastolic shock were palpable at the pulmonary area. On auscultation, there was an ejection systolic murmur maximal at the 2nd and 3rd intercostal spaces at the left sternal edge, accompanied by an ejection click and a loud second sound. No diastolic murmur was heard (Hb. = 77%).

Chest X-ray showed an enlarged heart with a cardio-thoracic ratio of 0.61, prominent branches of the pulmonary artery and an ischaemic peripheral lung field (Fig. 7).

Electrocardiogram showed severe right ventricular hypertrophy and some left ventricular overload pattern (Fig. 8).

Cardiac catheterisation was carried out and the findings are as follows (Table IV).

Comment: Right heart study showed a two-way shunt at the ventricular level and severe pulmonary vascular disease.

Diagnosis: Congenital Eisenmenger—V.S.D.

Addendum: This patient died at the age of 3 years and autopsy confirmed Eisenmenger—V.S.D. (Autopsy No. 1345/66).

Case No. 5. K.K.H. 9½ years. Chinese male. P. No. 52863

He was the second of five siblings. He was a premature baby weighing 4 lb. 15 oz. at birth. He had frequent chest infections during infancy. He was a difficult and slow feeder and was easily exhausted during feeding. There was no history of cyanosis. He perspired excessively especially during sleep. He was rather stunted in growth compared with the other siblings. However, after the first few years of life, episodes of chest infection became less frequent and he began to thrive.

He was first seen at the age of 4 years at the Paediatric Unit (by Dr. F. M. Paul) because of a cardiac murmur and the clinical findings were a marked precordial bulge with a systolic thrill and murmur, a loud pulmonary second sound. There was no cyanosis and a diagnosis of ventricular septal defect with pulmonary hypertension was made. His chest X-ray done at 4 years of age showed an enlarged heart with a cardio-thoracic ratio of 0.60, a prominent pulmonary conus and marked pulmonary plethora (Fig. 9).

He remained asymptomatic but was admitted at the age of 6 years for investigation. On examination, he was small for his age, weighing only 26 lbs. He had no cyanosis, BP = 80/65 mm. Hg. Clinically, the heart was not enlarged. There was no thrill. Grade 2/6 ejection systolic murmur with a loud pulmonary second sound was heard at the pulmonary area.

His chest X-ray done at the age of 6 years showed an enlarged heart with a cardio-thoracic ratio of 0.57, a very prominent pulmonary conus and mild pulmonary plethora (Fig. 10).

Cardiac catheterisation was done on 1.7.67 and it confirmed the severe pulmonary hypertension due to a ventricular septal defect with Qp/Qs = 1.2 and pulmonary vascular resistance of 8.9 units.

Since then, he had been closely observed in the Cardiac Clinic. He remained asymptomatic until 8 years of age, when he developed exertional dyspnoea and cyanosis after exercise. Cyanosis became more obvious during the following 12 months. At the age of 9½ years, a repeat cardiac catheterisation was performed.

On examination, he had cyanosis and clubbing, BP = 90/70. His pulse was regular but of poor volume. There was a precordial bulge. No thrill was palpable but a striking diastolic shock was felt at the pulmonary area. On auscultation, only a very faint systolic murmur was heard but there was an ejection systolic click followed by a loud pulmonary closure sound, Hb. = 14.0 gm.%, PCV = 45%.

His chest X-rays done at 9½ years of age showed a cardio-thoracic ratio of 0.53, a prominent pulmonary conus and branches of the

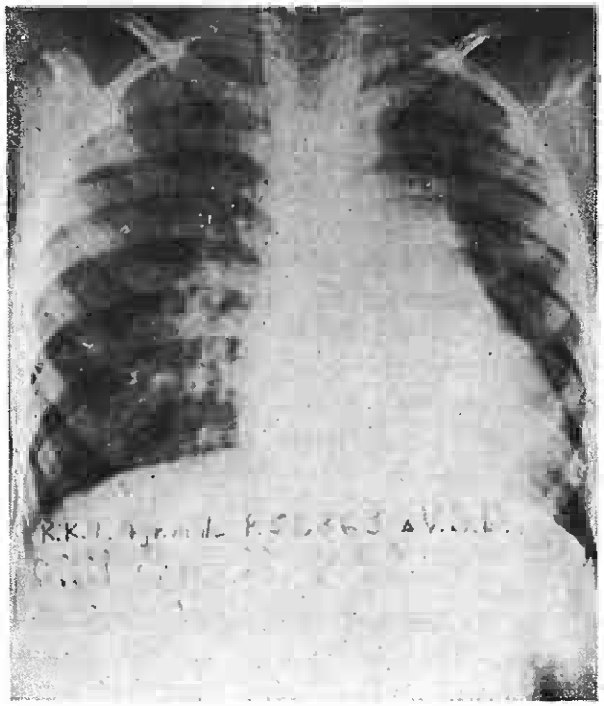

Fig. 9. This chest X-ray of Case 5 was taken at the age of 4 years. The heart is enlarged with a cardio-thoracic ratio of 0.60, a prominent pulmonary conus and marked pulmonary plethora.

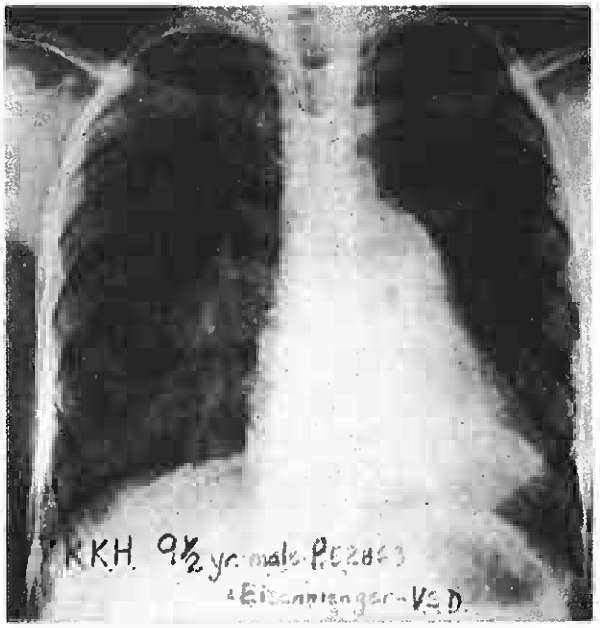

Fig. 11. This chest X-ray of Case 5 taken at 9½ years of age shows only a slightly enlarged heart (cardio-thoracic ratio of 0.53), a prominent pulmonary conus and right pulmonary artery and ischaemic lung fields.

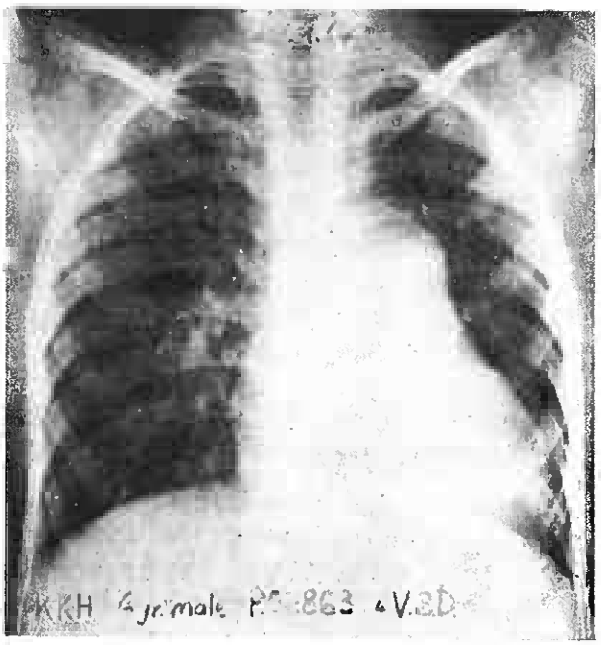

Fig. 10. This chest X-ray of Case 5 was taken at 6 years of age. The heart size is slightly less than that in Fig. 7 with a cardio-thoracic ratio of 0.57 and the lung fields show a reduction in pulmonary plethora.

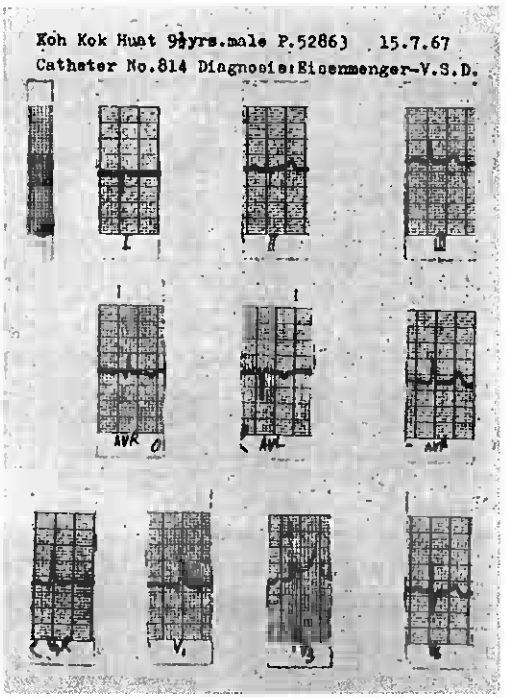

Fig. 12. The electrocardiogram of Case 5 shows a mean QRS axis of +135° and isolated right ventricular hypertrophy.

right pulmonary artery, and an ischaemic lung field (Fig. 11).

Electrocardiogram showed a mean QRS axis of +135° and isolated right ventricular overload pattern (Fig. 12).

The following is a comparison of the results of the two cardiac catheterisations done at 6 years and 9½ years of age (Table V).

Comments: Serial chest X-rays showed gradual decrease in heart size from a cardio-thoracic ratio of 0.60 to one of 0.53 and a diminution in the left-to-right shunt as shown in Figs. 10, 11 and 12. Serial right heart studies demonstrated progressive increase in pulmonary vascular resistance from 8.9 units to 25 units changing the left-to-right shunt to an Eisenmenger's state over a period of 36 months. This confirms the view that pulmonary vascular disease is a gradually acquired condition, a sequel to a ventricular septal shunt with hyperkinetic pulmonary hypertension.

Case No. 6. V.S.Y. 7½ years. Chinese female. P. No. 95500

She was the eldest of four siblings. Birth history was normal and her birth weight was 6 lbs. She was first seen as an outpatient at the age of 3 months because of a cardiac murmur. She had frequent chest infections during infancy but improved after the first two years of life. She remained asymptomatic, and was admitted for investigation at the age of 6 years.

Her effort tolerance was good. There was no history of cyanosis. On examination, she was well. There was no cyanosis or clubbing, BP = 90/60 mm. Hg. Her pulse was regular and of small volume. There was a precordial bulge with right ventricular hypertrophy. There was no thrill but a diastolic shock was felt at the pulmonary area. On auscultation, an ejection systolic murmur Grade 2/6 and a loud pulmonary closure sound followed by an early diastolic murmur were heard at the pulmonary area.

Chest X-ray showed a slightly enlarged heart with a cardio-thoracic ratio of 0.54, a prominent pulmonary conus and moderate pulmonary plethora (Fig. 13).

Cardiac catheterisation done at 6 years of age, confirmed V.S.D. with severe pulmonary hypertension with Qp/Qs = 3.0 and a pulmonary vascular resistance = 4.7 units. Closure of the defect was recommended. However, she had to wait 1 year before she was sent to Perth for surgery.

At 7 years of age, a repeat cardiac catheterisation followed by selective angiocardiography was done at Perth (Figs. 14 and 15).

She was found to be inoperable because of severe pulmonary vascular disease and a reversal of shunt. When she returned to Singapore, she was re-examined and found to be quite well. She had slight cyanosis and clubbing, BP = 110/90. Her pulse was regular and of poor volume. There was a prominent 'a' wave at the jugular venous pulsation. The heart was not enlarged clinically. There was no thrill but the pulmonary second sound was palpable. There was a faint systolic murmur with a loud second sound over the pulmonary area. No early diastolic murmur was heard (Hb. = 107%).

Chest X-ray showed a decrease of pulmonary plethora (Fig. 13). Electrocardiogram revealed a mean QRS axis of +150° and severe isolated right ventricular overloud pattern as shown in Fig. 16.

Findings at the two cardiac catheterisation are as follows (Table VI).

Comment: This patient had a large ventricular septal defect with severe pulmonary hypertension. The cardiologist at Perth remarked that we were witnessing a change here from a V.S.D. which was still shunting left-to-right when first investigated in Singapore to an Eisenmenger's situation over a period of 12 months. She was presented to Mr. W. P. Cleland, the Cardiac Surgeon of Hammersmith Hospital, London, when he happened to be in Perth on a short visit and he recommended that surgery should not be done. This patient confirms the view that pulmonary vascular disease is a gradually acquired condition secondary to a large pulmonary blood flow.

Case No. 7. C.B.C. 10 years. Chinese male. P. No. 9292

He was second of five siblings, born of a normal pregnancy and his birth weight was 6 lb. 12 oz. He was first referred at the age of 1½ months because of persistant chest infections and a cardiac murmur was discovered incidentally. He was admitted once at 6 months of age with chest infection and cardiac failure. He had repeated chest infections at monthly intervals but improved after the age of 1 year.

He remained well until the age of 8 years when he complained of giddiness—there no associated syncope.

TABLE V

Catheter No. 141 (1-7-64)

Pressure mm. Hg.

Pulmonary wedged	3 mm. Hg.
PA	83/52 (50) mm. Hg.
RV	90/0-6 mm. Hg.
RA mean	6 mm. Hg.
BP	80/65 (70) mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA	80%	16.0 Vol.%
RV	87%	16.0 Vol.%
RA	80%	15.5 Vol.%
SVC	81%	15.5 Vol.%
FA	98%	19.0 Vol.%
Capacity		19.5 Vol.%

	Systemic	Pulmonary
Cardiac Output	3.3 L/min.	3.8 L/min.
Cardiac Index	5.4 L/min./m.^{2}	6.3 L/min./m.^{2}
Qp/Qs	1.2	

Pulmonary vascular resistance = **8.9 units**

Systemic vascular resistance = 11.8 units

L-R shunt 0.9 L/min./m.^{2}

R-L shunt — nil

(Qp/Qs = Pulmonary to Systemic flow ratio)

Catheter No. 814 (13-7-67)

Pressure mm. Hg.

Pulmonary wedged	7 mm. Hg.
PA	109/61 (77) mm. Hg.
RV	109/0-4 mm. Hg.
RA mean	3 mm. Hg.
BA	90/70 (77) mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA	73%	13.5 Vol.%
RV	72%	13.5 Vol.%
RA	68%	13.0 Vol.%
SVC	66%	13.0 Vol.%
BA	92%	18.0 Vol.%
Capacity	100%	19.5 Vol.%

	Systemic	Pulmonary
Cardiac Output	2.4 L/min.	2.0 L/min.
Cardiac Index	3.4 L/min./m.^{2}	2.8 L/min./m.^{2}
Qp/Qs		0.8

25 units

10 units

L-R shunt 0.2 L/min./m.^{2}

R-L shunt 0.8 L/min./m.^{2}

TABLE VI

Catheter No. 574 (20-4-66) 6 years old

Pressure mm. Hg.

Pulmonary wedged mean	7 mm. Hg.
PA	81/40 (56) mm. Hg.
RV	93/0-3 mm. Hg.
RA mean	2 mm. Hg.
Aorta	87/58 (69) mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA	87%	15.5 Vol.%
RV	84%	15.5 Vol.%
RA	73%	12.5 Vol.%
SVC	69%	12.0 Vol.%
Aorta	97%	17.0 Vol.%
Capacity		17.0 Vol.%

	Systemic	Pulmonary
Cardiac Output	2.3 L/min.	6.8 L/min.
Cardiac Index	3.5 L/min./m.^{2}	10.5 L/min./m.^{2}

Pulmonary vascular resistance **4.7 units**

Systemic vascular resistance 19.2 units

Catheterisation at Perth 7 years old

Pressure mm. Hg.

PA	90/50 (63) mm. Hg.
RV	85/0-10 mm. Hg.
RA	0 mm. Hg.
Aorta	75/50 (58) mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA	75%	15.0 Vol.%
RV	74%	15.0 Vol.%
RA	62%	12.5 Vol.%
SVC	65%	13.0 Vol.%
Aorta	89%	18.0 Vol.%
Capacity		20.0 Vol.%

	Systemic	Pulmonary
Cardiac Output	2.2 L/min.	2.5 L/min.
Cardiac Index	3.4 L/min./m.^{2}	3.8 L/min./m.^{2}

R-L shunt = 1.27 L/min./m.^{2}

Pulmonary vascular resistance = **14.7 units**

Systemic vascular resistance = 17.1 units

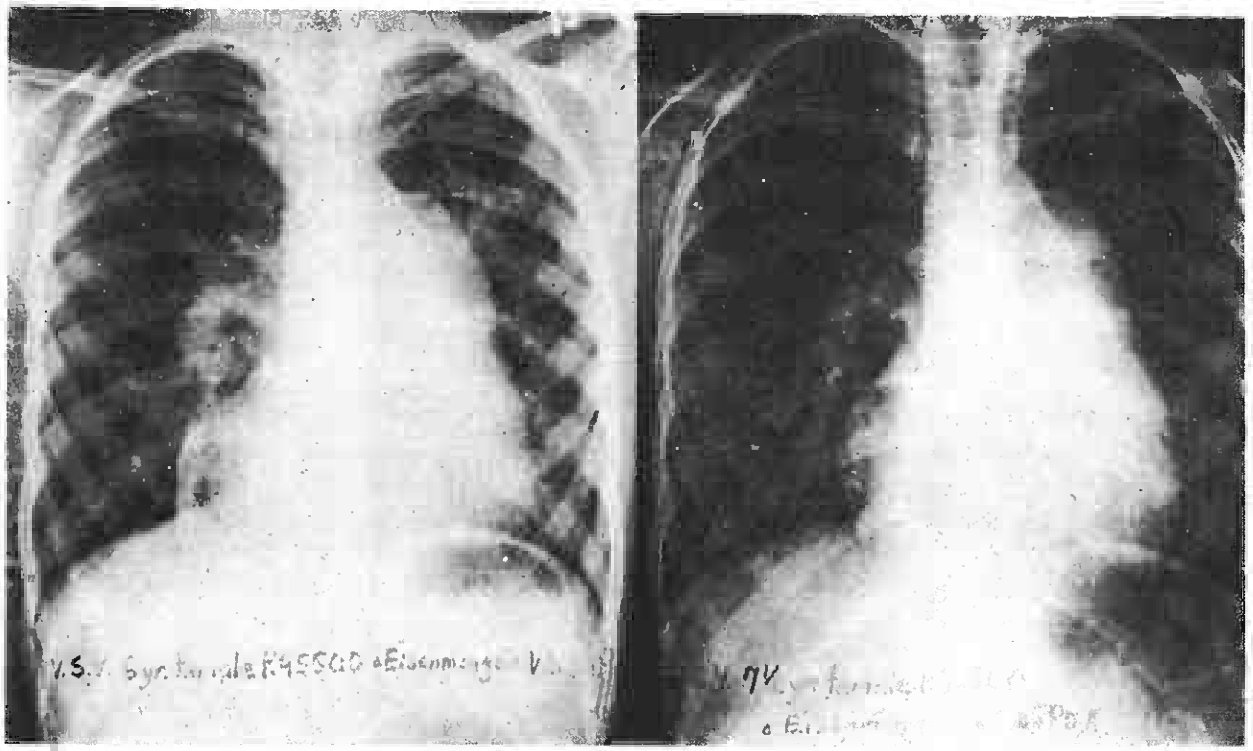

Fig. 13. The chest X-ray of Case 6 on the left done at 6 years of age shows moderate pulmonary plethora. The chest X-ray on the right done 1½ years later shows ischaemic lung fields.

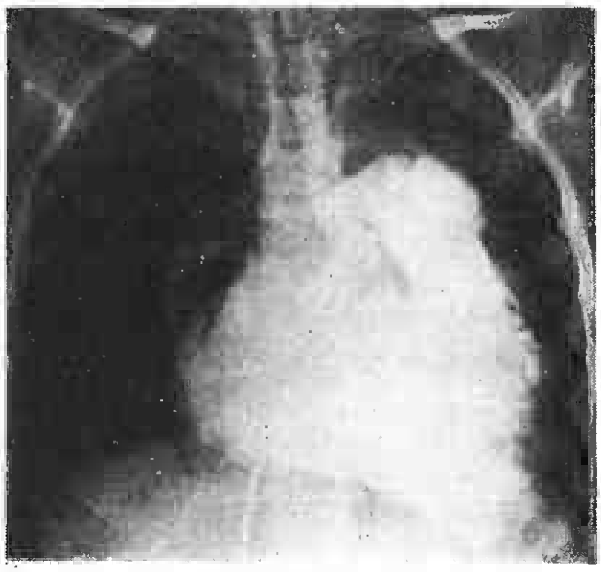

Fig. 14. Right ventriculogram (A-P view) shows opacification of a large pulmonary artery and a small aorta simultaneously.

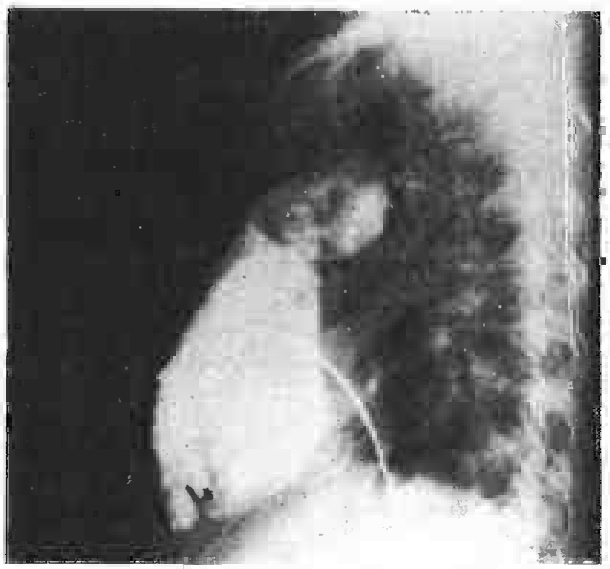

Fig. 15. Right ventriculogram (lateral view) shows a right-to-left shunt across the ventricular septal defect opacifying the left ventricle and aorta.

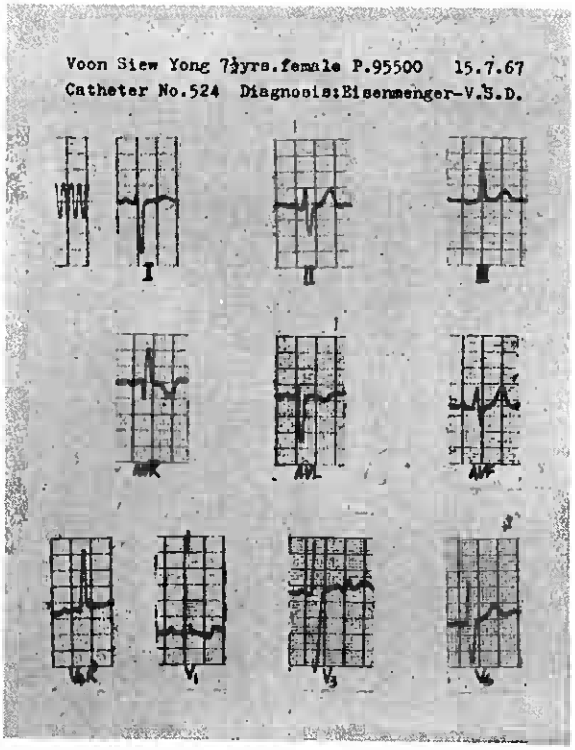

Fig. 16. The electrocardiogram of Case 6 shows a mean QRS axis of +150° and pure right ventricular hypertrophy.

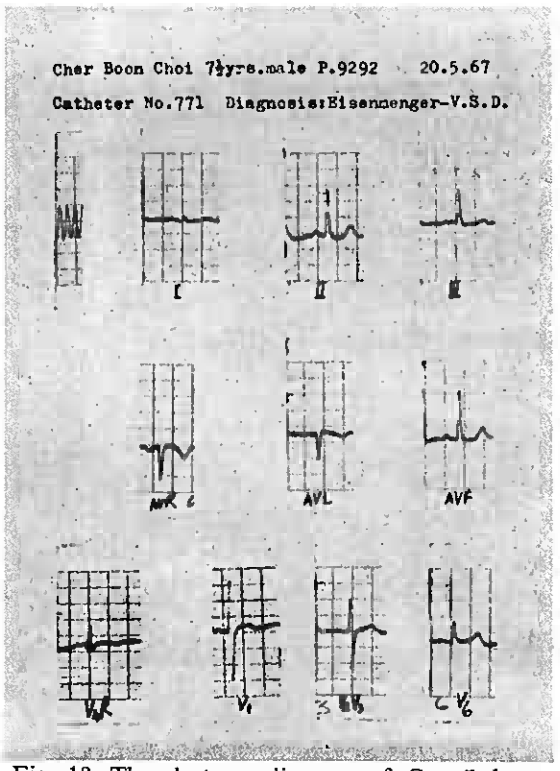

Fig. 18. The electrocardiogram of Case 7 shows no abnormality.

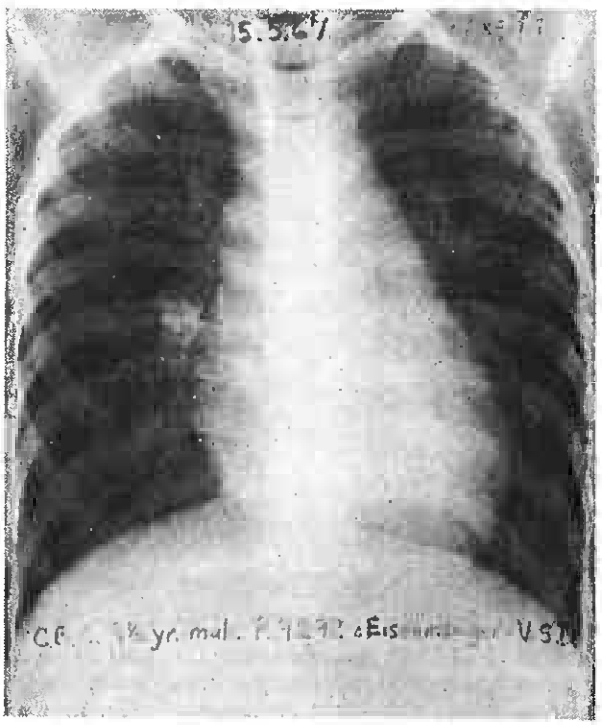

Fig. 17. The chest X-ray of Case 7 shows a slightly enlarged heart, a prominent pulmonary artery and ischaemic lung fields.

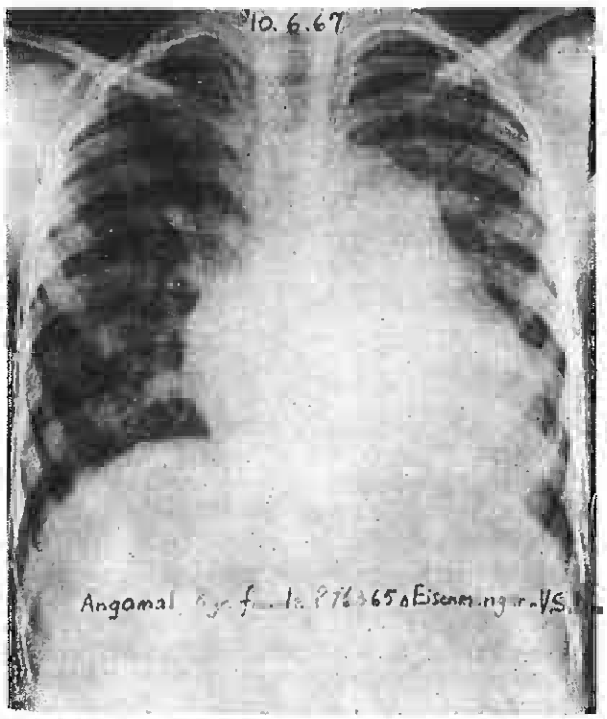

Fig. 19. The chest X-ray of Case 8 shows marked cardiomegaly, a prominent pulmonary conus and pulmonary plethora.

Cardiac catheterisation was done on 22.12.65 and he was diagnosed as a case of ventricular septal defect with severe pulmonary hypertension. He remained asymptomatic until he was 9 years old when he developed exertional dyspnoea and became cyanosed after exercise.

On examination, he had cyanosis and clubbing, BP = 95/80 mm. Hg. His pulse was regular but of small volume. There was a prominent 'a' wave in the jugular venous pulse. He had a precordial bulge and right ventricular hypertrophy. No thrill was present but a pulmonary diastolic shock was felt. There was a faint systolic murmur Grade 1/6 with an ejection click followed by a closely split and loud pulmonary second sound. No diastolic murmur, was heard, Hb. = 13.6 gm.%. His serial chest X-rays showed gradual decrease in heart size as well as in pulmonary plethora. The latest chest X-ray showed a slightly enlarged heart with a cardio-thoracic ratio of 0.55, a prominent pulmonary artery and branches, and oligaemic lung fields (Fig. 17).

Electrocardiogram surprisingly showed no right ventricular hypertrophy (Fig. 18).

However, a normal electrocardiogram may sometimes be recorded in the presence of combined ventricular hypertrophy. The balance of forces may not be sufficiently altered when both ventricles are symmetrically enlarged or when left ventricular hypertrophy counterbalances the right ventricular preponderance due to pulmonary hypertension.

A repeat cardiac catheterisation was done. Results of the two catheterisations done at 8 years and 10 years of age are shown in Table VII.

Comment: Although no cardiac catheterisation data were available during early childhood, there was clinical evidence of a large ventricular septal defect with a big shunt which gradually diminished over a period of 10 years due to acquired pulmonary vascular disease. The continued changed between 8 and 10 years of age were shown by serial catheterisation.

TABLE VII

Catheter No. 446 (22-12-65)

Pressure mm. Hg.

PA wedged mean	8	mm. Hg.
PA	99/57 (70)	mm. Hg.
RV	99/5	mm. Hg.
RA	mean 5	mm. Hg.
BA	105/75 (85)	mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA	90%	14.5 Vol.%
RV	93%	15.0 Vol.%
RA	79%	14.0 Vol.%
SVC	82%	13.5 Vol.%
IVC	78%	14.0 Vol.%
BA	98%	18.0 Vol.%
Capacity		18.0 Vol.%

BSA = 0.77 m.^{2} Oxygen consumption = 142 ml./min.

	Systemic	Pulmonary
Cardiac Output	3.6 L/min.	4.1 L/min.
Cardiac Index	4.6 L/min./m.^{2}	5.3 L/min./m.^{2}
Qp/Qs	1.1	

Pulmonary vascular resistance 13.2 units
Systemic vascular resistance 18.4 units

Catheter No. 771 (19-5-67)

Pressure mm. Hg.

PA wedged mean	8	mm. Hg.
PA	97/57 (70)	mm. Hg.
RV	97/0-4	mm. Hg.
RA	mean 5	mm. Hg.
BA	95/80 (85)	mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA	75%	12.0 Vol.%
RV	78%	13.0 Vol.%
RA	69%	11.5 Vol.%
SVC	68%	11.0 Vol.%
BA (exercise)	90%	15.5 Vol.%
BA (rest)	94%	16.0 Vol.%
Capacity		17.0 Vol.%

BSA = 0.85 m.^{2} Oxygen consumption = 175 ml./min.

	Systemic	Pulmonary
Cardiac Output	3.9 L/min.	3.5 L/min.
Cardiac Index	4.6 L/min./m.^{2}	4.1 L/min./m.^{2}
L-R shunt		0.3 L/min.
R-L shunt		0.7 L/min.
Net R-L shunt		0.4 L/min.

Pulmonary vascular resistance 15.1 units
Systemic vascular resistance 17.4 units

Diagnosis: Eisenmenger—V.S.D.

Case No. 8. Angamah. 8 years. Indian female. P. No. 76365

Birth history was not available. She was first referred from Johore Bahru General Hospital three years ago at the age of 5 years as a case of ventricular septal defect. Investigations including a cardiac catheterisation were done. Unfortunately, cardiac catheterisation was done under general anaesthesia and no shunt was detected. She was readmitted at the age of 8 years for a repeat study. Apparently she had had recurrent chest infections during the first two years of life and was looked after by her general practitioner. After then, she remained fairly well but complained of dyspnoea with cyanosis after moderate exercise.

On examination, she was small for her age weighing only 35½ lbs. at 8 years of age (33 lbs. 12 oz. at 5 years). She had slight cyanosis but no clubbing, BP = 110/70 mm. Hg. Her pulse was regular and of good volume. She had a prominent 'a' wave in the jugular venous pulse. There was a marked precordial bulge with clinical evidence of biventricular hypertrophy. There was a systolic thrill at the 5th left intercostal space at the sternal edge and a pulmonary diastolic shock has felt. On auscultation, there was an ejection systolic murmur Grade 2/6 with an ejection click and a closely split loud second sound over the pulmonary area. In addition, there was a pan-systolic murmur Grade 3/6 with a mid-diastolic rumble at the apex (Hb. = 12.6 gm.%, PCV = 40%).

Chest X-ray showed an enlarged heart with a cardio-thoracic ratio of 0.63, a small aortic knuckle, a prominent pulmonary conus and branches and marked pulmonary plethora (Fig. 19).

Her electrocardiogram showed a mean QRS axis of +90° and biventricular hypertrophy (Fig. 20).

The repeat cardiac catheterisation revealed a bidirectional shunt at the ventricular level. Data from the two studies are as follows (Table VIII).

Comment: After an interval of 3 years, the change of the haemodynamics, particularly after exercise is dramatic. This patient demonstrates the progressive nature of pulmonary vascular disease as a result of a large left-to-right shunt over a long period of time.

Case No. 9. A.b.A. 5½ years. Malay male. P. No. 108623

He was the sixth of seven siblings and his birth history was normal. His birth weight was 6 lb.

Apparently he had frequent chest infections during infancy and these became less frequent as he grew up. From the age of 1 year to 5 years, he was practically free from symptoms. He was referred to the Paediatric Department at 5½ years of age because of the onset of cyanosis, which increased after moderate exertion. On examination, he was of average build for his age. He had cyanosis and clubbing, BP = 75/55. His pulse was regular and of small volume. The 'a' wave of the jugular venous pulsation was prominent. He had a marked precordial bulge and right ventricular hypertrophy. No thrill was felt but the pulmonary closure was easily pulpable. There was a faint systolic murmur Grade 1/6 with an ejection click, and a loud pulmonary closure sound followed by an early diastolic murmur at the 2nd and 3rd left intercostal spaces at the sternal edge (Hb. = 13.9 gm.%).

His chest X-ray showed a slightly enlarged heart with a cardio-thoracic ratio of 0.53, a small aortic knuckle, a very prominent pulmonary artery and ischaemic peripheral lung field giving a pruned appearance of the pulmonary tree (Fig. 21).

His electrocardiogram showed a mean QRS axis of +150° and severe isolated right ventricular hypertrophy (Fig. 22).

Results of the cardiac catheterisation are as follows (Table IX).

Comments: Right heart study demonstrated a two-way shunt at the ventricular level with high pulmonary vascular resistance. From the history, the onset of cyanosis was very late and therefore, the reversal of the shunt probably occurred after the pulmonary vascular disease had progressed for some years.

Diagnosis: Eisenmenger—V.S.D.

Serial catheterisation has been done in four patients (Cases 5, 6, 7 and 8) who apparently had acquired severe pulmonary vascular disease as a sequel to their large ventricular septal defect with hyperkinetic pulmonary hypertension. The onset of the state of Eisenmenger—V.S.D. in the last five cases (Cases 5, 6, 7, 8 and 9) seems to occur only after the age of 5 years.

TABLE VIII

Catheter No. 179 (29-7-64)

Pressure mm. Hg.

PA wedged mean	18	mm. Hg.
PA	90/57 (70)	mm. Hg.
RV	90/0-5	mm. Hg.
RA	mean 5	mm. Hg.
FA	105/75 (85)	mm. Hg.
BP	95/40	mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA	86%	16.0 Vol.%
RV	86%	15.5 Vol.%
RA	82%	16.0 Vol.%
SVC	83%	16.0 Vol.%
FA	98%	18.0 Vol.%
Capacity		18.5 Vol.%

BSA = 0.68 m.^{2} Oxygen consumption = 128 c.c./min.

	Systemic	Pulmonary
Cardiac Output	6.4 L/min.	6.4 L/min.
Cardiac Index	9.4 L/min./m.^{2}	9.4 L/min./m.^{2}

No shunt

Pulmonary vascular resistance = 5.5 units
Systemic vascular resistance = 8.5 units

Catheter No. 794 (16-6-67)

Pressure mm. Hg.

PA wedged mean	18	mm. Hg.
PA	93/47 (61)	mm. Hg.
RV	107/0-4	mm. Hg.
RA	mean 4	mm. Hg.
BA	105/70 (82)	mm. Hg.
PA (exercise)	110/80 (90)	mm. Hg.

Oxygen	Saturation %	Content Vol.%
PA wedged	100%	17.0 Vol.%
PA	81%	13.5 Vol.%
RV	82%	13.5 Vol.%
RA	73%	11.5 Vol.%
SVC	73%	11.5 Vol.%
IVC	58%	10.0 Vol.%
BA (exercise)	83%	14.0 Vol.%
BA (rest)	94%	16.0 Vol.%
Capacity	100%	17.0 Vol.%

BSA = 0.75 m.^{2} Oxygen consumption = 142 ml./min.

At rest

	Systemic	Pulmonary
Cardiac Output	3.2 L/min.	4.1 L/min.
Cardiac Index	4.2 L/min./m.^{2}	5.4 L/min./m.^{2}
L-R shunt	1.5 L/min.	
R-L shunt	0.6 L/min.	
Net L-R shunt	0.9 L/min.	

Pulmonary vascular resistance = 8.1 units
Systemic vascular resistance = 18.0 units

After exercise

	Systemic	Pulmonary
Cardiac Output	5.7 L/min.	4.1 L/min.
Cardiac Index	7.6 L/min./m.^{2}	5.4 L/min./m.^{2}

L-R shunt 1.5 L/min.
R-L shunt 1.4 L/min.
Pulmonary vascular resistance = 13.3 units
Systemic vascular resistance = 10.3 units

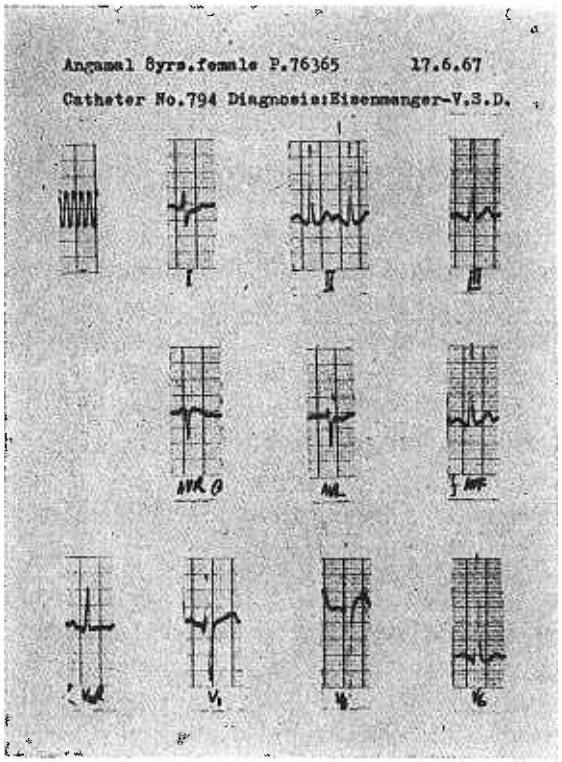

Fig. 20. The electrocardiogram of Case 8 shows a mean QRS axis of +90° and biventricular hypertrophy.

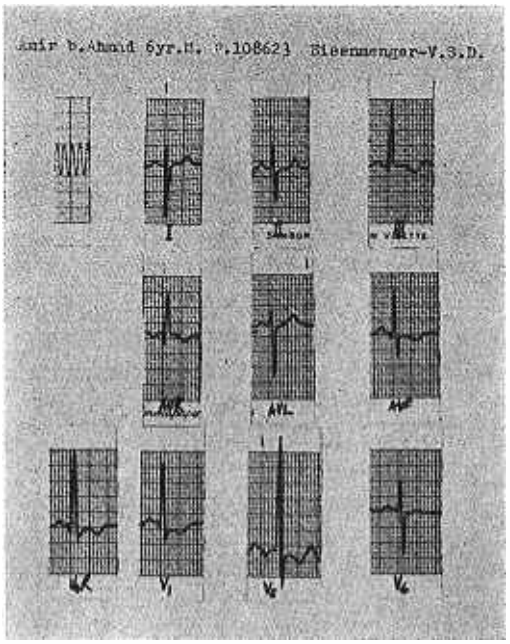

Fig. 22. The electrocardiogram of Case 9 shows a mean QRS axis of +150° and severe right ventricular hypertrophy.

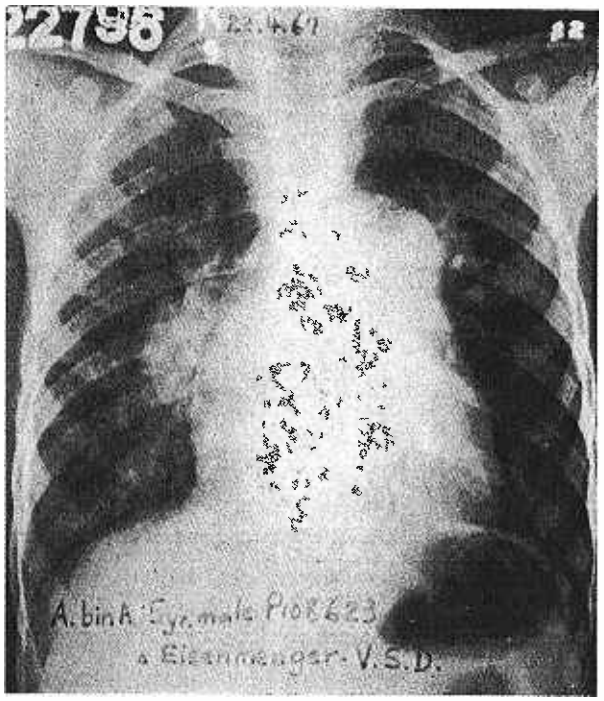

Fig. 21. The chest X-ray of Case 9 shows a slightly enlarged heart, a very prominent conus, a marked right pulmonary artery and ischaemic lung fields.

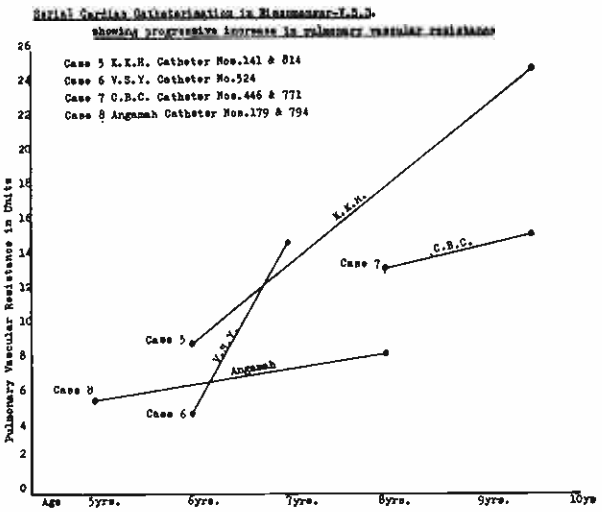

Fig. 23. The graph shows the increase in pulmonary vascular resistance in four patients with Eisenmenger —V.S.D. after the age of 5 years.

TABLE IX

Haemodynamic Data **Catheter No. 758 (2-5-67)**

Pressure mm. Hg.

PA wedged mean	5	mm. Hg.
PA	78/50 (60)	mm. Hg.
RV	78/0-4	mm. Hg.
RA mean	3	mm. Hg.
BA	82/55 (65)	mm. Hg.

BSA = 0.68 m.^{2}

Oxygen	Saturation %	Content Vol.%
PA	87%	14.0 Vol.%
RV	85%	14.0 Vol.%
RA	67%	11.0 Vol.%
BA	92%	15.0 Vol.%
Capacity		16.5 Vol.%

Oxygen consumption = 153 c.c./min.

	Systemic	Pulmonary	
Cardiac Output	3.8 L/min.	6.1 L/min.	L-R shunt 3.4 L/min.
Cardiac Index	5.6 L/min./m.^{2}	9.0 L/min./m.^{2}	R-L shunt 1.1 L/min.

Pulmonary vascular resistance = 6.1 units
Systemic vascular resistance = 11.1 units

The rise in pulmonary vascular resistance over varying periods of time in these four patients is as shown in Fig. 23.

DISCUSSION

Eisenmenger's syndrome may be defined as "pulmonary hypertension due to high pulmonary vascular resistance with reversed or bidirectional shunt at the aorta-pulmonary, ventricular or atrial level" (Wood, 1958).[11]

The present study is confined to 9 cases of Eisenmenger's syndrome due to ventricular septal defect (Loh).[7]

The aetiology of the high pulmonary vascular resistance is still not settled. Civin and Edwards (1950)[3] suggested the persistance of the foetal type of pulmonary circulation as a cause. Evans (1951)[5] concluded that an independent coincidental congenital anomaly of the pulmonary vessels was responsible. Whitaker (1958)[10] and Brotmacher and Campbell (1958)[1] believed that the cause was degenerative or thrombo-obstructive pulmonary vascular disease, secondary to high flow or hyperkinetic pulmonary hypertension. Wood (1952, 1956, 1958)[11] suggested that reactive pulmonary vaseconstriction, initiated by hyperkinetic pulmonary circulation was responsible initially and that degenerative or thrombo-obstructive pulmonary vascular disease developed with advancing years.

There are, therefore, many conflicting hypotheses concerning the origin and maintenance of this pulmonary hypertension. The author believes that there are probably multiple factors involved. The present study supports the theories of both the congenitally determined high pulmonary vascular resistance and the acquired one secondary to hyperkinetic pulmonary circulation. Four of the nine cases studied developed the Eisenmenger's state in infancy or very early in life. In this group, the high pulmonary vascular resistance must have been present at birth or in very early life. The remaining five developed it much later. Four of the latter patients, whose ages ranged from 5-10 years, had serial cardiac catheterisations demonstrating the progressive increase in pulmonary vascular resistance over the varying periods of 12, 18, 35 and 42 months.

It is not possible to assess the incidence of Eisenmenger—V.S.D. here since the number studied is so few and many others remain uninvestigated.

Eisenmenger's syndrome itself accounted for 8% of Wood's series of the first 1,000 cases of congenital heart disease and more than half of these was due to ventricular septal defect. The sex incidence was equal in his studies and the male predominance (7 males and 2 females) in the present study is probably of no significance as the cases represent a highly selected group.

Ritter *et al* (1965)[8] reported on incidence of 8% in their analysis of 273 cases of ventricular septal defect but Walker *et al* (1965)[9] found only one patient who had progressed to Eisenmenger's syndrome among their study of 415 cases. The cases studied, which account for 7% of cases in this series, have such severe pulmonary vascular disease that surgery is contra-indicated.

The clinical features in Eisenmenger—V.S.D. are quite uniform in all cases. When the pressures in both ventricles are balanced, the

pulmonary blood flow is normal or reduced and the patients are relatively free from pulmonary congestion and subsequent infection. In fact, many of them especially those in the paediatric age group, are asymptomatic, and do not consult the physician until the right-to-left shunt becomes so severe that marked effort intolerance occurs. Many of them continue normal activity in spite of their effort dyspnoea until the onset of congestive cardiac failure which is usually terminal.

Angina, syncope and haemoptysis are said to be common complications but they are usually seen only in early adult life. Haemoptysis is not a complication of pulmonary hypertension nor of pulmonary plethora per se but is due to pulmonary infarction secondary to pulmonary artery thrombosis.

None of the patients in the present study had haemoptysis probably because they were too young. However, haemoptysis occurred in 33% of Wood's series and only in patients more than the age of 24 years. This accounts for most of the deaths in patients with Eisenmenger's Syndrome.

Cyanosis at rest and clubbing of fingers are mild in the present series of 9 cases although cyanosis becomes more severe after exercise. The pulse is of small or normal volume. The presence of a precordial bulge suggests a right ventricular hypertrophy of long standing. Other findings are those of severe pulmonary hypertension characterised by a left parasternal heave due to right ventricular hypertrophy, a pulmonary ejection click, a loud pulmonary closure sound, followed frequently by an early diastolic murmur (Graham-Steel murmur). A soft pulmonary systolic murmur Grade 2/6 or less is often present. The murmur due to the ventricular septal defect itself is absent. If a pan-systolic murmur is heard at the left parasternal edge, it is probably due to tricuspid incompetence secondary to severe right ventricular hypertension.

Chest X-ray usually shows a normal sized or slightly enlarged heart, a very prominent main pulmonary artery and branches, and an ischaemic peripheral lung field.

Electrocardiogram in the majority of cases shows isolated right ventricular overload pattern with a clockwise frontal loop. The long-term prognosis is poor in view of the irreversible nature of pulmonary vascular disease. It is even worse if surgical closure is attempted in this group of patients. Immediate operative mortality is extremely high and pulmonary vascular resistance continues to rise even after successful closure of the defect.

Conservative management is the only line of treatment. The average age of natural death in Wood's[11] series was 33 years for both aorto-pulmonary and ventricular septal defects and 36 years for atrial septal defects. The maximum age reached was 65 for both the ventricular and atrial septal defects and 58 for the patent ductus arteriosus. Cartmill *et al* (1966)[2] reported that survival of up to 10 to 20 years after diagnosis of Eisenmenger—V.S.D. was not uncommon.

SUMMARY

Findings in nine patients with Eisenmenger—V.S.D. are described. In four of them, cyanosis occurred very early in life and they probably represent the group of congenitally determined pulmonary vascular disease.

The remaining five developed acquired pulmonary vascular disease secondary to a large defect and pulmonary hypertension over a period of many years. Serial catheterisations demonstrated the increase in pulmonary vascular resistance in four of them over a varying period of 12 months to 42 months and the Eisenmenger —V.S.D. state occurred after five years of age (in the present series).

The clinical features in both groups are discussed and the haemodynamic results are reported.

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