Management of Cyanotic Infant and Child

By

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Cyanosis due to cardiac malformations is a result of venous and arterial blood admixture. The concentration of reduced hemoglobin in execss of 5 G% in the systemic blood becomes clinically evident as blueness of the mucous membranes of the tongue and lips[1] Cyanotic children are often symptomatic and have shortness of breath and squat on exertion. Physical changes such as clubbing, retardation of growth and bony changes such as pulmonary osteo-arthropathy result after prolonged cyanosis. At times infants 3-4 months of age with tetralogy of Fallot present with hypercyanotic spells during which the infant is extremely irritable with incessant crying. Dyspnea and deep cyanosis are present and may result in convulsion and loss of consciousness[2-3-4]. During the spell, due to severe infundibular stenosis, the systolic mur mur disappears or is markedly reduced. In the newborn infant cyanosis is acute and leads to metabolic acidosis.

There are two major causes of cyanosis, respiratory and cardiac. Respiratory disturbances which produce cyanosis are ventilation/perfusion (V/Q) abnormalities, hypoventilation and, uncommonly, pure diffusion abnormalities. Hypoxemia (i.e., reduced arterial Pa02 $<$80 mm Hg) from hypoventilation and ventilaton-perfusion disturbances occurs in association with hypercapnia, i.e., elevated arterial PaC02 ($>$ 45 mm Hg). Adminisiration of 100% oxygen produces significant increase in the arterial Pa02 and correction of hypoventilation results in relief of hypoxemia and cyanosis. However, if the pulmonary hypoxemia is due to intrapulmonary right-to-left shunting, then the hypoxemia cannot be significantly corrected by the administration of oxygen alone.

Congential cardiac malformations produce central cyanosis by one of four meahanisms (Table I, II). First mechanism is the shunting of blood from system venous to arterial circuit i.e. right-to-left shunt. This shunt can occur at intracardiac sites, such as ventricular or atrial; and extacardiac level such as ductus arteriosus. Concomitantly, however an obstruction at various levels in the right heart such as tricuspid (Fig. 1) or pulmonary valve (Fig. 2) and pulmunary vasular bed, must be present which would elevate the right atrial, ventricular or pulmonary artery pressure.

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Table I

Mechanisms of Cyanosis

(i) Cardiac	(R—L Shunt)
(ii) Pulmonary	V/Q inequality (R—L Shunt) Hypoventilation
(iii) Mixed	R—L Shunt V/Q inequality Hypoventilation

Abbreviations
R—L=Right-to-Left.
V/Q=Ventilation/perfusion inequality

Table II

Cyanotic Diseases with Mixed cyanosis (Respiratory+cardiac origin).

(i) Hypoplastic left Ventricle Syndrome

(ii) Persistent Foetal Circulation. (P.F.C.)

(iii) Primary lung disease.

- (*a*) Hyaline Membarane diseas
- (*b*) Meconium Aspiration
- (*c*) Pulmonary haemorrhage
- (*d*) Pneumonia
- (*e*) Broncho pulmonary dys-plasia.

(iv) Mechanical Interference with lung Function

- (*a*) Diaphragmatic Hernia
- (*b*) Pneumothorax
- (*c*) Lopar Emphysema
- (*d*) Choanal Atresia.

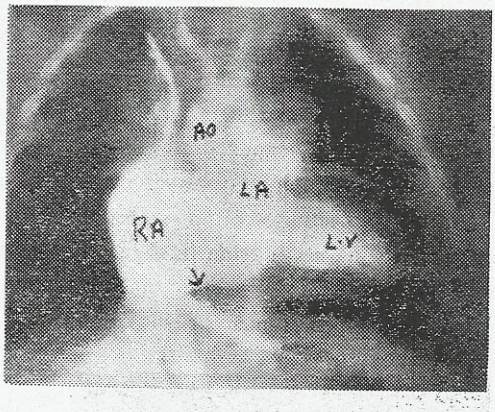

Fig. 1: Right atrial angiogram A-P view. Atresia of the Tricuspid valve is present (arrow). Right to left shunt at the atrial level opacifies left heart.

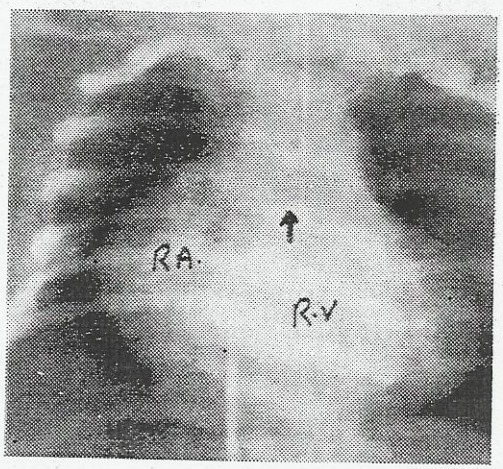

Fig. 2: Right ventricular (R.V.) angiogram, A-P view. Note complete atresia of the pulmonic valve (arrow). R.V. is mildly hypoplastic. R.A. right atrium.

The second mechanism is seen in patients with transposition of the great arteries where aorta arises from the right ventricle and all of the systemic venous blood is discharged into the systemic circuit and pulmonary artery arises from the left ventricle and the pulmonary venous blood recirculates within the pulmonary circuit[5]. (Fig. 3, 4). The third type of right-to-left shunt results from anomalous pulmonary venous connections i.e. pulmonary veins return to the

superior vena cava, right atrium or hepatic veins and the left atrium-to-left ventricle-to-aorta flow is an admixture of the pulmonary venous and systemic venous blood distal to the site of anomalous venous drainage. The fourth type of right-to-left shunt occurs in malformations where the ventricular septum is absent or when one single trunk arises from the heart with common supply to the systemic and pulmonary circulation as in truncus arteriosus communis.

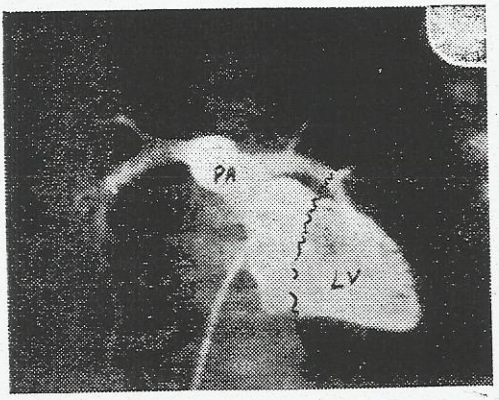

Fig. 3: Left ventricular (L.V.) angiograpm showing the origin of the pulmonary artery (PA) from the L.V. in a patient with d-transposition of the great arteries.

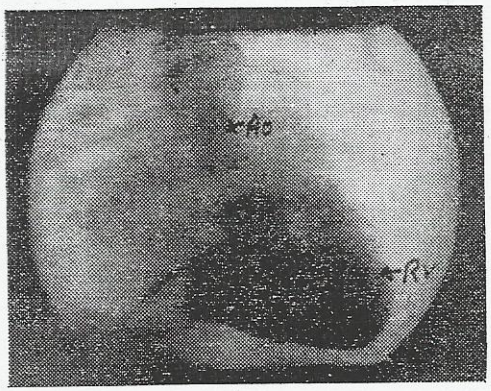

Fig. 4: R.V. angiogram of the same patient as in Fig. 3. Note the origin of aorta (AO) from the R.V.

The management of these abnormalities involves (a) precise anatomic diagnosis and (b) elucidation of physiologic disturbances and their metabolic consequences.

Diagnostic Workup

Clinical examination is extremely helpful in the initial assessment of the baby. The age at which an infant becomes cyanotic suggests certain types of malformation. Most babies with transposition of the great arteries and intact ventricular septum present within the first few hours to few days of age [5]. Infants with tetralogy of Fallot present within 6-12 months and it is the single most common cause of cyanosis after two years of life. The infant with pulmonary atresia with or without ventricular septal defect presents within the first few days of life. The hypoplastic left ventricle syndrome, comprising mitral and aortic atresia complex, presents in the first few days of life depending upon the size of the patent ductus arteriosus.

General Status: Respiratory distress (rate $\geq$ 40 per minute) in severely cyanotic newborn, suggests severe metabolic acidosis; and lack of spontaneous activity, suggests reduced cardiac output. Generally though the signs of shocked state suggest sepsis, intracranial pathology or shock due to blood loss. Respiratory distress and deep cyanosis suggests total anomalous pulmonary venous drainage or mitral atresia. Absence of cardiac murmurs suggests transposition of the great arteries or pulmonary atresia, or total anomalous pulmonary venous return with obstruction. In approximately half of the patients with pulmonary atresia continuous murmurs of patent ducturs arteriosus or systemic to plmonary collaterals can be detected [6]. The presence of ejec-

tion systolic murmur at the left upper sternal border suggests stenosis of the right ventricular outflow tract, or the pulmonary valve as in tetralogy of Fallot or critical pulmonary valve stenosis. A diastolic murmur which occurs slightly earlier in time than mid-diastole suggests increased tricuspid flow as would be expected in cases of total anomalous pulmonary venous return[7].

Normal second heart sound has two components. A2, due to aortic valve closure which precedes P2 which is due to pulmonary valve closure. Absence of P2 suggests pulmonary atresia or severe stenosis of the pulmonary valve as in tetralogy of Fallot. Closely split and accentuated P2 suggests pulmonary arterial hypertension and points to persistent fetal circulation in the newborn period. In this condition the pulmonary vascular resistence fails to decrease in a normal fashion after birth. Severe cyanosis develops within the first 3 days of age. The arterial blood gases obtained from the umblical artery shows lower PaO2. Compared to PaO2 in the blood obtained from the brachial artery. This differential Cyanosis is due to a right to left shunt at the ductal level. on chest X-ray cardiac size is often increased but the pulmonary vascularity is markedly reduced. These infants may show a considerable improvement in the arterial PaO2 following intra-venous administration of tolazoline in 1-2 mg/kg. stat doses over 10-20 min. period. If satisfactory increase in arterial PaO2 occurs maintenance dose of Tolazoline (Priscoline) can be employed (2-3 mg/Kg/Hour).

Second heart sound can be normally split in about one-third to one-half of the patients with transposition of the great arteries in the newborn period and single or narrowly split in the remaining[7].

The degree of cyanosis can also be helpful in the evaluation of the anatomic lesion. Patients with obstruction of the right heart, (such as pulmonary atresia or tricuspid atresia), total anomalous pulmonary venous return below the diaphragm, and transposition of the great arteries with intact ventricular septum show intense cyanosis. Patients with single ventricle, transposition of the great arteries with ventricular septal defect, supradiaphragmatic total anomalous pulmonary venous return, and truncus arteriosus without pulmonary stenosis show mild to moderat cyanosis.

Radiologic Assessment: On chest roentgenogram the right aortic arch can be diagnosed by noting its impression on the trachea. Right aortic arch is often found in tetralogy of Fallot and truncus arteriosus. On the chest roentgenogram the cyanotic lesions produce three main abnormalities of the pulomnary vasculature (1) decreased pulmonary vascularity; (2) increased pulmonary vascularity; and Table III (3) pulmonary edema.

Table III

Obstructive lesions of the right heart. decreased Pulmonary rascularity
1. Pulmonary atresia with Intact Ventricular septum
2. Pulmonary atresia with ventricular septal defect
3. Tetrology of Fallot.
4. Tricuspid atresia with pulmonary stenosis.
5. Ebstein's anomaly
Cyanotic Lesions with increased pulmonary vascularity
Transposition of the great arteries
Total anomalous pulmonary venous drainage.
Truncus Arteriosus communis.

Pulmonary atresia with or without ventricular septal defect, and tricuspid atresia without ventricular septal defect show decreased pulmonary blood flow and oligaemic lung fields. Transposition of the great vessels, total anomalous pulmonary venous returns, and truncus arteriosus communis show increased pulmonary vascularity. The heart size is normal to mildly increased (Cardiothoracic ratio ≥ 0.5) obstructve lesions of the left heart produces pattern of passive venous congestion. Moderate to severely increased heart size is present in those with increased pulmonary blood flow. Pulmonary edema characterizes infants with obstructive form of total anomalous pulmonary venous return or pulmonary vein stenosis. The shape of the heart at times is diagnostic however, in the newborn period the heart shape is often a typical. Egg-on-side shape with narrow vascular pedical and increased pulmonary vascularity suggests transposition of the great vessels; Concave pulmonary segment and uplifted boot shaped apex suggests tetralogy of Fallot. Snowman or figure-of-8 appearance is characteristic of total anomalous pulmonary venous return to the superior vena cava, but this appearance is usually seen in older infants.

Assessment of Metabolic Status:(8) Arterial blood gas analysis shows a reduced arterial PaO2 (<60 mm Hg) and failsto adequately increase (≥ 150 mm Hg) with adnministration of 100% oxygen. The PaCO2 (partial pressure of CO2) is reduced or within normal limits (35-45 mm Hg). The newborn achieves PaO2 of 45 mm Hg by one hour of age and 60 mm Hg by one day of age[8]. In patients in whom hypoxemia is due to respiratory causes, such as hypoventilation or ventilation perfusion abnormalities, the arterial PaCO2 is increased ($\geq$ 50 mm Hg) and during 100% oxygen inhalation for 7-10 minute period the PaO2 increases to $\geq$ 150 mm Hg.

In severely cyanotic infant the arterial pH may be reduced due to metabolic acidosis (<7.35). The clinical manifestations of severely acidotic infant (pH 7.0) are lethargy with rapid respirations without respiratory distress and a reduced arterial PaCO2.

Estimation of Blood glucose helps in the diagaosis of hypoglycemia and elevated potassium levels of adrenal insufficiency. Hematorcrit level of $\geq 65\%$ and hemoglobin of 22G suggest polycythemia of the newborn which can result in congestive heart failure. Renal status should be evaluated by urine output and blocd urea nitrogen and serum creatinine measurements.

Electrocardiogram: Certain electrocardiographic patterns are fairly characteristic of a particular anatomic lesion, left axis deviation with left ventricular hypertrophy suggests tricuspid atresia; Lack of right ventricular forces with normal QRS axis is usually seen in patient with pulmonary atresia with intact ventricular septum while right axis deviation ($\geq 90°$ in older children and $\geq 120°$ in infants) and right ventricular hypertrophy suggests pulmonary atresia with ventricular septal defect. The electrocardiogram in the newborn infant with transposition of the great arteries and intact ventricular septum is often within normal limits, however, in older infants right ventricular hypertrophy is dominant. Right ventricular hypertrophy is present in lesions with total anomalous pulmonary venous return and combined ventricular hypertrophy and left ventricular hypertrophy in truncus arterious communis.

Echocardiogram: Recently echocardiography has enormously helped in the anatomic evaluation of congential cardiac malformations [9-10]. Both the atrioventricular and semilunar valves and sizes of the right and left ventricles can be defined both on M-mode and two-dimensional sector scan echocardiography. On M-mode ecocardiography pulmonary atresia with intact septum shows a small hypoplastic right ventricle, but pulmonary valve echoes cannot be detected. However on two-dimensional sector scanning the atretic pulmonary value can be identified. The size of the main pulmonary artery and often the right pulmonary artery can be precisely defined. Tricuspid atresia shows as a linear echo on M-mode or the tricuspid valve cannot be detected, but sector scan defines the atretic valve and hypoplastic right ventricle. Transposition of the great vessels and associated lesions can be diagnosed with great precision by econocardiography [11-12-13]. On M-mode the aortic valve is located to the right and anteriorly; the pulmonary valve is posterior and connected to the left ventricle. The opening of the anterior semilunar (Aortic) is later than posterior semilunar valve (Pulmonic). In normally related great vessels the anterior semilunar valve (Pulmonic valve) is located anteriorly and to the left of the poster semilunar valve (Aortic valve) and opens earlier. Two dimensional echo cardiography has helped in the diagnosis of transposed great arteries as well as associated lesions such as Venlricular Septal Defect and Left Ventsicular Outflow tract stenosis[13].

Tetralogy of Fallot can be diagnosed on M-mode echo cardiography by aortic over riding above the ventricular septum and small left atrium. (Fig. 5). Pulmonary valve is often not visualized. Two-dimensional sector scan can however delineate the anatomic features, of tetrology of Fallot i.e., infundibular stensosis size of the

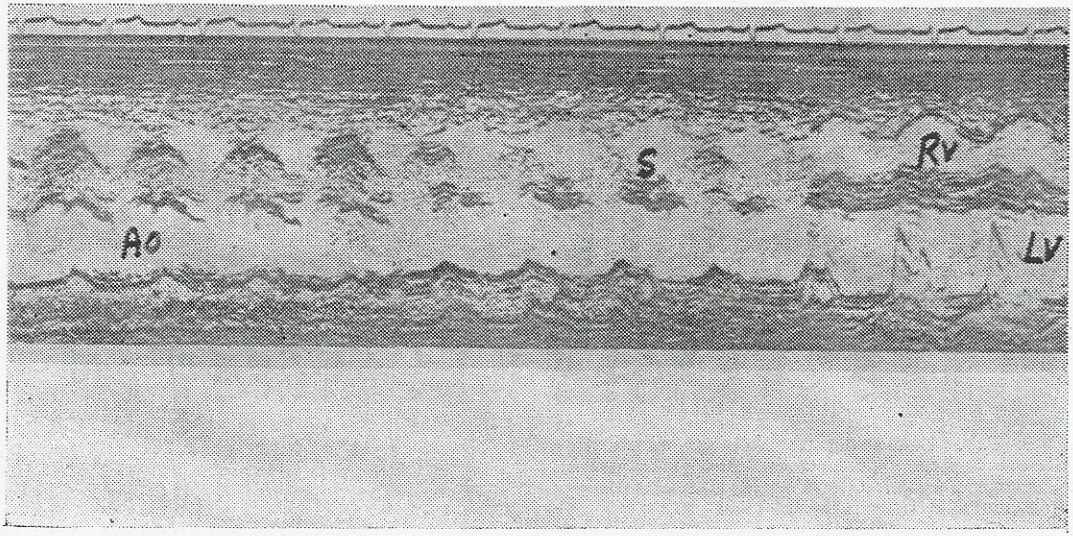

Fig. 5: M-mode echocardiogram in a patient with Tetralogy of Fallot. Note overriding of AO above the ventricular septum(s). R.V. is markedly hypertrophied.

pulmonary annulus and pulmonary arteries (Fig. 6). Total anomalous pulmonary venous drainage is a difficult lesion for anatomic diagnosis on echocardiography[14]. The characteristic features of M-mode are (1) anomalous echo with phasic motion behind the left atrium (2) large and hyper trophied right ventricle and paradoxic ventricular septal motion i.e., anterior motion during systole as opposed to normal posterior systolic motion. Two-dimensional sector scan shows common pulmonary venous chamber behind the left atrium and at times entry of the Common pulmonary venous chamber into the superior vena cava or coronary sinus.

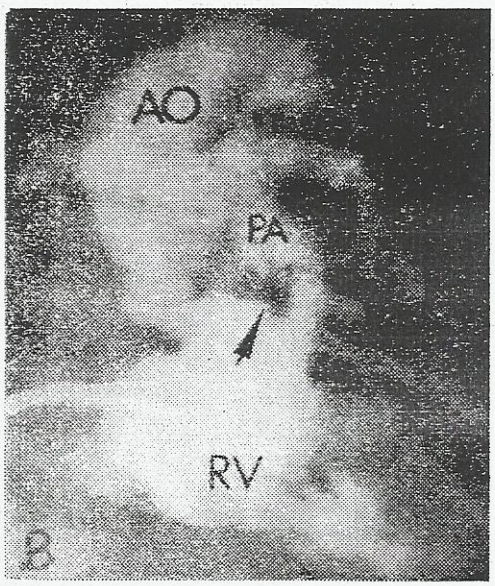

Fig. 6A: R.V. Cine angiogram showing infundibular stenosis due to hypertrophied crista (arrow) in a patient with Tetralogy of Fallot. Overriding AO is seen O pacifying from the right ventricle.

Single ventricle can be easily diagnosed by the absence of central septum and location of both atrioventricular valves in one ventricle.

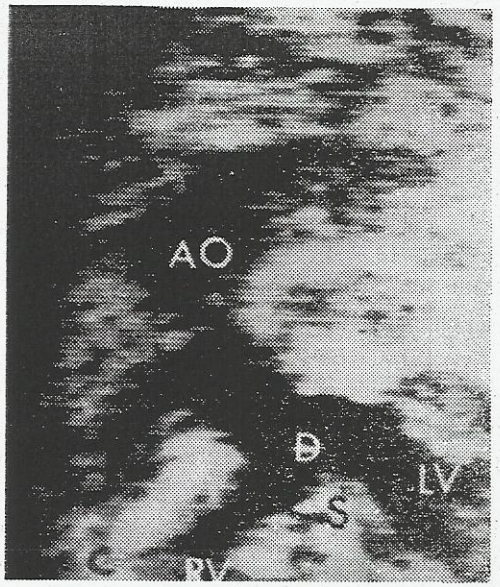

Fig. 6B: Long axis 2-D Echo subxiphoid view. Note overriding of AO above the V.S.D. (D) Ventricular septum (S) is clearly seen between the R.V. and L.V..

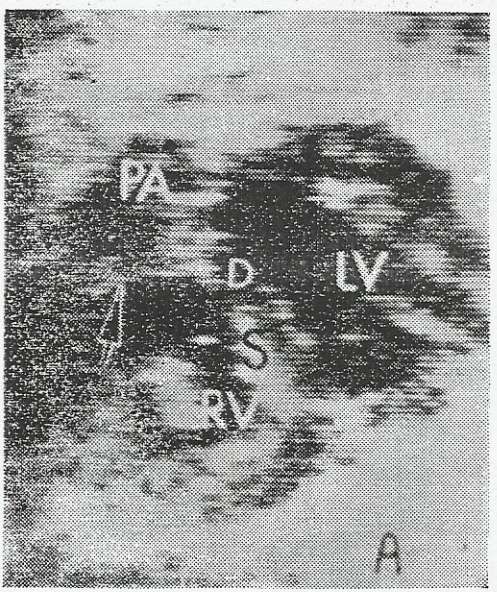

Fig. 6C: Sagittal plane 2-D Echo subxiphoid view. Subcristal V.S.D. (D) is seen above the ventricular septum (S). The outflow tract of the R.V. shows hypertrophied muscle, seen as band of trans-verse echoes (arrow) below the P.A. and represents hypertrophied crista.

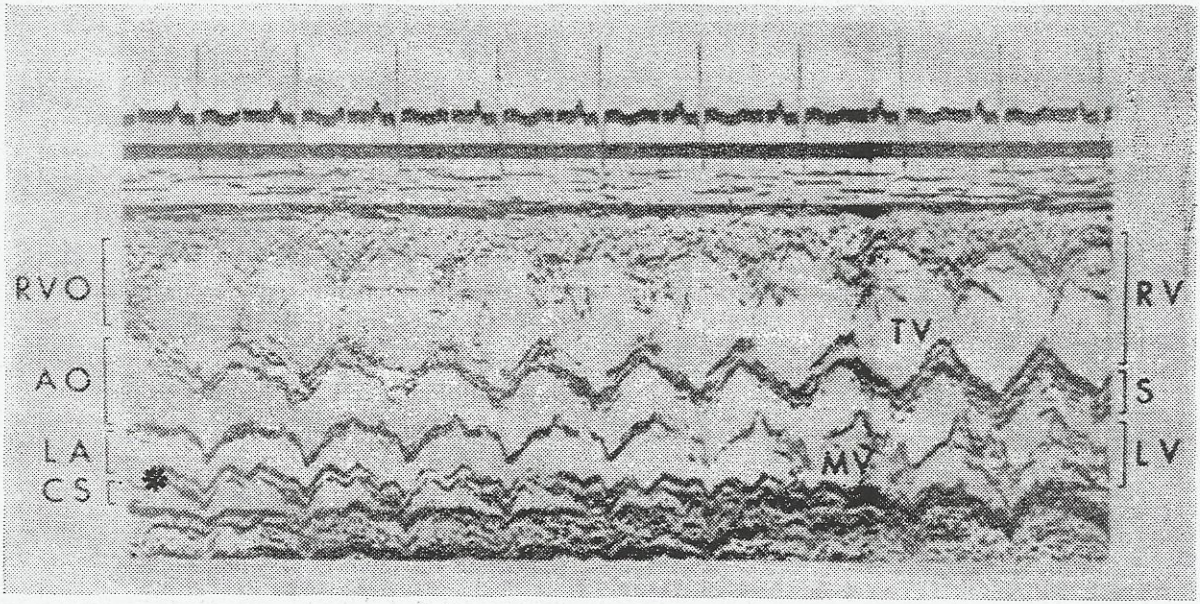

Fig. 7: M-mode echo L.V. sweep scan in a patient with total anomalous pulmonary venous drainage into the coronary sinus. Note amomalous echos (asterisk) which represent anterior coronary sinus wall and left atrial posterior wall complex. M-V—Mitral valve; R.V.O.—right ventricular outflow tract.

Treatment of Cyanotic Infant and Child

Cyanotic Infant: Assessment of ventilatory status is done by noting the respiratory rate and Signs of repiratory distress which is evidenced by intercostal or subcostal recession. Arterial blood gases help in determining the degree of respiratory insufficiency, ($PaCO_2 > 45$ mm Hg and PaO_2 of < 60 mm Hg indicate beginning of respiratory insufficiency). Ventilatory support with artificial ventilation should be considered when indicated.

Cardiovascular Status is determined by clinical examination listless, grey looking infant with reduced systemic pressure (< 60 mm Hg) should alert one to the need for circulatory support. In such an infant systemic venous pressure is evaluated by the catheter placed in the umbilical vein. Hypovolemic state responsible for the collapsed infant can be diagnosed by the low level of central venous pressure (< 3 cm water). Congestive cardiac failure produces elevation of the central venous pressure: (> 12 cm water).

In infants with severe congestive cardiac failure or prolonged severe cyanosis the circulatory support is provided by chemical inotropic myocardial stimulation. Such support is generally not required for most cyanotic babies seen early in the course of the disease.

Digitalization is often indicated for cyantoic infants with large hearts due to increased pulmonary blood flow. Most cyanotic infants with reduced pulmonary blood flow do not require digitalis. Digitalization in children under one year of age is achieved with a total 24 hour oral dose of 0.03 mg/pound, body wt; half of the digita-

lizing dose can be given as a stat dose, and the rest in 2 doses at 8 hour intervals. Intravenous dose is 2/3rd the oral dose. The maintenance dose of digoxin is 1/4 or 1/5th of the total digitalizing dose divided into two 12-hour interval doses. The dose of digoxin is withheld if infant's heart rate is <100/minute.

Ionotropic stimulation with Isoproterenol (Isuprel) is given by diluting 1 mg Isuprel in 100 cc which gives 10 mcg/ml concentration and infused at 6 ml/hour rate. Future doses can be adjusted to provide 0.1-0.5 mcg/kg/min depending upon infant's response.

Dopamine is a recent addition and can be given alone in 10-40 mcg/kg/min doses or combined with Isuprel.

Correction of Hyporemia and Metabolic Acidosis: All infants with severe cyanosis should be placed in 100% oxygen and further reduction of inspired oxygen can be adjusted by arterial PaO2 response. Metabolic acidosis should be initially corrected with 1.0 m Eq/Kg dose of NaHCO3 and further correction can be achieved by calculation of sodium bicarbonates required by the formula 0.3 x wt in "Kg" x Base "deficit" = MEq NHCO3. Recently in infants with reduced pulmonary blood flow, Prostaglandin E1 has been administered intravenously preferably in the aorta, or by a large vein[15-16]. The dose is 0.1 mcg/kg which can be reduced depending upon the infant's response. The effect is immediate. The side effects are common but transient. Most commonly encountered are pyrexia, cessation of respiration (apnea), convulsions and erythematous rashes. These are to some extent dose dependent and disappear with the reduction of the dosage .The Prostaglandins are a temporary measure but provide invaluable support for improving the baby prior to catheterization and surgery.

Management of Cyanotic Spells: Older infants (3-6 months of age) with tetralogy of Fallot are prone to hypercyanotic spells. These are rare after 5 years of age. The cause is infundibular spasm. The treatment involves placing the baby in knee-chest position, administration of oxygen and morphia 0.1-0.2 mg/kg subcutaneously. In a prolonged spell arterial gases should be obtained and metabolic acidosis if present be corrected with NaHCO3 .Most spells would settle with above regime, however, if it is prolonged, then general anesthesia can be given which often relieves the spell. Inderal (Propranolol) intravenously has been used with success in the dose of 0.01 mg/kg over a 2-5 minute period, followed by an oral daily dose of 1 mg/kg in divided doses[17]. Elevation of systemic pressure is beneficial and reduction of systemic pressure is deleterious to such infants.

Correction of Polycythemia in Chronic Cyanosis: In older infants with presistent cyanosis due to uncorrected cardiac malformation, very high hematocrit develops (>65%) with hemoglobin in excess of 22G%. The danger of high hematocrit is increased blood viscosity and the complication of cerebral thrombosis. The replacement of blood with plasma or sodium free albumin (Plasmaphoresis) should be done if hematocrit is above 65%18. The exchange should be done slowly in small measures so as to avoid systemic hypotension which may be dangerous. The effects on hemoglobin reduction is transient, however it produces symptomatic relief from headach, fatigue and irritability[18]. All efforts should be made to relieve the cysnosis by primary corection wherever feasible. Proper hydration should be undertaken in all cyanosed children,

particularly in hot climates; to prevent hyperviscosity and cerebrovascular accidents.

Brain abscess has a high association with cyanotic heart disease. Appropriate management with neurosurgical service is then indicated.

Surgical Management: Obstructive lesions such as tricuspid atresia without ventricular septal defect, pulmonary atresia with intact septum, require balloon atrial septostomy which should be undertaken during cardiac catherization [19-20]. Rashkind's balloon atrial Septostomy has made significant contribution to the management of infants with transpostion of the great arteries. The balloon catheter can be introduced into the femoral vein either by direct exposure or by percutaneous technique. The balloon cathater is then advanced into the left atrium across the atrial septum and inflated with. 1.5-2.0 cc radio opaque dye. It is then pulled ocross the atrial septum into the right atrium tearing a hole in the atrial septum. This atrial septal defect so created usually provides adequate interatrial mixing for 6-9 months.

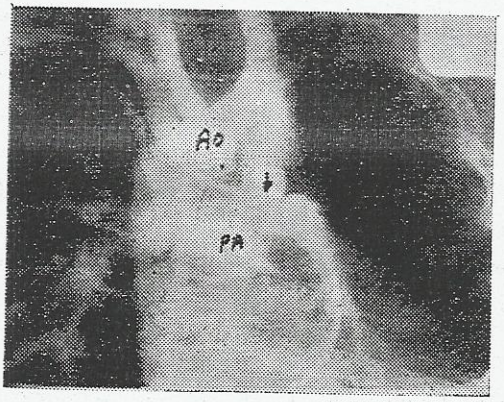

Fig. 8: Aortogram in A-P view. Arrow shows the position of left Blalock Taussig shunt.

Blalock-Taussig shunt, where one of the sub-clavian artery is connected to the pulmonary artery, usually on the side opposite to the aortic arch, has recently been reported to be technically feasible (Fig. 8) in the newborn infants. In the past, Waterston-Cooley shunt (Side-to-side anastomosis of right pulmonary artery and ascending aorta Fig. 9) has given a satisfactory palliation of these desperately sick infants with obstructive lesions of the right neart. Pulmonary valvotomy can be combined with shunt procedure in patients with pulmonary atresia and intact vencular septum[20].

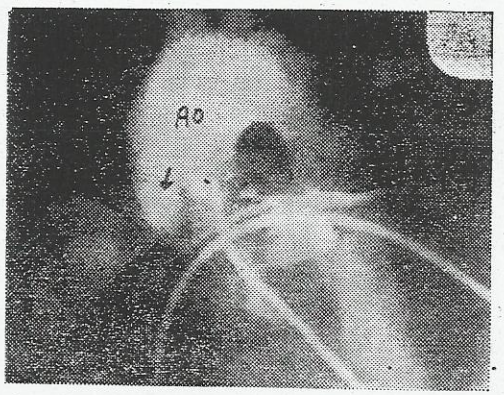

Fig. 9: Aortogram in A-P view. Arrow shows the position of Waterston Cooley shunt i.e. Ascending aorta to right pulmonary artery connection.

In patients with pulmonary atresia and ventricular septal defect, only shunt surgery is indicated without prior balloon atrial septostomy.

In older infants complete repair of tetraolgy of Fallot is now recommended after 6 months of age [21-22-23]. Transpostion of the great vessels with intact ventricular septum requires balloon atrial septosotomy which is done at the time of Cardiac catheterization, and Mustard operation, whereby pulmonary and systemic venous returns are directed to the right and left ventricles

respectively, can then be undertaken at 6 months-1 year of age [24]. In patients with critical pulmonary valve stenosis and adequate right ventricle, pulmonary valvotomy alone should be done[25-26].

The patients with increased pulmonary blood flow such as truncus arteriosus communis or single ventricle without pulmonary stenosis or transposition of the great vessels with ventricular septal defect, can be palliated by pulmonary artery banding. Recently there has been a trend toward complete correction of these defects during infancy [27]. During infancy Mustard operation and closure of ventricular septal defect for transposed great arteries can be undertaken in units equipped for handling these very small infants.

In older children with tricuspid atresia and single ventricle, right atrium to pulmonary artery connection by a valved conduit (Fontan procedure) has recently been introduced with satisfactory results during short postoperative followup [28-29]. Long-term results are not yet known.

In summary, the management of cyanosis in children requires a team effort on the part of pediatrician, pediatric cardiologist, pediatric cardiac surgeon, and anesthesiologist. With this combined approach great strides have recently been made in the care of very complicated cardiac abnormalities.

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