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# Pattern of symptomatic congenital heart disease among Oriental neonates—a decade's experience

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**Abstract**   Between 1981 and 1990, 765 symptomatic neonates with major congenital heart malformations were admitted into the Grantham Hospital. This represented an incidence of 10 per 10,000 live births for Hong Kong. The figure was comparable to those reported for Caucasians. Among the 744 Oriental neonates, obstruction of the pulmonary outflow tract occurred most frequently (281, 37.8%), followed by left ventricular outflow tract obstruction (169, 22.7%), left-to-right shunting (115, 15.5%), complete transposition (92, 12.4%), common mixing situations (62, 8.3%), and miscellaneous causes (25, 3.3%). When compared with the available reports from the West, Chinese neonates had a high preference for pulmonary outflow tract obstruction (p<0.005), especially the anomaly of pulmonary atresia and intact ventricular septum. This correlated well with cyanosis as the commonest neonatal presentation (64%). Contrary to previous reports that aortic coarctation was rare among Orientals, this abnormality was observed frequently in our study. The rare occurrence of critical aortic valvar stenosis among Chinese, however, was supported by our present analysis. Other lesions, such as left-to-right shunting and complete transposition, showed no significant racial difference in the frequency of occurrence. Such knowledge concerning the pattern of congenital heart disease amongst Oriental neonates can facilitate early diagnosis and timely referral of babies to the appropriate center for management.

Key words: Neonate; congenital heart disease

THE MAJORITY (76–95%) OF CHILDREN WITH SYMP-tomatic congenital heart disease tends to present in the first year,[1-5] and mostly in the first weeks of life.[6,7] During the early neonatal period, drastic circulatory changes would bring on major hemodynamic disturbances in association with significant cardiac malformations. Consequently, in the past, one–third to half of these symptomatic babies died within the first month of life.[5,8] Recent advances in diagnosis and treatment, however, have improved the survival of many of these sick newborns. Early recognition of the underlying correctable cardiac lesions, with appropriate referrals, also contribute to the better prognosis of this group.[9] To avoid any delay or misdiagnosis, doctors looking after newborns must be aware of the clinical presentations and patterns of symptomatic congenital

heart disease during this critical period.[9] Previous reports on the overall incidence of congenital heart disease,[1-5] including the New England Regional Infant Cardiac Program,[10] usually failed to highlight the problem relating to newborns, and included a large number of asymptomatic infants. Studies of necropsy materials from infants dying in the first month of life[11,12] tend to bias towards the worst end, and cannot truly reflect the whole spectrum of congenital heart disease. The purpose of this study, therefore, was to review the pattern and clinical profile of Oriental neonates with symptomatic congenital heart disease admitted into our hospital over the past decade. We then attempted to identify any differences in the frequency of occurrence of the various heart lesions between Oriental and Caucasian babies.

## Patients and methods

### Study population

Symptomatic neonates (younger than 30 days) present-

ing with one or more of the four clinical signs and symptoms of tachypnea, cyanosis, heart failure and heart murmur who were admitted into the Grantham Hospital, University of Hong Kong, between January 1981 to December 1990 were included into the study. The Grantham Hospital serves as the major tertiary referral cardiac center for Hong Kong for surgical treatment of neonates with congenital heart disease. Since the city itself is small, and none of its six million population is living remotely from the 12 regional and nine private hospitals, all have good pediatric care. The majority (19 of 21 hospitals) also have an obstetrical unit with neonatologists screening for babies who develop cardiorespiratory symptoms. Moreover, pediatricians and neonatologists all over the territory are closely linked with the pediatric cardiologists at the Grantham Hospital. Except for one regional hospital, where small numbers of simple aortopulmonary shunts and ductal ligation could be performed since 1987,[13] it can safely be assumed that over 95% of all symptomatic newborns with suspected congenital heart diseases are being referred to the Grantham Hospital for assessment and treatment. This includes babies with dysmorphism and chromosomal abnormalities who have relative good prognosis, but excludes syndromes with universal guarded outcome (such as Edward's & Patau syndromes).

### Definitions and diagnosis of congenital heart diseases

Our definition of congenital heart diseases was adopted from the studies performed by Mitchell et al[14] and Scott et al.[6] We included structural abnormalities of the heart or intrathoracic great vessels that are of potentially functional significance. We also included isolated persistent arterial duct which caused symptoms of heart failure, but excluded it from the study if it formed part of the presentation of persistent pulmonary hypertension of the newborn.

The definitive diagnosis of each neonate was based on either cardiac catheterization, echocardiography, surgery and/or autopsy findings. When either echocardiography or catheterization (or both) had been performed, the complete diagnosis achieved was based on the sequential segmental approach.[15] Previous studies from this center had confirmed that echocardiography alone could safely be used for the definite diagnosis of symptomatic neonates with suspected congenital heart diseases.[16,17]

We classified congenital heart diseases according to the major functional hemodynamic disturbances. Babies with complex cardiac malformation were grouped according to the dominant lesion which demanded early treatment. Hence, aortic coarctation in the setting of hearts with univentricular atrioventricular connection was categorized into the subgroup of coarctation,

under the major grouping of left ventricular outflow tract obstruction. Similarly, when pulmonary atresia occurred, irrespective of intracardiac anatomy, great arterial relationship, or atrial arrangement, the anomaly would be grouped under pulmonary outflow tract obstruction.

### Method

From the hospital records, we retrospectively reviewed the following clinical profiles for each baby: age, sex, maturity and weight at birth, year of admission, ethnic group, age of presentation, symptomatology, associated congenital anomalies, method of definitive diagnosis before treatment (clinical, echocardiography, catheterization) and forms of treatment received.

The incidence of symptomatic congenital heart disease for Oriental neonates was calculated from our local birth rate. That for Caucasians was derived from published data of the Brompton Hospital study,[6] the New England Regional Infant Cardiac Program[10] and the Baltimore-Washington Infant Study.[18] Since these latter reports included infants (older than one month) and asymptomatic babies, only those admitted into hospital during the neonatal period were included. For the same reason, only three studies[6,19,20] among the medical literature documented the incidence of specific cardiac lesions within the neonatal period. They were selected for comparison with the present study. The frequency of occurrence of each specific group of cardiac malformation was compared. Chi-square with Yates' correction was utilized and statistical significance assumed at 5% level. Despite a time gap which existed between the present and the published studies, the comparison can give a general impression on whether significant differences occur between the various groups of congenital cardiac malformations seen in Orientals and Caucasian neonates.

### Results

Over the ten years, 871 neonates with suspected congenital heart disease were admitted. Of these, 57 did not have any structural cardiac abnormalities, 17 had isolated disturbances of the cardiac rhythm, and 32 records were not available at the time of study. The remaining 765 babies formed our study group. Their demographics are shown in Table 1. With reference to the local birth rate,[21] the incidence of neonates with symptomatic congenital heart disease was 10.0 per 10,000 live births for the period of study. This figure was very similar to that published for Western babies (Figure).

Echocardiography was first introduced into the unit in late 1982. Prior to this, definitive diagnoses were achieved by catheterization, with the exception of eight babies who had their diagnoses based on clinical find-

**Table 1.** Demographics of the neonates with congenital heart disease.

| Description | n | Percent |
|---|---|---|
| Sex | | |
| Male | 475 | 62 |
| Female | 290 | 38 |
| Ehnic origin | | |
| Chinese | 744 | 97 |
| Caucasian | 21 | 3 |
| Gestation | | |
| Mature | 661 | 86 |
| Premature | 104 | 14 |
| Body weight | | |
| >2.5 kg | 612 | 80 |
| <2.5 kg | 153 | 20 |
| Time of presentation | | |
| Week one | 627 | 82 |
| Week two | 79 | 10.5 |
| Week three | 26 | 3 |
| Week four | 33 | 4.5 |
| Clinical manifestations | | |
| Cyanosis | 503 | 64 |
| Heart failure | 148 | 19 |
| Tachypnea | 79 | 10 |
| Heart murmur | 35 | 5 |
| Associated anomalies (extracardiac) | | |
| Chromosomal | 28 | 3.7 |
| Non-chromosomal | 14 | 2.8 |
| Other | 60 | 11.9 |

**Table 2.** Interventional procedures performed as guided by echocardiography.

| Types of interventional procedures | n |
|---|---|
| Balloon septostomy | 53 |
| Repair of coarctation* | 50 |
| Shunt operation | 40 |
| Ligation of patent arterial duct | 29 |
| Ligation of patent arterial duct and PAB | 8 |
| Closed pulmonary valvotomy | 29 |
| Repair of TAPVC | 17 |
| Pulmonary arterial band (PAB) | 7 |
| Arterial switch operation and septostomy | 7 |
| Others (e.g., balloon angioplasty) | 11 |

* ± Ligation patent arterial duct; ± pulmonary arterial band; ±septostomy; TAPVC: totally anomalous pulmonary venous connection.

ings alone. Over the years, there was an increasing trend of relying on echocardiography to arrive at a definitive diagnosis and implement interventional procedures (including balloon septostomy or other surgery). Of the 466 neonatal procedures (61% of all admissions) performed, 251 (54%) were based on echocardiographic findings alone (Table 2). Among the 765 neonates, there were 238 (31%) hospital deaths.

*Pattern of congenital heart diseases*

Depending on the functional hemodynamic disturbances on presentation, the 744 Oriental neonates were classified into six major groups with further subgroupings (Table 3).

Pulmonary outflow tract obstruction occurred most frequently (n=281, 37.8%) and correlated with the highest incidence of neonatal cyanosis. Babies suffering from left ventricular outflow tract obstruction was second commonest (n=169, 22.7%). These patients presented with heart failure with or without cyanosis. The group with left-to-right shunting (n=115, 15.5%) and common mixing situations (n=62, 8.3%) usually developed heart failure.

When compared with the published series of congenital heart disease among neonates[6,19,20] (Table 4), our present study has the highest proportionate frequency for pulmonary outflow tract obstruction. In particular, the anomaly of pulmonary atresia and intact ventricular septum occurred commonly amongst Orientals. On the other hand, our frequency of occurrence of left ventricular outflow tract obstruction and left-to-right shunting were either lower, comparable, or higher than the reported series. Complete transposition (concordant atrioventricular and discordant ventriculoarterial connections) was observed with similar frequency amongst all four studies, but aortic stenosis occurred rarely in Chinese babies (Table 4).

*Pulmonary outflow tract obstruction*

Among 281 babies, 157 had pulmonary atresia while 124 had valvar and/or subvalvar pulmonary stenosis. There was a high preference of pulmonary atresia and intact ventricular septum. Most babies with significant cyanosis and/or ductal dependent pulmonary circulation received infusions of prostaglandin followed by early construction of an aortopulmonary shunt (mostly modified Blalock-Taussig shunt). As for babies with pulmonary atresia/stenosis and intact ventricular septum (n=69) with a hypoplastic right ventricle, structured surgical management was introduced and the data have been published elsewhere.[22]

*Left ventricular outflow tract obstruction*

Of the 169 babies, 99 and 22 had coarctation and interruption of the aortic arch, respectively, 46 had hypoplastic left heart syndrome (mitral and aortic atresia), while two had severe aortic stenosis with a hypoplastic left heart. Conservative management was implemented for the babies with hypoplastic left heart (with aortic atresia or stenosis) and all 48 died. Prostaglandin $E_2$, dopamine, and ventilator supports were liberally

**Table 3.** Neonates with congenital heart disease—diagnostic classification and proportionate frequency among Orientals referred to Gratham Hospital between 1981-1990.

| Diagnostic classification | n | (%) |
|---|---|---|
| Pulmonary outflow obstruction | 281 | (37.8) |
| Pulmonary atresia + intact ventricular septum | 69 | |
| Pulmonary atresia + univentricular atrioventricular connection | 40 | |
| Pulmonary atresia + ventricular septal defect | 35 | |
| Pulmonary atresia + other intracardiac anomalies | 13 | |
| Pulmonary stenosis + univentricular atrioventricular connection | 38 | |
| Tetralogy of Fallot | 36 | |
| Tetralogy of Fallot complex | 12 | |
| Pulmonary stenosis + intact ventricular septum (critical) | 26 | |
| Pulmonary stenosis + other intracardiac anomalies | 12 | |
| Left ventricular outflow obstruction | 169 | (22.7) |
| Coarctation complex | 99 | |
| Interruption of aorta | 22 | |
| Aortic stenosis | 2 | |
| Aortic atresia (± hypoplastic left heart) | 46 | |
| Left-to-right shunt | 115 | (15.5) |
| Patent arterial duct | 49 | |
| Ventricular septal defect | 47 | |
| Atrioventricular septal defect | 11 | |
| Atrial septal defect ± patent arterial duct | 6 | |
| Aortopulmonary window | 2 | |
| Anomalous origin of the right pulmonary artery | 1 | |
| Complete transposition | 92 | (12.4) |
| Simple | 52 | |
| + Ventricular septal defect | 26 | |
| + Ventricular septal defect + pulmonary stenosis | 12 | |
| Common mixing | 62 | (8.3) |
| Totally anomalous pulmonary venous connection | 36 | |
| Univentricular atrioventricular connection without outflow obstruction | 13 | |
| Common arterial trunk (Truncus arteriosus) | 10 | |
| Double outlet right ventricle | 3 | |
| Others | 25 | (3.3) |
| Ebstein's malformation/valvar diseases | 15/2 | |
| Arteriovenous fistula | 4 | |
| Cardiac tumor | 2 | |
| Cardiomyopathy | 2 | |

used for most sick neonates with obstruction in the aortic arch (n=123). Medical treatment alone (n=18) was offered when surgery could not be carried out because of the critical condition or, rarely, because of parental refusal. Otherwise, repair of the coarctation (n=82) by subclavian flap aortoplasty or end-to-end anastomosis was carried out with ligation of the arterial duct (and banding of the pulmonary trunk when large intracardiac shunt existed). Interruption of the aortic arch was repaired (n=19) by either end-to-end anastomosis or interposition of a Gore-Tex® graft between the interrupted arch (together with ligation of the duct and banding of the pulmonary trunk).

*Left-to-right shunting*

Persistent arterial duct (n=49, 43%) and ventricular septal defect (47, 41%) were the commonest lesions for this group. Of the total 115 babies, 65 were offered medical and 50 surgical treatment.

*Complete transposition*

Among the 92 neonates with simple complete transposition and complete transposition with complex intracardiac anatomy, 89 underwent balloon septostomy. The procedure was not required in four babies who had an adequate atrial septal defect. Seven babies were referred for neonatal arterial switch operation, and 69 other neonatal survivors underwent further surgery including Mustard's or Senning's operation with or without closure of a ventricular septal defect (n=62), modified Blalock–Taussig Shunt (n=3), arterial switch operation (n=1) and other complex surgery (n=3).
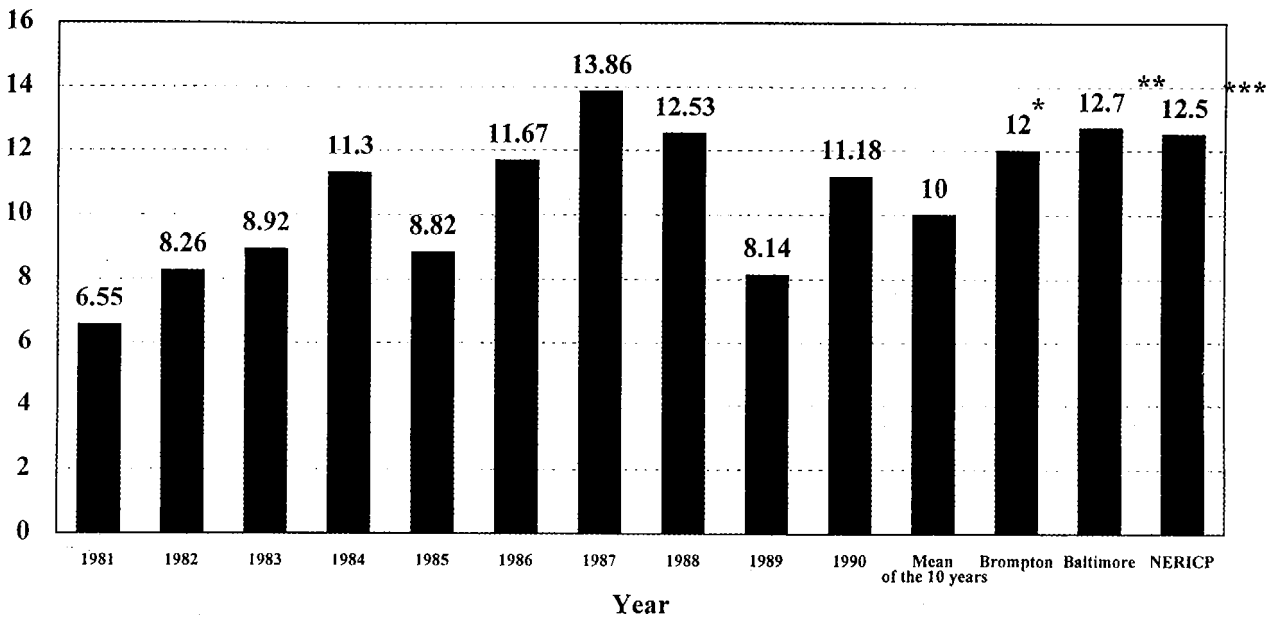
\*        derived from Table VI and the reported birth rate of 61,920 per year of the Brompton Hospital's series
\*\*      derived from Table I (prevalence) and Figure I (% of the livebirths diagnosed before 4 weeks) of the Baltimore-Washington Infant Study
\*\*\*     derived from Table IV and the reported 58% of admissions during the first month of the New England Regional Infant Cardiac Programme

**Figure.** *Neonates with symptomatic congenital heart disease—incidence per 10,000 live births.*

## Common mixing

The major subgroups for these babies include those with totally anomalous pulmonary venous connection (n=36), hearts with univentricular atrioventricular con-nection without any outflow obstruction (n=13), common arterial trunk (n=10) and double outlet right ventricle (n=3).

Medical treatment alone was offered to 27 babies

**Table 4.** Comparison of the pattern of various groups and subgroups of congenital heart disease.

| Congenital heart disease | Present study n=744 | Lambert n=165 | Izukawa n=258 | Scott n=704 | $p_1$ | p value $p_2$ | $p_3$ |
|---|---|---|---|---|---|---|---|
| Pulmonary outflow obstruction | 281 | 38 | 29 | 81(+73)* | <0.005 | <0.0001 | <0.0001 |
|   Pulmonary atresia + intact ventricular septum | 69 | (11)* | 5 | 29 | NS | <0.0005 | <0.0005 |
|   Univentricular atrioventricular connection | 78 | 9 | 8 | (73) | NS | <0.001 | NS |
|   Tetralogy of Fallot | 37 | 12 | 8 | 40 | NS | NS | NS |
|   Others | 97 | 6 | 8 | 12 | | | |
| Left ventricular outflow obstruction | 169 | 69 | 33 | 164 | <0.0001 | <0.05 | NS |
|   Coarctation complex | 99 | 25 | 13 | 94 | NS | <0.05 | NS |
|   Interruption of aorta | 22 | 1 | 0 | 0 | NS | | <0.0001 |
|   Hypoplastic left ventricle | 46 | 37 | 20 | 61 | <0.0001 | NS | NS |
|   Aortic stenosis | 2 | 4 | 0 | 9 | <0.01 | | <0.05 |
| Left-to-right shunts | 115 | 15 | 106 | 74 | NS | <0.0001 | <0.01 |
|   Patent arterial duct | 49 | 4 | 80 | 19 | NS | <0.0001 | 0.001 |
|   Atrioventricular septal defect | 11 | 7 | 0 | 14 | | | NS |
|   Septal defects | 52 | 4 | 26 | 41 | | NS | NS |
|   Others | 3 | 0 | 0 | 0 | | | |
| Complete transposition | 92 | 25 | 23 | 111 | NS | NS | NS |
| Common mixing | 62 | 13 | 7 | 138 | NS | <0.005 | NS |
| Others | 25 | 5 | 52 | 114 | | | |

* Hearts with univentricular atrioventricular connection but pulmonary stenosis not specified by Scott et al. $p_1$: comparison between present and Lamberts' series; $p_2$: comparison between present and Izukawa' series; $p_3$: comparison between present and Scott' series.

while corrective (as in total correction for anomalous pulmonary venous connection) and palliative (such as banding of the pulmonary trunk) operations were performed on 35 neonates.

### Miscellaneous lesions

The miscellaneous group consisted of 25 babies with Ebstein's malformation of the tricuspid valve and other rare anomalies (such as cardiac tumors).

### Discussion

The increasing awareness that any "off-colored" neonates might be suffering from congenital heart disease has prompted early referrals of these sick babies to a cardiac center. Yet very few reports[6,7,19] have focused on the pattern of disease presented at this critical period. Furthermore, no studies have been carried out, to the best of our knowledge, among Oriental neonates. Our study provides the only data of this kind among the Chinese population. The very condensed environment of Hong Kong has greatly facilitated the extension of pediatric services to rural areas. Widely distributed Government regional hospitals over the whole territory ensure that no family will refrain from sending their sick babies to a hospital because of poverty. Obstetrical care is available in 19 of the 21 hospitals, and is fully supported by neonatal screening with easily available echocardiographic assessment. With the exception of about ten symptomatic babies referred to one regional hospital during this period of study,[13] practically all symptomatic newborns with suspected congenital heart diseases were concentrated at the Grantham Hospital. The estimated number of babies (10.0 per 10,000 live births) with obvious symptoms was practically a true representation of the incidence of major congenital heart defect presenting in the neonatal period requiring assessment and treatment. Excluded from these data were babies who had chromosomal abnormalities with dismal prognosis, but their referrals would have no impact on the policy of management. Again the small number of babies with a dominant heart lesion who were dead before arrival to a regional hospital (Coroner's registry less than five cases during the period—personal communication) had little effect on the pattern of congenital heart lesions described in this series.

Our incidence of congenital cardiac malformation closely resembles figures derived from three studies[6,10,18] and suggests that the occurrence of major symptomatic congenital heart lesions presenting in neonates are similar for Chinese and Caucasians. Because the prevalence of specific lesions published in most series have focused on infants (younger than one year) and included asymptomatic babies, comparison with these data would not be logical. Moreover, we believe that

symptomatic neonates are at higher risk and frequently require urgent medical and surgical treatment. In contrast, most older infants can compensate better for the disturbed hemodynamics. We have, therefore, selected series which documented admissions of symptomatic neonates and compared the frequency of occurrence of each specific lesion. We are aware of the time gap which existed between the present and the published series, and the changing diagnostic practice over this period (echocardiography versus catheterization). Yet it is reported that the incidence of major congenital heart defect has remained constant over time.[23,24] Hence, a comparison on the frequency of occurrence of a specific group of cardiac anomaly between Oriental and Western babies would seem to be valid. We observed that the proportionate frequency for pulmonary outflow obstruction was markedly different between Orientals and Caucasians. In particular, the anomaly of pulmonary atresia with intact ventricular septum showed a high preference for Chinese neonates. This allowed us to accumulate our experience and to evolve a policy for management[22] which was guided by the tripartite classification of the hypoplastic right ventricle.[25,26] On the other hand, the frequency of occurrence of left ventricular outflow obstruction, especially of hypoplastic left heart, was either lower, comparable or higher than the reported series, suggesting no true difference in occurrence of the congenital malformation. Contrary to previous reports,[27-30] aortic coarctation is not rare among Chinese. Our observed proportional frequency is comparable to those reported by Scott et al.[6] A hint for the frequent occurrence of coarctation among Orientals might be found in the report from Singapore,[31] which included 8.3% of the 121 post-mortem studies on babies dying at birth or in the neonatal period. We postulate that, since neonates with coarctation usually present in a "collapsed" state, their underlying heart lesions might have been masked by their "septic" look when they were first admitted into the general hospital. In our situation, the close proximity of the rural areas to the city, the relationship between cardiologists and pediatricians, the wide availability of echocardiographic machines in the regional hospitals with experienced personnel who had been trained by our cardiologists, all contributed to the early diagnosis and referrals of these neonates. Hence, most of the babies (92.5%) in our study were referred within the first two weeks of life. Our data, however, supported the findings that critical aortic valvar stenosis may be genuinely rare among the Chinese population.[23,24] The anomalies of complete transposition or left-to-right shunts showed no significant racial difference in occurrence, since the discrepancy between our series with Western reports could be in either direction.

Neonatologists and pediatricians looking after Ori-

ental babies in Asia and Western countries should be aware of our observed patterns of congenital heart disease. This is especially true with the increasing influx of Asian immigrants to Europe and North America. Doctors should be alerted concerning the high frequency of cyanosis in Oriental neonates, and relate the presentation to pulmonary outflow obstructive lesions. They should also remember that aortic coarctation frequently causes early heart failure among Chinese, but critical aortic stenosis is a rarity. Such knowledge will greatly facilitate future early diagnosis and referral of affected babies to the appropriate centers for management.

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