

Nonstructural heart disease in the newborn

Observations during one year in a perinatal service

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SUMMARY One-third of 327 newborn infants referred to the perinatal service of the Hospital for Sick Children during 1975 with suspected cardiopulmonary disorders proved to have nonstructural heart disease. Most of these were term infants with transient tachypnoea or cyanosis who recovered. A history of fetal distress or difficult delivery was commonly associated. The haemodynamic disorder for most was a delay in the normal progress of the transitional circulation. Evidence of myocardial ischaemia was present in 40%, and about half of these developed congestive heart failure. Aids to diagnosis of the ischaemic complication included echocardiography and myocardial perfusion scanning. For a small proportion specific metabolic disturbances, myocarditis, or dysrhythmia seemed the primary cause but even for these there were reasonable grounds to suspect a prenatal origin. Current general supportive measures were of value in treatment.

Congenital malformations of the heart constitute an important diagnostic and management problem in infancy. Over one-third of these patients have critically severe congenital heart disease and are usually identified very early because of the development of cyanosis or congestive heart failure (Rowe, 1970; Mitchell *et al.*, 1971; Campbell, 1973; Nadas *et al.*, 1973).

It has been recognised for many years that there exists another group of newborn infants who present with signs suggestive of heart disease, often of a rather severe nature, in whom the basis for the clinical picture has eventually proved not to be that of heart malformation. In 1975 there were 101 newborn infants in this category seen by cardiologists at the request of our perinatal service.

This report examines the composition of this particular group of patients, and indicates some of the newer approaches to diagnosis and to team management.

Material

The perinatal service of the Hospital for Sick Children serves as a tertiary care centre for the newborn for metropolitan Toronto and neighbouring

parts of Ontario, servicing an area in which approximately 60 000 deliveries take place annually, of whom approximately 1300 (2%) are referred.

Patients classified as having nonstructural heart disease in this particular service are carefully selected and only those with an obvious additional cardiac disturbance or suspicion of it during the course of the illness are likely to be referred by neonatologists to the cardiologist. The respiratory distress syndrome of prematurity, patients with trivial or transient murmurs, and infants with diaphragmatic hernia or tracheo-oesophageal fistula are examples of the situation in which only selected patients would receive a specific cardiac evaluation. Patients for whom such an opinion would be requested could include those with intense cyanosis failing to respond to high ambient oxygen breathing, those with frank or strongly suspected congestive heart failure, those with heart murmurs, or with abnormal pulses or blood pressures.

For 1975 a prospective evaluation was designed to examine this type of nonstructural heart disease. The 101 patients for whom cardiac consultation was requested were seen first by a fellow in cardiology and shortly afterwards by a staff cardiologist. Preliminary investigations beyond the physical examination for all such patients included blood gas measurements, a chest x-ray, and an electrocardiogram. Echocardiography was performed in 34

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patients. The preliminary investigations and recommended treatments were communicated to the appropriate staff. Further investigation by cardiac catheterisation and angiocardiology was performed after such consultations in only 6 patients. Subsequent evaluations on the ward were performed by cardiologists, usually daily, but more or less frequently according to need. Follow-up after discharge, arranged through the referring physician, depended on the severity of the residual cardiac anomaly and the possibility of future problems.

Results

The broad diagnostic categories found among 101 cardiac consultations of this type are identified in Table 1. Almost 90% of the nonstructural heart disease seen in our unit presented with cardio-respiratory distress and we arbitrarily separated arrhythmia and polycythaemia because of obvious clinical differences.

Respiratory distress. Most children in this category were full-sized and for approximately 85% of them a serious perinatal disturbance in adapting to extra-uterine life was eventually thought to be the likely explanation for symptoms. Within the subdivisions of simple and complex chosen for the broad classification we found several groups of patients, of roughly equal size, having rather similar presenting features. So it was that in simple respiratory distress, although most patients had tachypnoea and differing degrees of cyanosis there were 20 with predominant cyanosis and 21 with predominant respiratory difficulty. Another 20 patients in this general category had either predominant cyanosis or respiratory difficulty but these also showed ST/T changes in the electrocardiogram, suggesting myocardial damage.

The mean P_{aO_2} for each group, with a mean F_{IO_2} of 0.45, was 44 mmHg (5.87 kPa) and we were not able to find other differentiating features for the groups in regard to known prenatal events, conduct of labour, or Apgar score. The sequence of recovery

Table 2 *Clinical associations in newborns with respiratory distress complicated by heart failure*

| | |
|---------------------------------|----|
| Birth asphyxia | 5 |
| No obvious cause | 4 |
| Meconium staining or aspiration | 3 |
| Viral or widespread infection | 3 |
| Infant of diabetic mother | 2 |
| Fetomaternal transfusion | 1 |
| Fluid overload | 1 |
| Multiple anomalies | 1 |
| Hydrops | 1 |
| | 21 |

in the 3 groups was also similar, the electrocardiographic signs in those with change reverting eventually to normal. Heart size was not appreciably different within the groups nor were murmurs more common in those with electrical abnormalities. The principal differential diagnoses for these [types of simple respiratory distress were cyanotic congenital heart disease and heart malformation with equivocal early congestive heart failure.

In the simple form of respiratory distress without evidence of myocardial ischaemia, there were 12 deaths among the 41 patients—almost 30%. Of this number 5 were premature infants. The cause of death was subependymal plate and intraventricular bleeding (5), severe birth asphyxia (2), meconium aspiration (2), hyaline membrane disease (1), extreme immaturity (1), and sepsis (1). In the simple form with ST/T segment changes in the electrocardiogram there were 2 deaths among the 20 patients. The necropsy showed cerebral and pulmonary haemorrhage (1), and hyaline membrane disease (1).

Quite different from these 60 patients with simple respiratory distress was the group of 21 patients we classified as having complex respiratory distress. These were infants, often with similar backgrounds to the simple type of respiratory distress, in whom the respiratory difficulty became severe during the first 48 hours culminating in frank congestive heart failure. Table 2 shows the precipitating events recognised for the cases with this symptom complex. It will be seen that a rather wide range of physical, infectious, and metabolic disturbances existed for these patients as for the other groups. The mean P_{aO_2} for them was higher (53 mmHg, 7.07 kPa) at a lower F_{IO_2} (0.39) than was the case for the babies with simple respiratory distress. There were 3 deaths among these 21 patients. One patient died with widespread Coxsackie B4 infection including myocarditis, one infant with severe birth asphyxia, and one with fetomaternal exsanguination syndrome and tentorial tears.

Table 1 *Categories of nonstructural heart disease in newborns*

| | | |
|----------------------------------|----|-----|
| Respiratory distress | | |
| Simple, + - cyanosis | | 41 |
| ST/T changes | | 20 |
| Complex, with myocardial failure | | 21 |
| Other forms | | |
| Arrhythmias | 15 | |
| Polycythaemia | 3 | |
| Renal hypertension | 1 | 19 |
| | | 101 |

Other

(a) *Arrhythmias*. There were 4 examples in term infants of congenital atrial flutter, all seriously ill with gross heart failure on admission. All survived. There were no other examples of arrhythmias as a significant isolated event in this particular year. Of the remaining 11 patients, 7 were premature infants with birthweights ranging from 680 to 2200 g. They had a variety of types of heart block or ectopic pacemakers in association with metabolic and pulmonary disturbances or with sepsis. Lastly 4 term babies had ventricular premature contractions (2), or bradycardia (2), all associated with other disease.

(b) *Polycythaemia*. All 3 infants had Hb values above 21 g/dl but although they appeared cyanosed the PaO_2 in all cases in room air exceeded 53 mmHg (7.07 kPa) and none had developed severe symptoms or sequelae at the time of discharge.

Discussion

The need to differentiate patients with congenital heart disease from those with disorders mimicking this condition has long been appreciated by paediatricians caring for the newborn. Kreutzer *et al.* (1956) referred to this group of patients as having 'pseudocardiopathy' and more recently the term nonstructural heart disease has been in vogue. Neither is entirely appropriate because in some instances there is true cardiopathy and in others a structural defect may be present.

The group of patients with simple respiratory distress and predominant cyanosis fits a picture which has been called 'persistent fetal circulation' (Gersony *et al.*, 1969). These babies are in a state of pulmonary vasoconstriction and usually have a wide-open ductus arteriosus. For many this is relieved by high environmental oxygen concentrations and attention to general supportive aspects—such as raising a lowered body temperature, blood sugar, or blood calcium, or by reducing metabolic acidosis, or by measures which relieve pneumothorax or pneumomediastinum. Some babies fail to improve with simpler approaches and require more active treatment with vasodilator drugs, such as tolazoline, under carefully controlled conditions (Goetzman *et al.*, 1976; Levin *et al.*, 1976). Such is likely to be the case for patients with meconium aspiration or diaphragmatic hernia in the postoperative phase and in the 10% of patients for whom there is no obvious cause for the findings. The major differential diagnosis is cyanotic congenital heart disease, particularly D-transposition of the great arteries.

Differential blood sampling from arteries above and below the ductus arteriosus, hyperoxic tests, and echocardiography are often helpful in differential diagnosis but severe cases unresponsive to enriched inspired oxygen usually require cardiac catheterisation and angiocardiography.

Those babies with major respiratory difficulty almost always have obvious lung problems of which the 'wet lung' or transient tachypnoea of the newborn is most important for term babies. Premature infants prove most often to have very severe respiratory distress syndrome, and mortality was particularly high as might be expected.

Patients with respiratory distress and ST/T segment changes without congestive failure resembled in most respects the simpler cases who do not show electrocardiographic alterations suggesting myocardial damage.

It is not clear yet what relationship these patients may have to the more striking subgroup of complex respiratory distress in which congestive failure is a prominent feature. Perhaps the infant with hydrops is a reasonably simple diagnostic problem but for few of the others does the aetiology emerge easily. The association of congenital heart disease and non-structural heart disease in infants of diabetic mothers makes the need for strenuous and complete diagnostic assessment mandatory in this group of patients (Keith *et al.*, 1961; Rowland *et al.*, 1973; Poland *et al.*, 1975; Wolfe and Way, 1977), particularly when cardiac dilatation is associated with hypoglycaemia (Reid *et al.*, 1971).

Myocarditis can be very difficult to diagnose. In the present series one patient also had toxoplasmosis, one had Coxsackie B4 infection, and a third patient also had cytomegalic virus infection. Transient myocardial ischaemia is a term we have applied to newborn infants with respiratory distress, congestive heart failure, and signs of atrioventricular valve regurgitation or vascular collapse (Rowe and Hoffman, 1972; Emmanouilides and Siassi, 1975; Bucciarelli *et al.*, 1977). This picture simulates severe congenital heart disease and can mimic hypoplastic left heart syndrome, absent pulmonary valve, Ebstein's anomaly of the tricuspid valve, and hypoplastic right heart syndrome, to mention only a few. The electrocardiogram can show signs of ST/T segment alteration early or late and often that of posterior myocardial infarction. Despite the fact that segmental disturbance of myocardial function usually limits the value of single transducer echocardiography in adult ischaemic heart disease, the echocardiogram is usually helpful in newborn infants with these disturbances and often shows impaired myocardial function. Such patients appear desperately ill and often require cardiac catheterisation for

complete diagnosis. The response to anticongestive measures, myocardial stimulants and, occasionally, to vasodilator drugs is good. A tendency to digitalis toxicity from rather ordinary doses of digoxin has been encountered in a manner similar to that seen in patients with myocarditis. These infants may clearly improve yet continue to have rapid respirations and residual murmurs for a week or more after birth. We recently confirmed by myocardial imaging techniques that widespread myocardial ischaemia does in fact exist in these patients (Rowe *et al.*, 1977). The early resolution of heart failure, reduction in heart size, and disappearance of the murmurs are not usually matched by the electrocardiogram which often takes weeks and sometimes months to return to normal. Similarly, normal myocardial uptake of thallium is seldom completely established before age 3 months. Follow-up beyond infancy is not yet available for these subjects. Most survivors show a spectacular improvement and at least during infancy their progress from the cardiovascular point of view appears to be perfectly normal after the newborn period. Whether the early myocardial insult has any relation to the sudden infant death syndrome, later arrhythmias, or to the prolapsed mitral valve leaflet syndrome is as yet unknown and remains speculative.

Babies with congenital flutter are rather dramatic in presentation but fortunately respond well to treatment (Radford *et al.*, 1976). They are often delivered by caesarean section for 'fetal distress' manifested by fetal tachycardia. Other disturbances are usually either minor in degree or arise as late complications of major disease in premature babies. Although polycythaemia is a serious disorder demanding prompt action to avoid cerebral and other complications (Gross *et al.*, 1973), it is not today often confused with cyanotic congenital heart disease because of the availability of blood gas measurements.

Despite the selected nature of the nonstructural heart disease patients who presented during this year it is disturbing to see that 20% of them died. Almost half of these deaths were in premature babies and at least half were caused by bleeding disorders.

Although the cause of nonstructural heart disease in the newborn is undoubtedly multifactorial, hypoxia and resulting pulmonary vasoconstriction appear to be the main precipitating causes of disturbed circulatory dynamics and myocardial function at this age. The response of a particular newborn to the stimulus of hypoxia is governed by a great many additional factors of which the degree of hypoxia is one, the amount of medial muscle in small muscular pulmonary arteries another, and the degree of patency of the ductus arteriosus as well as the myocardial fuel supply at the time yet

others. The myocardium is also affected by acute perinatal blood volume changes of either extreme, by infection, by metabolic disorders, and by severe electrolyte disturbances. Frequently a number of factors are mutually reinforcing. For example, a premature infant, asphyxiated at birth, may be cold, stressed, and hypoglycaemic and subsequently develop pulmonary oedema and 'wet' respiratory distress syndrome with persisting ductal patency followed by congestive heart failure. Alternatively one could cite the 43-week postmature infant who is asphyxiated at birth, with high haematocrit, hyperviscous, and hypoglycaemic—all inimical to myocardial function. It is not surprising that sub-endocardial ischaemia is becoming a matter of increasing concern for these babies (Rowe and Hoffman, 1972; Bucciarelli *et al.*, 1977; de Sa, 1977; Nelson *et al.*, 1978).

The history—prenatal, natal, and immediate post-natal—is therefore of great importance in raising a suspicion of nonstructural cardiac disease neonatally. Final diagnosis rests on the exclusion of structural causes and the association of specific clinical conditions with the cardiac findings.

Anticipation of secondary cardiac involvement from the perinatal history and clinical findings now enables diagnostic and supportive measures to be instituted early, thus improving prognostic ability, treatment, and eventual prognosis. The ultimate objective of prevention rests with improved methods of identification and appropriate management for the high risk pregnancies and deliveries involved.†

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