

## CONGENITAL HEART DISEASE

# Neurodevelopment at 1 year of age in infants with congenital heart disease

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**Objective:** To assess psychomotor development and neurological sequelae in infants after surgery for congenital heart defects.

**Design and setting:** Single institution prospective cohort study.

**Patients:** 90 of 112 consecutive surviving infants of less than 1 year of age, without brain anomalies, conditions, or syndromes associated with delayed mental development, who underwent cardiac surgery during an 18 month period; 20 control infants with minor or no congenital heart defects.

**Main outcome measures:** Griffiths developmental scales and standardised neurological examination at 1 year.

**Results:** Mean (SD) developmental quotient (DQ) in index infants was 99 (10.6), compared with 106.7 (6.6) in controls ( $p < 0.001$ ). DQ was lower in infants after palliative surgery ( $n = 16$ ; 88 (12.2)) than after corrective surgery ( $n = 74$ ; 101.4 (8.6)) ( $p < 0.001$ ). Of the 90 index infants, 24 (27%) had a DQ below 93.5 (more than 2 SD below the mean of controls). Developmental delay (DQ  $< 93.5$ ) was more common after palliative surgery (10/16, 63%) than after corrective surgery (14/74, 19%) ( $p < 0.001$ ). Of the 90 index infants, 29 (32%) had neurological abnormalities, compared with only one of the 20 controls (5%) ( $p = 0.013$ ). Neurological abnormalities were more frequent after palliative surgery (11/16, 69%) than after corrective surgery (18/74, 24%) ( $p < 0.001$ ).

**Conclusions:** There is a considerable rate of neurodevelopmental impairment at 1 year of age in infants after cardiac surgery. Psychomotor impairment and neurological sequelae are apparently more severe in infants in whom only palliative surgery is possible.

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Congenital heart defects (CHD) are among the most common birth defects, and nearly one third of them will require surgical intervention in infancy.<sup>1</sup> Thanks to advances in cardiothoracic surgical methods, extracorporeal circulation techniques, and intensive care medicine, it is now possible to undertake definitive corrective surgery early in life. However, infants with complex CHD require a multistep approach and often undergo palliative surgery first to improve oxygen saturation and haemodynamic conditions. Increasing survival rates have been associated with a shift in focus from heart related morbidity and death to concern for brain integrity,<sup>2–5</sup> and developmental and neurological outcome has come under increasing scrutiny. Several studies evaluating various surgical procedures in subsets of children with CHD have found evidence of developmental delay and neurological deficits in selected groups of infants.<sup>6–15</sup> However, the extent of neurodevelopmental impairment in otherwise normal children with CHD who are subjected to cardiac surgery in early infancy still has to be defined.

To investigate this problem, we undertook prospective neurological and neurodevelopmental examinations before surgery (when possible) and at 1 year of age in a single institution cohort of consecutive infants with various types of CHD who had undergone corrective or palliative surgery within the first year of life. In contrast to most other studies, enrolment of infants was not limited to those with a specific diagnosis, such as transposition of the great arteries, but covered the whole spectrum of CHD, to reduce the chances of selection bias. Within the same tertiary care paediatric cardiology centre setting, a control group was recruited of infants not requiring any cardiac surgery or catheterisation during the first year of life, who were examined alongside the surgically treated infants with CHD at 1 year of age.

## METHODS

### Subjects

In the 18 month period between 15 April 1998 and 14 October 1999, 135 infants with CHD underwent cardiac surgery within their first 11 months at the German Heart Institute Berlin, and had none of the following exclusion criteria: previous cardiac surgery in another hospital; gestational age  $< 32$  weeks; umbilical artery pH  $< 7.1$ ; five minute Apgar score  $< 7$ ; brain malformation as detected by ultrasound; or syndromes associated with neurodevelopmental disability such as Down's syndrome or DiGeorge syndrome. One hundred and twelve of these infants were discharged alive after corrective or palliative surgery. Of those 112 eligible infants, 99 (88%) were enrolled in the neurodevelopmental follow up programme with informed parental consent. The parents of 13 infants decided against participating because they lived too far away ( $> 300$  km,  $n = 8$ ) or for other unspecified reasons ( $n = 5$ ).

We also recruited 20 control outpatients with no or only minor cardiac defects without haemodynamic significance (for example, a small ventricular or atrial septal defect). Those infants were seen for echocardiography in our hospital clinics. The control infants were born within the same time period as the infants with CHD who had undergone open heart surgery. The control infants had never been admitted to hospital for heart disease, nor had received any specific drug treatment.

The study was approved by the institutional review board of the Charité Medical Centre.

### Operative and perioperative data

Cranial ultrasound examinations were undertaken before and after surgery. The type of surgical procedure, the use of cardiopulmonary bypass and deep hypothermic circulatory arrest (DHCA), the number and duration of cardiopulmonary bypass and DHCA procedures, the lowest rectal temperature,

**Table 1** Diagnostic categories of congenital heart defects

<i>Corrective surgery (n=74)</i>	
Transposition of the great arteries	17
Transposition of the great arteries with aortic arch hypoplasia	1
Anomalous pulmonary venous connection	3
Coarctation of the aorta	10
Coarctation of the aorta with ventricular septal defect	1
Atrial or ventricular septal defect or combination of both	21
Atrioventricular septal defect	3
Anomalous origin of the left coronary artery	1
Tetralogy of Fallot	11
Pulmonary atresia with ventricular septal defect	1
Hypertrophic obstructive cardiomyopathy	1
Interrupted aortic arch	1
Patent ductus arteriosus Botalli	2
Double outlet right ventricle with transposition of the great arteries	1
<i>Palliative surgery (n=16)</i>	
Tetralogy of Fallot	3
Transposition of the great arteries with ventricular septal defect and pulmonary valve stenosis	1
Tricuspid atresia (including one with transposition of the great arteries and one with pulmonary valve stenosis)	4
Pulmonary atresia with:	
– ventricular septal defect	3
– combined atrioventricular septal defect	2
– double outlet right ventricle with transposition of the great arteries	1
Tricuspid hypoplasia and hypoplastic right ventricle	2

age at operation, duration of sedation and mechanical ventilation, length of stay in the intensive care unit, and overall length of hospital stay during the first year of life were noted.

Clinical seizures after surgery were recorded by the nurses or the physicians caring for the infant. The criteria for a definite clinical seizure included the occurrence of a single or a recurrent motor event with tonic or clonic movements of an extremity or cranial muscles, associated with change in consciousness not responsive to manipulation.

### Neurodevelopmental assessment

Neurological examinations were carried out before surgery except in critically ill infants who required sedation, mechanical ventilation, or emergency surgical intervention; and again in all infants at 1 year of age, at least six weeks after the last surgical procedure. Standardised neurological examinations<sup>16</sup> included assessment of muscle tone, movement patterns, posturing, deep tendon reflexes, and special senses (hearing and vision). Activity level was taken into account. Findings were classified as normal or abnormal, and abnormalities were

scored as mild, moderate, or severe. Children with definite cerebral palsy were excluded from classification into any other categories except that of special senses (hearing and vision).

The Griffiths developmental scales,<sup>17</sup> translated and standardised for a German reference population,<sup>18</sup> were used to assess the developmental status of the infants; they covered locomotor skills, personal/social skills, hearing/speech, eye-hand coordination, and cognitive performance. Total developmental quotients (DQ) were calculated by dividing the number of items successfully executed by the infant's age (in months). Corrections were made for preterm birth and any period of time an infant had been sedated and mechanically ventilated, assuming that psychomotor development is minimal or non-existent under sedation/mechanical ventilation. This conservative approach tends therefore to underestimate neurodevelopmental delay, especially in infants with complex CHD requiring prolonged intensive care. At the time of assessment, investigators were blinded to the type of cardiac defect and to the medical history. Measuring of somatic data (weight, length, head circumference) was undertaken by the same investigator.

### Statistical analysis

We used SPSS for Windows 9.0 (SPSS Inc, Chicago, Illinois, USA) for all calculations. Probability values of  $p < 0.05$  were considered to be significant. Data are given as mean (SD) or median with minimum and maximum. Categorical variables between groups were analysed by  $\chi^2$  contingency tables, with Fisher exact calculations if one expected cell value was below 5. Continuous variables were compared by the Mann-Whitney U test or the Kruskal-Wallis test.

## RESULTS

### Patient characteristics and surgical intervention

Of the 99 infants with CHD originally enrolled, 98 were alive at one year of age. One infant was excluded after suffering severe hypoxic brain injury during a surgical procedure unrelated to CHD at 8 months of age. The parents of seven infants did not show up for the 1 year examination. Of the 90 infants actually examined at 1 year of age, 61% were male, 39% female, and 82% were from German mother tongue households. In the study group of 90 CHD infants examined, there were 50 cyanotic and 40 acyanotic heart defects. Sixty eight of the 90 infants (76%) were examined neurologically before their first cardiac operation.

Seventy five infants underwent surgery during cardiopulmonary bypass, and two infants during deep hypothermic circulatory arrest. Fourteen infants underwent more than one cardiac operation. Seventy four (82%) underwent anatomical correction of CHD, and 16 (18%) underwent palliative procedures and remained cyanotic after surgery.

**Table 2** Surgical interventions of infants with congenital heart disease

Variable	Corrective surgery (n=74)	Palliative surgery (n=16)
Infants with two surgical procedures	8	4
Infants with three surgical procedures	0	2
Number of operations with CPB	69	17 (central aorto-pulmonary shunt, n=6; central aorto-pulmonary shunt + outflow tract reconstruction, n=7; Glenn op, n=4)
Number of operations without CPB	13 (repair of coarctation of the aorta, n=11; ligation of patent ductus arteriosus Botalli, n=2)	7 (central aorto-pulmonary shunt, n=7)
Number of operations with deep hypothermic circulatory arrest	2 (repair of interrupted aortic arch, n=1; repair of transposition of the great arteries with aortic arch hypoplasia, n=1)	0

CPB, cardiopulmonary bypass.

**Table 3** Characteristics of infants with congenital heart disease

Variable	Corrective surgery (n=74)	Palliative surgery (n=16)	Controls (n=20)
<i>Preoperative characteristics</i>			
<i>Birth data</i>			
Body weight <3rd centile	–	1 (6%)	–
Body length <3rd centile	1 (1%)	–	–
Head circumference <3rd centile	–	1 (7%)*	–
Gestational age (weeks)	40 (32 to 42)	40 (35 to 40)	40 (35 to 41)
Apgar score at 5 minutes	10 (7 to 10)	9 (7 to 10)	10 (8 to 10)
Age at first surgery (months)	3 (0 to 11)	3 (0 to 10)	–
<i>Heart defect</i>			
Cyanotic	34 (46%)	16 (100%)	–
Oxygen saturation before surgery (%)	96 (33 to 99)	77 (40 to 95)	–
Oxygen saturation at time of neurodevelopmental testing (%)	99 (98 to 100)	85 (78 to 93)	–
<i>Surgical data</i>			
CPB	62 (84%)	13 (81%)	–
Circulatory arrest	2 (3%)	–	–
Lowest rectal temperature (°C)	30 (15 to 36)	36 (30 to 36.5)	–
Repeated cardiac surgery†	8 (11%)	6 (38%)	–
<i>Perioperative data</i>			
Length of stay on intensive care unit (days)‡	4 (1 to 22)	6 (2 to 52)	–
Duration of hospital stay (days)§	22 (7 to 166)	62 (19 to 315)	0 (0 to 3)
<i>Sociodemographic factors</i>			
Maternal age at birth (years)	30 (26 to 33)	28 (17 to 43)	30 (20 to 39)
Maternal education			
Completed high school or more	66 (89%)	14 (88%)	19 (95%)
Marital status			
Married or living with partner	65 (88%)	14 (88%)	18 (90%)
Family income per year (euros)			
<15 000	21 (28%)	4 (25%)	5 (25%)
15 000 to 30 000	40 (54%)	12 (75%)	10 (50%)
>30 000	13 (18%)	–	5 (25%)
<i>Follow up data at 1 year</i>			
Age at examination (months)	12.2 (10.8 to 14.4)	12.1 (10 to 14.1)	12.4 (10.6 to 14)
Body weight <3rd centile¶	15 (20%)	7 (44%)	–
Body length <3rd centile	8 (11%)	3 (19%)	–
Head circumference <3rd centile**	7 (10%)	7 (44%)	–

Data are numbers (percentages) for categorical, or median (range) for numerical variables.

\*Data available from 14 children.

†Corrective v palliative surgery;  $p=0.016$ .

‡Corrective v palliative surgery;  $p=0.050$ .

§Corrective v palliative surgery;  $p=0.001$ .

¶Corrective v palliative surgery;  $p=0.053$ .

\*\*Corrective v palliative surgery;  $p=0.003$ .

The diagnostic categories of CHD of the infants with corrected heart defects and the infants who underwent palliative surgery are shown in table 1.

The control group comprised the following cardiac diagnoses: ventricular septal defect (9), atrial septal defect (7), normal heart (2), aneurysm of the coronary arteries (1), patent ductus arteriosus Botalli (1); 45% were male, 55% female, and 75% were from German mother tongue households.

Surgical interventions in the infants with CHD are given in table 2, and their characteristics are shown in table 3. The three groups (corrective surgery, palliative surgery, and controls) did not differ with respect to maternal age, maternal education, marital status, family income, birth data (weight, lengths, head circumference), gestational age, Apgar scores, and age at neurodevelopmental examination. Infants who underwent corrective surgery did not differ from the palliative surgery group with respect to age at first surgery or use and duration of cardiopulmonary bypass; infants with corrected heart defects scored lower for rectal temperature during surgery than infants who underwent palliative surgery ( $p = 0.001$ ). Infants in the corrective surgery group had a shorter duration of hospital stay than those in the palliative surgery group ( $p = 0.001$ ). Also, the percentage of infants with repeated cardiac operations was smaller in the corrective group than in the palliative surgery group ( $p = 0.016$ ). At the

time of follow up, the percentage of children with microcephaly (head circumference < 3rd centile) and low body weight (weight < 3rd centile) was smaller in the corrective group than in the palliative surgery group ( $p = 0.053$  and  $p = 0.003$ , respectively).

#### Neurodevelopmental examination before surgery

Of the 68 infants who underwent neurodevelopmental examination before first cardiac surgery, 25 (37%) had neurological abnormalities that were judged to be mild in 23 (92%) and moderate in two (8%). Neurological abnormalities were seen in 19 of 58 infants (33%) before corrective surgery, compared with six of 10 infants (60%) before palliative surgery ( $p = 0.1$ ) (table 4).

#### Early clinical course after surgery

All infants had normal cranial ultrasound scans before surgery. Two infants had intracranial haemorrhage after surgery, one with interrupted aortic arch who underwent corrective surgery, and one with tetralogy of Fallot who received a central aortopulmonary shunt. Both suffered clinical seizures. Four further infants developed seizure activity during the early postoperative course without abnormal findings in the cranial ultrasound scans. Thus, six of the 90 infants (7%) had seizures during the postoperative course (3/74 (4%)

**Table 4** Neurological findings in infants before corrective or palliative cardiac surgery (some infants had multiple neurological abnormalities)

	Corrective surgery (n=58)	Palliative surgery (n=10)
Overall abnormalities	19 (33%)	6 (60%)
Hypotonia	10 (17%)	2 (20%)
Hypertonia	7 (12%)	3 (30%)
Asymmetria	5 (9%)	2 (20%)
Strabism	3 (5%)	2 (20%)
Cerebral palsy	0	0

after corrective surgery compared with 3/16 (19%) after palliative surgery;  $p = 0.066$ ). None of these infants had seizures after discharge.

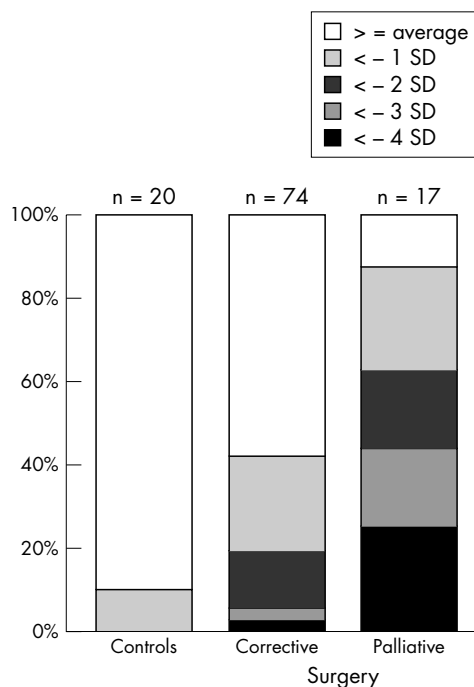
Both infants with intracranial haemorrhage showed developmental delay at 1 year of age (more than 2 SD below the mean of controls, see below). One suffered from cerebral palsy and the other had muscular hypotonia. All four infants with postoperative seizures but normal ultrasound scans had a normal developmental outcome at 1 year of age (developmental quotient within the mean  $\pm$  2 SD range of controls), with a normal neurological examination in three and muscular hypotonia in one.

#### Developmental testing

The time elapsed between the last date of cardiac surgery and the date of the neurodevelopmental examination was 9.6 months (range 1.8–13.7 months) in the corrective surgery group, and 9.8 months (range 2.1–13.2 months) in the palliative surgery group. Seventy nine per cent (71/90) were examined at least six months after the last cardiac surgical procedure. Only three infants (5%) underwent cardiac surgery during the two months before follow up, with a duration of hospital admission not exceeding three weeks.

The mean (SD) DQ in children who underwent cardiac surgery was 99 (10.6), and in the controls it was 106.7 (6.6) ( $p < 0.001$ ). DQ values were lower in infants after palliative surgery (88 (12.2)) than after corrective surgical procedures (101.4 (8.6);  $p < 0.001$ ). The DQ of the children who underwent only one surgical intervention was slightly higher than in children with more than one cardiac operation ( $p = 0.022$ ). However, DQ did not differ between children with one surgical intervention and those with repeated operative procedures in either the corrective surgery group (101.8 (8.4)  $v$  98.5 (10.6);  $p = 0.38$ ) or the palliative surgery group (89.7 (17.3)  $v$  85.1 (9.7);  $p = 0.33$ ).

Twenty four of the 90 infants (27%) who underwent cardiac surgery and none of the controls had a DQ below 93.5, equivalent to more than 2 SD below the mean of controls. Thus defined, developmental delay (DQ  $<$  93.5) was more common among infants who had undergone palliative surgery (10/16, 63%) than in the group who had undergone corrective surgery (14/74, 19%) ( $p < 0.001$ ). The relative percentage of infants with more severe developmental impairment was consistently higher in the palliative surgery group than in the corrective surgery group (fig 1). The differences in psychomotor development between controls and infants who had undergone cardiac surgery, as well as those between infants who had undergone corrective or palliative surgery, were evident throughout all five subscales (locomotor skills, personal and social skills, hearing and speech, eye–hand coordination, and cognitive performance), as shown in table 5. In all subscales, differences were significant for the comparison of cardiac surgery versus controls, with  $p$  values ranging from 0.001 to 0.046, and for the comparison of palliative versus corrective surgery, with  $p$  values ranging from  $<$  0.001 to 0.015.



**Figure 1** Developmental quotients at 1 year of age in infants with congenital heart disease who had undergone corrective or palliative surgery, respectively, compared with controls. Data of controls were used to calculate mean and standard deviation, and infants were then grouped accordingly.

The main categories of CHD that were surgically corrected showed comparable psychomotor developmental scores, with no differences noted in the statistical tests: transposition of the great arteries ( $n = 17$ ), DQ 103.9 (6.5); coarctation of the aorta ( $n = 10$ ), DQ 103.2 (8.9); atrial or ventricular septal defect or combination of both ( $n = 21$ ), DQ 101.7 (7.3); tetralogy of Fallot ( $n = 11$ ), DQ 101.2 (7.8). All groups scored higher than the infants with palliative cardiac surgery, with  $p$  values ranging from  $<$  0.001 to 0.005.

#### Neurological examination

Of the 90 infants who underwent cardiac surgery, 29 (32%) had neurological abnormalities—judged to be mild in 22 (76%) or moderate in seven (24%)—compared with one of the 20 control infants (5%) ( $p = 0.013$ ) (table 6). Neurological abnormalities were seen in 18 of 74 infants (24%) after corrective surgery, compared with 11 of 16 infants (69%) after palliative surgery ( $p = 0.0005$ ).

Of the 68 children who had neurological examination before surgery, 25 (37%) had neurological abnormalities. Nine (36%) also showed neurological abnormalities at 1 year (six children with corrected heart defects and three who underwent palliative surgery).

Of the 22 children who could not be examined neurologically before surgery, 10 (45%) had abnormal neurological status at 1 year (four of six children with palliative surgery and six of 16 children with corrected heart defects).

#### Infants not followed up

In all, 13 infants were lost to follow up, either because they lived too far away or because the parents were worried about subjecting the child to stress. With one exception, those infants had undergone corrective surgery. Otherwise, the 13 infants lost to follow up and the 90 infants who actually underwent neurodevelopmental assessment at 1 year of age did not differ significantly with respect to any of the variables in table 3.



**Table 5** Scores of developmental subscales in infants who had undergone corrective or palliative surgery, respectively, compared with controls

Scores	Corrective surgery (n=74)	Palliative surgery (n=16)	Controls (n=20)
Locomotor skills	99.4 (20.1)	73.5 (16.4)	108.2 (19.7)
Personal and social skills	103.0 (9.1)	91.3 (14.0)	107.7 (8.9)
Hearing and speech	94.9 (11.4)	85.1 (14.6)	98.6 (8.5)
Eye and hand coordination	101.7 (9.6)	91.6 (14.6)	109.8 (9.8)
Cognitive performance	102.5 (13.6)	92.5 (12.3)	109.7 (10.3)

**Table 6** Neurological findings at 1 year of age in infants who had undergone corrective or palliative cardiac surgery or controls (some infants had multiple neurological abnormalities)

	Corrective surgery (n=74)	Palliative surgery (n=16)	Controls (n=20)
Overall abnormalities	18 (24%)	11 (69%)	1 (5%)
Hypotonia	5 (7%)	7 (44%)	0
Hypertonia	6 (8%)	0	0
Asymmetry	8 (11%)	2 (13%)	1 (5%)
Strabismus	6 (8%)	2 (13%)	0
Cerebral palsy	0	1 (6%)	0

## DISCUSSION

Although the majority of children who underwent cardiac surgery in the first year of life had neurodevelopmental scores within the normal range at 1 year of age, we found an association between cardiac surgery in the first year and a significantly poorer performance on tests of developmental and neurological function compared with a control population tested at the same time. The magnitude of the effect was considerable, as the difference between the neurodevelopmental scores of the two groups was approximately 1.1 SD, and more than one quarter of all children studied after cardiac surgery were considered to be developmentally delayed. In addition, mild and moderate neurological deficits became apparent in nearly a third of the infants at the age of 1 year. More severe heart defects not amenable to surgical correction in the first year of life were accompanied by an increased risk of developmental and neurological abnormalities at 1 year. Nearly two thirds of the infants with complex cardiovascular malformations not amenable to corrective surgery showed developmental delay, and a similar number of infants displayed neurological deficits.

Our study group included infants with various types of CHD presenting the whole spectrum of congenital heart defects, with a variety of haemodynamic situations before and after surgery. These infants also differed with respect to the mode of surgical approach, the number of surgical interventions, and the chronological age at which surgery was performed. Therefore a multitude of risk factors may have contributed to the low developmental scores and the high neurological morbidity at 1 year in our cohort.

A subset of the children with complex CHD may have subtle congenital cerebral dysgenesis<sup>3 19 20</sup> not detected by cranial ultrasound before surgery, as well as submicroscopic chromosomal aberrations, both of which may influence neurodevelopmental outcome. The haemodynamic and homeostatic implications of CHD carry a significant risk for brain injury before cardiac surgery. Damage may be caused by cerebral venous thrombosis, thromboembolism, infarction, abscess formation, mycotic aneurysms, and hypoperfusion.<sup>6 21-24</sup> In this cohort of patients, minor neurological abnormalities were

found before surgery in more than a third of the infants examined, which is in agreement with findings from other centres.<sup>4 25-27</sup> However, only a third of infants with neurological abnormalities before surgery still had these at 1 year of age. In contrast to a recent study,<sup>27</sup> microcephaly in our cohort was a rare finding at birth. However, it was present in a quarter of the children at 1 year, the majority of whom had undergone palliative cardiac surgery. These findings underline the heterogeneous factors that may have an adverse influence on the developmental outcome of infants with CHD before and after surgery.

During surgery with cardiopulmonary bypass, the infant's brain may be subjected to global or focal ischaemia caused by gaseous and particulate microemboli and hypoperfusion.<sup>28-32</sup> Haemodynamic instability and medical complications during postoperative intensive care may then have additional adverse effects on the central nervous system.<sup>5 33</sup> The developing brain shows great vulnerability during synaptogenesis, also known as the brain growth spurt, which in humans extends from the sixth month of gestation into the first year of life.<sup>34</sup> During this time, exposure of the brain to barbiturates, benzodiazepines, and several other neurotropic drugs commonly used in paediatric anaesthesia and intensive care medicine may cause widespread apoptotic neurodegeneration, deleting millions of neurones.<sup>35</sup> Excitotoxic sequelae of ischaemic events may be aggravated in the developing neonatal brain, showing patterns that are quite different from those observed later in life.<sup>36</sup>

In calculating the age at evaluation we subtracted any time during which an infant was sedated or mechanically ventilated, and this led to a conservative estimate of the infant's psychomotor retardation, using mean and SD of the population standard (105.6 and 8.0) dating from the 1970s<sup>18</sup> instead of those of the control group (106.7 and 6.6). This could have reduced the number of infants with CHD who were considered to have developmental delay. Higher scores in an actual control group, as compared with scores that would be expected from the standardised norms of the Griffiths test, have also been observed recently in England.<sup>7</sup> While these considerations may be important for the interpretation of the data gathered, they do not change the pattern of the results. Interestingly, the overall magnitude of neurological deficits and psychomotor retardation of the children with corrected heart defect in this investigation was similar to that in a study of 1 year old infants with transposition of the great arteries who had undergone open heart surgery using cardiopulmonary bypass with or without circulatory arrest.<sup>9</sup>

In addition to conditions causing frank or subtle brain damage, developmental delay in children with severe CHD has been attributed to four further factors<sup>7</sup>:

- children with cyanotic CHD are often physically less able to interact with their environment, limiting their exploratory behaviour
- maternal overprotectiveness may limit the child's social interaction
- the inconsistent human and physical environment encountered during prolonged and repeated hospital admissions may compromise psychomotor development

- feeding difficulties may make parents feel inadequate, causing them to withdraw emotional support from their infant.

These factors are apparently related to illness severity, and the CHD infants having palliative surgery not only comprised those with the most severe illness, as measured by prolonged and repeated hospital admissions, but they also had the worst neurodevelopmental outcome. However, the data from this investigation are not suitable for identifying the relative contributions of medical and psychosocial factors.

Although developmental tests such as the Griffiths developmental scales have concurrent validity, there are several limitations inherent in testing at the age of 1 year. The scores of 12 month old children have limited predictive validity.<sup>37, 38</sup> Domains such as language or visual-motor integration are not easily tested in very young children,<sup>39</sup> and the abilities of these children will become more evident in the ensuing years.

## Conclusions

Infants undergoing cardiac surgery have an increased risk for poor neurodevelopmental outcome at 1 year of age. Neurodevelopmental deficits are especially prominent in infants with complex cardiac malformations in whom only palliative surgery is possible in the first year of life. As the majority of these infants are candidates for additional surgical procedures (for example, a Fontan operation), their overall risk for neurodevelopmental deficits later in life may increase even further. We conclude that neurodevelopmental monitoring is highly desirable for infants and children with complex cardiac malformations, to provide more information about the risk factors, about when to institute preventive measures, and about when to start early intervention programmes. It is important that all children needing surgical intervention be monitored neurodevelopmentally, starting in early infancy, and that those with developmental deficits be identified. Early intervention programmes may have a positive influence on these children's development.<sup>40</sup> Assessments of the children during the ensuing years of life will clarify the degree to which they can compensate for their deficits, and whether our findings have clinical importance for later academic achievement.

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