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Arch Dis Child Educ Pract Ed 2010 95: 98-104
doi: 10.1136/adc.2007.126672

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Accepted 7 March 2010

There is an increased incidence of congenital heart disease among children with Down syndrome. The most common lesion is complete atrioventricular septal defect (cAVSD). Failure to recognise this defect early in life can have very serious consequences. Hence, in this paper, we have chosen to focus more on this lesion than on others. Children with cAVSD and already irreversible pulmonary vascular disease continue to present in paediatric cardiology clinics too late for corrective surgery to be carried out. The child's future health, and indeed survival, may be severely compromised by late diagnosis. This suggests that the importance of diagnosis in the first few weeks of life is not universally recognised.

The early recognition of cAVSD and other major shunt lesions is of paramount importance, but despite this, we explain that urgent indiscriminate referral to paediatric cardiologists of all newborns with the syndrome is not necessary. We will outline surveillance principles that should allow child health teams to develop effective screening protocols appropriate to local service provision and level of clinical experience and specialist interest available.

BACKGROUND

In a population not affected by prenatal diagnosis, between 40% and 60% of babies born with Down syndrome have congenital heart defects. Of these, 30%–40% are cAVSDs.[1–3] Conversely, approximately 80% of all cAVSDs occur in children with Down syndrome.[4–6]

With regard to the prevalence of other cardiac anomalies, we have not found any contemporary studies that describe, in samples of reasonable size, the frequency and range of lesions identified by echocardiography. There are several earlier studies from which we have chosen, as an illustration, two population-based studies.[1 2] (table 1).

In these two studies, because very few lesions were identified by echocardiography, findings from clinical examination, electrocardiogram (ECG), cardiac catheterisation, surgery and autopsy were used instead. Direct comparison of the two studies cannot be made. There are differences in classification of defects that are further compounded by a mixture of natural variation, differences in ascertainment, diagnostic methods and the longer follow-up of Frid's study. Both studies, however, serve to illustrate the range and the frequency of lesions that may be present.

It is not clear how prenatal diagnosis impacts on these figures. Data from Oxford (2000–2007; T Boyd and N Manning, John Radcliffe Hospital, Oxford, personal communication, 2007) show that of 28 families of babies with prenatal diagnoses of Down syndrome and cAVSD, 11 (39%) opted for termination. Of 256 families of babies with Down syndrome (cardiac status unknown), 174 (69%) opted for termination. Hence, the presence of cAVSD does not seem to be a powerful predictor for termination.

With a risk figure for Down syndrome of 1.1 per 1000 live births and 722 500 UK live births in 2005,[7] the number of children born with Down syndrome in 2005 would be predicted as 795. Hence, there are likely to be around 397 babies born every year in the UK who have Down syndrome and a congenital heart defect, of whom around 139 can be expected to have cAVSD. It is for these 139 children that early diagnosis is of paramount importance. The drive towards early identification of cAVSD will of course also reveal the presence or absence of other cardiac lesions.

- In the UK, there are likely to be 795 babies born with Down syndrome every year.
- Three hundred and ninety-seven are likely to have congenital heart disease.
- One hundred and thirty-nine are likely to have cAVSD.
- Early diagnosis of cAVSD is of paramount importance.
- Specific early screening programmes are effective in achieving this.
- Surgical intervention for those with cAVSD must take place in early infancy.

NATURAL HISTORY OF cAVSD IN CHILDREN WITH DOWN SYNDROME AND RESPONSES TO INTERVENTION

Irreversible pulmonary vascular disease develops earlier in individuals with Down syndrome with particular structural cardiac lesions than in those without the syndrome. This is particularly important in cAVSD[8–11] but is not universal. Pulmonary vascular disease may very occasionally be present at birth but should not be confused with persistent pulmonary hypertension of the newborn (discussed later), which may occur in the absence of cardiac disease. A few cases are reported by age 3 or 4 weeks. Suzuki *et al*[10] reported irreversible pulmonary vascular disease in three children with

Table 1 Cardiac lesions in children with Down syndrome

Distribution of lesions among those with CHD	
Torfs *et al*[2]	cAVSD 30%
Californian Birth Defects Monitoring Programme	Tricuspid valve defects 20%
Births 1983–1993	ASD and foramen ovale 11.2%
No. babies with Down syndrome 2894	Ventricular septal defects 11.4%
Follow-up to age 1 year	Coarctation and other aortic anomalies 10%
Proportion with CHD 56%	Tetralogy of Fallot 4.5%
	Isolated PDA 6.0%
Frid *et al*[1]	cAVSD 11.2%
Northern Sweden. Down syndrome mortality study	Partial AVSD 5.8%
Register based	Secundum ASD 7.7%
Births 1973–1980	Ventricular septal defects 32.7%
No. babies 219	Tetralogy of Fallot 1.9%
Follow-up to minimum 14 years	PDA persisting after first year 1.9%
Proportion with CHD 47.5%	

ASD, atrial septal defects; cAVSD, complete atrioventricular septal defect; CHD, congenital heart disease; PDA, patent ductus arteriosus.

cAVSD aged 3–4 months. Clapp *et al*[8] reported 12% with irreversible changes by age 1 year. Hence, surgical intervention must take place in early infancy to ensure optimum outcome. Similar considerations with respect to the need for early diagnosis apply to other lesions that may allow high pressure and/or flow into the lungs, such as ventricular septal defect, patent ductus arteriosus and partial atrioventricular septal defect.

Persistent pulmonary hypertension of the newborn. Physicians caring for newborns with Down syndrome will have experienced those with persistent pulmonary hypertension of the newborn who do not have cardiac disease. For most of the survivors, the condition resolves spontaneously, but follow-up should continue until that time.[12]

The impact of corrective surgery

The possibility and the advisability of effective corrective surgery for cAVSD in children with Down syndrome were being discussed widely in the UK by the early 1980s. Reports from Birmingham, Alabama and elsewhere were indicating that operative outcome could be very good. Before this, some children had pulmonary artery banding to protect the pulmonary vascular bed until such time as the child was large enough for full correction to be considered. Others were only offered standard cardiac medical treatment. Mortality and morbidity were high. A key issue in the debate about corrective surgery concerned long-term survival and quality of life after operation. One view was that surgery would confer little benefit and that long-term survival would be a little different from that which could, in any case, be expected for children with Down syndrome. The opposite view was that later death due to the Eisenmenger complex among those who had not undergone corrective surgery was barely tolerable and no child should be subjected to this outcome if it could be prevented by surgery.

In 1985, Bull *et al*[13] reporting from the paediatric cardiology department at the Brompton Hospital reviewed the mortality and the morbidity of 67 children with Down syndrome and cAVSD who had had no surgical intervention. Eight (12%) had died in infancy from the consequences of excessive pulmonary blood flow. Eighty per cent were alive, most with Eisenmenger complex, but with a reasonable quality of life at age 15 years. Thereafter, death became more common. A further review from the same unit 9 years later[14] revealed increasing deaths from age 20 years. Among the survivors, cardiac disability increased as they got older. None was asymptomatic. Most had either mild symptoms of cardiac dysfunction on exertion or had markedly restricted exercise capacity. None was bed bound or totally wheelchair-dependent. The oldest was aged 40 years.

It has been questioned whether those with Down syndrome form a high-risk group and, therefore, impose an unreasonable burden on healthcare resources. In 2006, Roussot and colleagues addressed this issue in relation to their own surgical practice in Cape Town, South Africa. They compared outcomes of early cardiac surgery in children with Down syndrome and those without who had undergone cardiac surgery between 1998 and 2003. There was no significant difference between the two groups in the burden that was placed on the healthcare system. Similar complication rates, reoperation rates and early mortality were recorded for both groups. The Down syndrome group seemed to benefit more from cardiac surgery than the non-Down syndrome group. They concluded that "denying cardiac surgery to children with Down syndrome does not improve the efficiency of resource allocation".[15]

The evidence, therefore, is that without surgical intervention, the outcome of cAVSD is death or significant cardiac disability; there are no contraindications in resource allocation; hence, the case for surgery now seems irrefutable.

Outcome after early corrective surgery

Only 20 years later, the almost-universal referral of all babies with Down syndrome and cAVSD for early full corrective surgery represents the single most radical advance in the care of children with Down syndrome. UK national data for 2007/2008 gives 3.6% overall mortality for all infants for correction of cAVSD.[16] Data from Goteburg[4] from the early 1990s show only 3% mortality for operations carried out in the first year of life. Many of those children had Down syndrome. For those with Down syndrome operated on in the first year of life, Suzuki and colleagues from Japan report 8% mortality, but three of the five who died already had irreversible pulmonary vascular disease at the time of operation.[10]

There are as yet few reports about long-term outcome of cardiac surgery for those with Down syndrome, but there is accumulating evidence that surgical outcome is best if surgery takes place in the first year and surgery is increasingly practiced before age 4 months. Suzuki *et al*[10] followed-up 75 survivors for a median period of 6 years. Only 13% of those operated on in the first year had

residual pulmonary vascular disease as against 46% of those operated at a later age. Michielon *et al*[17] used survival analysis to show 92.9% survival at age 14 years of those operated on before 4 months as against 75.9% survival at age 15.4 years of those operated on after 4 months. Tubman and colleagues reported in 1996 that most of those teenagers who had survived corrective repair in Belfast in the 1970s and 1980s were currently in good health and free of cardiac medication (B Craig, conference presentation, Belfast, personal communication, 1996).

SURVEILLANCE AND SCREENING

Are early screening programmes effective in reducing morbidity and mortality?

The possibility of serious cardiac disease must be considered urgently whenever a baby is born with Down syndrome. Every child health team needs to be aware of this and must have an agreed screening protocol in place to ensure early diagnosis. The impact of changing attitudes, a specific screening programme and universal screening by neonatal cardiac echocardiogram is highlighted by Amark and Sunnegårdh.[4] In 1970, the calculated median age of diagnosis of cAVSD in Goteburg was 861 days in children with Down syndrome as against 56 days in infants without Down syndrome. In 1996, after screening had been introduced, children with Down syndrome were found to have cAVSD earlier than those without, the median ages being 4 and 33 days, respectively. There is no doubt, therefore, that specific screening programmes are effective in identifying those conditions that if unrecognised or recognised too late, result in death or serious lifelong morbidity.

Overall aim of early screening programmes

Because of the grave consequences of failure to diagnose cAVSD and other major shunt lesions, the overall aim of early screening must be to identify those babies with these defects sufficiently early to ensure that by the time surgery can take place, very few will already have irreversible pulmonary vascular changes.

The Down's Syndrome Medical Interest Group (DSMIG UK) recommends that by age 6 weeks the cardiac status of every child should be established and, for those with lesions, an action plan set in place.[18] They believe that from a practical point of view, this should be achievable over the very wide range of clinical settings that exist in the UK.

A knee-jerk reaction to this recommendation may be to think that all babies with the syndrome should have an echocardiogram in the first few days. Indeed, in many areas, this is what happens. However, we are aware (DSMIG membership, personal communication, 2009) that in some cases, newborn babies referred for a cardiological opinion have not been seen until well after the 6-week deadline. Delays occur for a variety of reasons including unavailability of clinic time, illness in the child and parental non-attendance. Awareness of these failures has led us to suggest that where early neonatal echocardiography is not available, an alternative two-stage diagnostic pathway can be followed. We suggest that this can be used when necessary to reduce the load of urgent referrals to paediatric cardiological services while still achieving the 6-week diagnostic goal.

The administrative protocols followed will vary from district to district according to local service provision and the level of clinical expertise and specialist interest available. Local audit of cases diagnosed and missed will provide useful background to inform service planning.

Diagnostic methods

Clinical examination

There is no doubt that clinical examination alone is insufficient to detect all of even the most serious heart disease in newborns and young babies.[6] A retrospective case review of all babies born with Down syndrome in Ireland from 1987 to 1989 showed that clinical examination in the early neonatal period missed 5 (39%) of 13 cases of cAVSD,[3] although the training and expertise of the staff doing the screening was very different from that likely to apply today. Wren *et al*[6] reviewed retrospectively an ad hoc policy where some but not all were referred for assessment simply because of Down syndrome. They found that only 41% of newborns had a cardiovascular abnormality on clinical examination. Thirty-four per cent of those with congenital heart disease remained undiagnosed at 6 weeks; and 24%; at 12 weeks.

ECG and chest *x* ray

In 1999, Narchi[19] carried out neonatal ECG on 37 newborns with Down syndrome and reported that in this small group, sensitivity and specificity of a superior QRS axis to diagnose complete cAVSD were 100% and 96.8%, respectively. However, the predictive value of neonatal ECG for other congenital heart disease was poor. Ten years earlier, Tubman and colleagues[3] had carried out a retrospective screening survey of all babies with Down syndrome born in Northern Ireland between November 1987 and November 1989 comparing chest *x* ray (CXR) and ECG with the criterion standard of echocardiography. CXR alone missed 39% of the cases of cAVSD, whereas ECG missed only 17%. Combining CXR, ECG and clinical examination gave little added benefit with only 15% missed (see fig 1). Hence, there is no evidence that CXR is a useful addition for neonatal diagnosis of serious heart disease.

Echocardiography

Paediatric echocardiography is now widely accessible in the UK. Although acknowledging that trained and experienced observers using clinical examination and ECG in the neonatal period rarely miss major cardiac lesions (discussed previously), it has become standard practice in many areas to refer all babies with the syndrome for echocardiography. It must, however, be born in

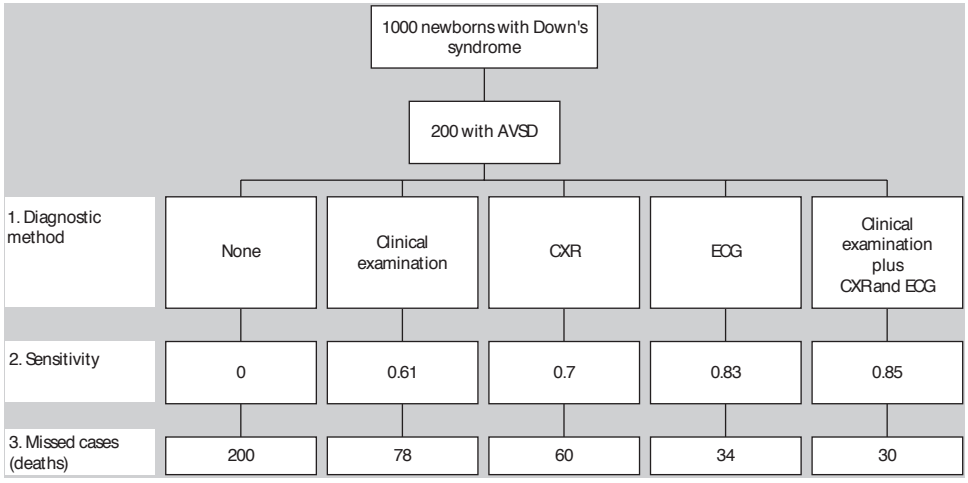

Figure 1 Atrioventricular septal defect: prediction of missed cases of cAVSD in 1000 newborns with DS according to diagnostic methods used in the neonatal period (adapted from Tubman *et al*).[3]

mind that although neonatal echocardiography is undoubtedly the most effective single diagnostic procedure, it is

- not necessarily the only effective screening method;
- to some extent, subjective and must be carried out by an appropriately trained person;
- not 100% effective in identifying lesions, particularly in the first week or so of life;
- likely to identify many babies with shunts through ductus arteriosus and foramen ovale, which are physiological and are going to resolve, but in the meantime, place burdens on families and healthcare resources.

In 1998, Chong *et al*[20] reviewed retrospectively a birth cohort of 94 children with Down syndrome born between 1982 and 1996. There had not been a policy of routine echocardiography or paediatric cardiology referral. Twenty five children had never had an electrocardiogram, but all had had, as newborns, careful clinical examination and ECG. Twenty of these were recalled in later childhood for echocardiogram to see if any lesions had been missed. There were none. The remaining five were reported as being in excellent health. All the cases of cAVSD had been suspected within the first 3 days, and in all of those born since 1983, cAVSD was confirmed within 1 week of birth. Hence, in some clinical settings, neither routine echocardiography nor cardiology referral is essential to diagnose all cases of congenital heart disease before 6 weeks. It is important, however, to emphasise that this finding derives from an area where there was, at the time, a specific dedicated, integrated medical and surgical service for babies and young children with Down syndrome and hence an overall heightened awareness of possible problems among these children.

Key points for developing a screening protocol

A simplistic solution to ensure adequate screening could be the immediate referral of all newborns for urgent echocardiography. In some localities, however, this may be impractical, and where this is so, it is important to recognise that other diagnostic routes are available. In recommending a screening protocol, it is essential to bear in mind that the goal is more important than the pathway chosen, and it is up to those developing local screening pathways to decide how best local services and resources can be used to achieve the 6-week diagnostic goal. The following questions may arise.

Diagnostic key points

- Clinical examination alone is insufficient to detect all of even the most serious heart disease in newborns and young babies.[3 6]
- Superior QRS axis on ECG is highly predictive of cAVSD.[19]
- CXR is not useful for diagnosing cAVSD in the neonatal period.[3]
- Neonatal echocardiography is undoubtedly the most effective single diagnostic procedure, but it is not 100% effective in identifying lesions in the early neonatal period and has drawbacks and resource implications (see text).
- Neonatal echocardiography must always be carried out by an appropriately trained person. However, even in the most expert hands, it is not foolproof.

1. Is it necessary to refer all babies to a paediatric cardiologist?

Formerly, in the UK, paediatric echocardiography was carried out only by paediatric cardiologists or specialist echocardiographers. However, the situation is now evolving, whereby increasing numbers of paediatricians are receiving training in cardiology and echocardiography. Hence, it is not always necessary to refer babies to a specialist paediatric cardiologist for echocardiography or indeed for expert cardiovascular screening.

2. *The availability of appropriate neonatal echocardiography services varies throughout the country. How can available services best be used? Is it possible to prioritise those newborns most urgently in need of echocardiography?*

On the basis of the above evidence, it is clear that abnormal clinical signs and/or ECG abnormality, in particular a superior QRS axis in the neonatal period, are predictors of cAVSD and, therefore, of a group at risk of early pulmonary vascular disease. Hence, it is reasonable to suggest that these babies should be prioritised for very early expert assessment. Hence, DSMIG[18] recommends that

> **Where facilities for expert neonatal echocardiography are not readily available all newborns with the syndrome should have a careful clinical examination and ECG and those with abnormalities as above should be prioritised for very early echocardiogram (by age 2 weeks). Expert cardiovascular assessment by someone with appropriate paediatric cardiological training should have been carried out and an action plan set in place by 6 weeks.**

The prioritisation to 2 weeks for those likely to be most at risk is not evidence based but is suggested as a way in which to reduce the load of urgent referrals for expert cardiovascular assessment.

There is no doubt that those without abnormal clinical signs and with a normal ECG on initial evaluation may, nevertheless, have cardiac disease, including occasionally cAVSD. To achieve the 6-week overall diagnostic goal, DSMIG recommends that

> **Newborns with no abnormal clinical signs and normal ECG should be referred and seen by age 6 weeks for echocardiogram followed by expert cardiological assessment by someone with appropriate paediatric cardiological training.**

3. *Will echocardiogram screening in the first weeks of life fail to detect any significant lesions?*

We caution against overreliance on negative echocardiogram findings in the early weeks. A few children continue to present in specialist clinics with previously undiagnosed cAVSD and other large shunt lesions that were missed on a single early echocardiogram. In some of these cases, the echoes had been carried out at tertiary paediatric cardiology centres. Even in the most expert hands, the procedure is not foolproof (N Archer; R Tulloh; J Dennis, DSMIG, Oxford, and C Ward, Emeritus Professor Paediatrics, Dublin, personal communication)

> **It is, therefore, essential to carry out a careful clinical appraisal of the cardiovascular system for all children who present in routine clinics even if they are said to have had a normal echocardiogram in the neonatal period. There should be a low threshold for ECG and referral for further echocardiography if there are signs or symptoms that suggest the possibility of cardiac disease at any age.**

Newborns who have had fetal echocardiography

Routine antenatal obstetric screening using the usual four-chamber heart view in fetuses not known to have any problems misses around two thirds of cAVSD cases.[21 22] The pickup rate after detailed fetal echocardiography in those known to have trisomy[21] is likely to be much higher. However, it is prudent to follow the above neonatal pathway for all babies with Down syndrome even if fetal echocardiography has been negative.

Screening outside the neonatal period

It is not unusual for older children who have never had an echocardiogram to present for assessment. There may have been a late diagnosis of Down syndrome; the diagnosis may be suspected for the first time in the clinic; the child may previously have been looked after overseas; or

Newborn surveillance key points

- Every child health team needs to have an agreed screening protocol in place to ensure the early diagnosis of serious heart disease in babies with Down syndrome.
- Around 397 babies with Down syndrome and congenital heart disease are born every year in the UK, of whom 139 can be expected to have cAVSD.
- Without surgical intervention, the outcome of cAVSD is significant cardiac disability and premature death.
- The cardiac status of every baby with Down syndrome should be established, and where appropriate, an action plan should be set up by age 6 weeks.
- Surgical intervention for major shunt lesions must take place in early infancy to ensure optimum outcome.
- All newborns with the syndrome in addition to careful clinical examination should have either neonatal echocardiography or ECG.
- Those with abnormal early neonatal echocardiogram should have an expert cardiological assessment by age 2 weeks and an action plan set in place by age 6 weeks.
- Those who have not had early neonatal echocardiography but who have abnormal clinical signs or ECG should be referred and seen for echocardiogram and expert cardiological assessment within 2 weeks of birth, and an action plan should be set in place by 6 weeks.
- Babies who have not had neonatal echocardiography but have no abnormal signs or ECG abnormality should have an echocardiogram by age 6 weeks in conjunction with an expert cardiological assessment.

echocardiography has simply never been carried out. All should have a careful clinical examination and ECG. Those who are symptomatic and/or have abnormal clinical signs or ECG should be referred urgently to someone with appropriate paediatric cardiological training. Those with no symptoms or clinical signs and normal ECG should be referred routinely for specialist cardiological assessment and possible echocardiography.

Other considerations for long-term care and surveillance

Management of other cardiac lesions

If early cardiac surveillance protocols are in place as suggested above, lesions other than major shunt lesions will also be identified by age 6 weeks. Thereafter, it is likely that most of these children will come under ongoing surveillance by someone with appropriate cardiological training and will be managed as for any child in the population. However, it is always possible that a cardiac lesion is missed on initial screening, and vigilance on this account is always necessary when carrying out routine reviews that are recommended for all children with Down syndrome.[23]

Infective endocarditis risk

Current endocarditis preventive measures apply to individuals with Down syndrome and structural congenital heart disease.[24] Therefore, for those with cardiac disease presenting at routine clinics, paediatricians should check that parents and carers have been made aware of endocarditis risk and have written information appropriate to their own child. Information cards from the British Heart Foundation (BHF)[25] are useful, and local paediatric centres and cardiology clinics are also likely to have their own preferred literature. The BHF recommends that those with flu-like symptoms and high temperature lasting more than a week should go to their general physician, taking the BHF card with them. They stress the importance of good oral hygiene and avoiding body piercing, tattooing and injection of recreational drugs.

Cardiovascular problems secondary to airway/respiratory disease

As with other children, those with Down syndrome and a normal heart can develop pulmonary vascular disease and right heart failure secondary to airway/respiratory problems. Sleep related breathing disorders have a high prevalence among those with the syndrome, and enquiry about symptoms should always be made as part of ongoing child health surveillance.[26]

Mitral valve prolapse and aortic regurgitation in late adolescence

From late adolescence onwards, there is evidence of an increased incidence of asymptomatic mitral valve prolapse and aortic regurgitation.[27–30] Some guidelines recommend echocardiography in late adolescence to identify these conditions, but we can find no evidence of long-term benefit of such screening. We and some of our colleagues have carried out late adolescent cardiac echocardiography on small samples of our local clinic populations with no positive results. It cannot be predicted which of those with mitral valve prolapse and/or aortic regurgitation will progress later in life to mitral valve regurgitation, which for a minority, may become symptomatic.

The presence of mitral valve regurgitation and/or aortic regurgitation is an indication for ongoing cardiac follow-up and endocarditis advice. These lesions are usually identified on auscultation.

We, therefore, recommend that auscultation should always be carried out as part of the transition medical assessment. Relevant information should be given to the family and passed on to adult services concerning the need for ongoing clinical vigilance in this area.

Acknowledgements The authors are indebted to those other members of the steering group who revised the DSMIG cardiac guideline: Drs Pat Charleton, Marian McGowan and Rob Tulloh, and to Mrs Penny Green who represented the Down's Heart Group.

Competing interests None.

Provenance and peer review Commissioned; externally peer reviewed.

REFERENCES

1. **Frid C**, Drott P, Lundell B, *et al.* Mortality in Down's syndrome in relation to congenital malformations. *J Intellect Disabil Res* 1999;**43**:234–41.
2. **Torfs CP**, Christianson RE. Anomalies in Down syndrome individuals in a large population-based registry. *Am J Med Genet* 1998;**77**:431–8.
3. **Tubman TR**, Shields MD, Craig BG, *et al.* Congenital heart disease in Down's syndrome: two year prospective early screening study. *BMJ* 1991;**302**:1425–7.
4. **Amark K**, Sunnegårdh J. The effect of changing attitudes to Down's syndrome in the management of complete atrioventricular septal defects. *Arch Dis Child* 1999;**81**:151–4.
5. **Hanley FL**, Fenton KN, Jonas RA, *et al.* Surgical repair of complete atrioventricular canal defects in infancy. Twenty-year trends. *J Thorac Cardiovasc Surg* 1993;**106**:387–94; discussion 394–7.
6. **Wren C**, Richmond S, Donaldson L. Presentation of congenital heart disease in infancy: implications for routine examination. *Arch Dis Child Fetal Neonatal Ed* 1999;**80**:F49–53.
7. Office for National Statistics. Key population and vital statistics. Series VS No 32. Table 4.2a, 2005. http://www.statistics.gov.uk/downloads/theme _ population/KPVS32 _ 2005/KPVS2005.pdf.
8. **Clapp S**, Perry BL, Farooki ZQ, *et al.* Down's syndrome, complete atrioventricular canal, and pulmonary vascular obstructive disease. *J Thorac Cardiovasc Surg* 1990;**100**:115–21.
9. **Soudon P**, Stijns M, Tremouroux-Wattiez M, *et al.* Precocity of pulmonary vascular obstruction in Down's syndrome. *Eur J Cardiol* 1975;**2**:473–6.
10. **Suzuki K**, Yamaki S, Mimori S, *et al.* Pulmonary vascular disease in Down's syndrome with complete atrioventricular septal defect. *Am J Cardiol* 2000;**86**:434–7.
11. **Yamaki S**, Yasui H, Kado H, *et al.* Pulmonary vascular disease and operative indications in complete atrioventricular canal defect in early infancy. *J Thorac Cardiovasc Surg* 1993;**106**:398–405.
12. **Shah PS**, Hellmann J, Adatia I. Clinical characteristics and follow up of Down syndrome infants without congenital heart disease who presented with persistent pulmonary hypertension of newborn. *J Perinat Med* 2004;**32**:168–70.
13. **Bull C**, Rigby ML, Shinebourne EA. Should management of complete atrioventricular canal defect be influenced by coexistent Down syndrome? *Lancet* 1985;**1**:1147–9.

14. **Shinebourne EA**, Carvalho JS. Atrioventricular septal defect and Down's syndrome. In: Yacoub M, Pepper J, eds. *Annual of cardiac surgery.* 7th *edn.* London: Current Science, 1994:60–77.
15. **Roussot MA**, Lawrenson JB, Hewitson J, *et al.* Is cardiac surgery warranted in children with Down syndrome? A case-controlled review. *S Afr Med J* 2006;**96**:924–30.
16. Central Cardiac Audit Database. Congenital heart disease. Specific Procedures National Data, 2005 http://www.ccad.org.uk/002/congenital.nsf/WBenchmarksYears?openview&RestrictToCategory=2005&start=1&count=500.
17. **Michielon G**, Stellin G, Rizzoli G, *et al.* Repair of complete common atrioventricular canal defects in patients younger than four months of age. *Circulation* 1997;**96**:II–316–22.
18. DSMIG UK. Guidelines for essential medical surveillance for people with Down's syndrome, 2007. http://dsmig.org.uk/library/articles/guideline-cardiac-5.pdf.
19. **Narchi H**. Neonatal ECG screening for congenital heart disease in Down syndrome. *Ann Trop Paediatr* 1999;**19**:51–4.
20. **Chong ESF**, Dennis J, Archer N. The effectiveness of screening for congenital heart disease in a 14 year birth cohort of children with Down's syndrome. Proceedings of the RCPCH Annual Spring Meeting. *Arch Dis Child* 1998;**2**:63; Abstract G94.
21. **Chew C**, Stone S, Donath SM, *et al.* Impact of antenatal screening on the presentation of infants with congenital heart disease to a cardiology unit. *J Paediatr Child Health* 2006;**42**:704–8.
22. **ter Heide H**, Thomson JD, Wharton GA, *et al.* Poor sensitivity of routine fetal anomaly ultrasound screening for antenatal detection of atrioventricular septal defect. *Heart* 2004;**90**:916–17.
23. DSMIG UK. *Insert for personal child health record for babies born with Down's syndrome*. 2nd edn. South Shields: Harlow Printing, 2000. http://www.harlowprinting.co.uk.
24. NICE Guideline. Prophylaxis against infective endocarditis. http://www.nice.org.uk.
25. British Heart Foundation. Endocarditis warning card. 2008. http://www.bhf.org.uk.
26. **Fitzgerald DA**, Paul A, Richmond C. Severity of obstructive apnoea in children with Down syndrome who snore. *Arch Dis Child* 2007;**92**:423–5.
27. **Geggel RL**, O'Brien JE, Feingold M. Development of valve dysfunction in adolescents and young adults with Down syndrome and no known congenital heart disease. *J Pediatr* 1993;**122**:821–3.
28. **Goldhaber SZ**, Brown WD, Sutton MG. High frequency of mitral valve prolapse and aortic regurgitation among asymptomatic adults with Down's syndrome. *JAMA* 1987;**258**:1793–5.
29. **Hamada T**, Gejyo F, Koshino Y, *et al.* Echocardiographic evaluation of cardiac valvular abnormalities in adults with Down's syndrome. *Tohoku J Exp Med* 1998;**185**:31–5.
30. **Pueschel SM**, Werner JC. Mitral valve prolapse in persons with Down syndrome. *Res Dev Disabil* 1994;**15**:91–7.