

CHARGE association looking at the future — the voice of a family support group

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Summary CHARGE association is a non-random collection of congenital anomalies. The condition is becoming more widely known to medical and educational professionals. The number of children diagnosed is increasing, probably because of the greater awareness of this condition. This paper considers some of the long-term management problems which are often deferred in the early months, when acute life threatening problems take priority.

Questionnaires were sent to parents via the CHARGE Association Family Support Group, UK. Thirty-nine were returned and incomplete information was sought by personal contact or telephone. The majority of children were known professionally to one or both authors and information was therefore checked from medical and educational notes.

There is still widespread misunderstanding about the impact of multiple disability, especially when this includes multi-sensory impairment, on the early development of the child. Therefore, the information collected from the study has been from an educational and medical perspective, thereby aiding the understanding of these complex problems.

At the parents request, information was gathered about certain teratogens, of which Lindane, an organophosphate, is highlighted.

Keywords CHARGE association colobomata choanal atresia deaf blind multi-sensory impairment

INTRODUCTION

CHARGE Association was first described by Hall (1979) but the acronym 'CHARGE' was first used by Pagon *et al.* (1981). This is, therefore, a relatively newly-recognized condition. The acronym 'CHARGE' is used to describe a heterogeneous group of children who exhibit at least four of the features prefixed by the letters of the acronym and including one or other of choanal atresia and colobomata.

C = Coloboma: these may be of the iris and/or retina. Anophthalmos or microphthalmia are also part of the coloboma spectrum.

H = Heart defect: heart lesions may be simple acyanotic defects (i.e. patent *ductus arteriosus*) or complex cyanotic conditions (i.e. Tetralogy of Fallot).

A = choanal Atresia: a blockage of the passage between the nasal cavity and the naso-pharynx, which can be unilateral or bilateral, membranous or boney.

R = growth Retardation (developmental delay).

G = Genitalia anomalies: microphallus and/or cryptorchidism in boys. Anomalies in girls are rare.

E = Ear anomalies: these can affect the external ear (lop or cup shaped), middle ear (ossicular malformations, stapedius tendon anomalies, chronic serous otitis) and/or internal ear (sensori-neural deafness).

In addition to the features listed above, evidence has been offered to support the inclusion of other anomalies within the spectrum of CHARGE association. These include large tongue size (Lin *et al.* 1990) facial palsy, orofacial clefts, renal anomalies and oesophageal atresia (Oley *et al.* 1988) laryngeal malformations and skeletal anomalies (Blake *et al.* 1990).

Mental retardation was thought to be a characteristic feature of the association. However, in the literature of the 1990s the developmental delay that the children exhibit is now thought to be as the result of the other anomalies rather than an integral part of the association itself. There is a growing number of children who do not quite meet the criteria for inclusion within the CHARGE mnemonic which makes us believe that this is a spectrum and the condition may have a heterogeneous aetiology.

METHOD

The study was initiated by parent members of the CHARGE Association Family Support Group (UK). A parent questionnaire was prepared by a paediatrician (K.D.B.) and a teacher of multi-sensory impaired children (D.B.). Forty-eight questionnaires were sent out to parents who had children diagnosed with the CHARGE association. The questionnaire was administered via the Family Support Group and was mostly circulated with their national newsletter. Thirty-nine questionnaires were completed and returned, missing or inadequate data was obtained by telephone or correspondence.

There were four families who answered the questionnaire, although their child with the CHARGE association had died. The continued involvement of these parents with the Family Support Group offers a valuable extra dimension to the group, and their co-operation with this project was greatly appreciated.

The data were collected into a paradox data base running on an IBM-PC and were analysed on an EPI-INFO version 5 epidemiological analysis package, Centres for Disease Control, Atlanta, Georgia, USA 1990 and stored on a paradox data base. All Chi-squared results include the Yates continuity corrector. For comparison of frequencies, where expected values were less than five, the Fishers Exact Test has been used and the two-tailed result presented. A non-parametric test (Mann-Whitney *U*-test) has been used when one or both distributions were significantly skewed.

RESULTS

Table 1 shows the frequency of occurrence of each of the anomalies that make up the CHARGE mnemonic including extra criteria suggested more recently (Oley *et al.* 1988). All cases were sporadic but in five families there was a past family history of congenital malformations. These were unilateral choanal atresia, tracheoesophageal atresia, cleft lip and ventricular septal defect, cleft lip and webbed fingers, and Cri du chat.

The age range of the children was 18 months–20 years with a mean age 6.0 years. The boys (22) outnumber the girls (17). Male children often have characteristically small external genitalia (20 out of 22) which is far less obvious in the girls, thus resulting in a greater likelihood of medical opinion being sought for the boys. There were

TABLE 1. Frequencies of the defects that make up the CHARGE association including the extra criteria

Defect	%	Number
Coloboma Iris	53 (50% bilateral)	19
Retina	89 (60% bilateral)	32
Heart defect	80	31
Atresia Choanae	64	
Bilateral	36	14
Unilateral	28	11
Retardation growth (height < 3rd centile)	74	25
Genitalia hypoplasia*	91	21
Ear anomalies		
External	87	34
Middle (grommets)	62	23
Internal (aids)	70	26
Facial palsy	58	22
Renal anomalies	31	12
Cleft lip/palate	18	7
Bony anomalies	32	12

*% from male population only ($n = 22$).

no girls with documented abnormal external genitalia in this group although there have been previous reported cases (Davenport *et al.* 1986).

There was some geographical clustering of the cases and certainly a north-south divide. The increased numbers in the south of the country probably reflect heightened awareness, and the location of the Support Group organizers, rather than any environmental factors.

Vision

There was information from 36 children about their eyes. Coloboma of the iris and/or retina was present in 92% ($n = 33$). Retinal coloboma (88% $n = 32$) was more prevalent than iris coloboma (53% $n = 19$).

Functional visual impairment (vision problem so severe that it interferes with the child's learning process [Langley 1980]) was present in 75% ($n = 24$) of the children. There was a weak trend towards children with functional visual impairment having retinal colobomata but this was not statistically significant (Fisher exact test $P = 0.08$). However, there was a statistically significant relationship between children with functional visual impairment having iris colobomata (Yates corrected $P = 0.01$).

When one considers that 75% of children had functional visual impairment, there was a disappointingly small proportion of children who had received input from a teacher of the visually impaired (31%). The children with bilateral retinal colobomata walked later than the children without both retinae being affected (Table 2) and all the children who wore tinted glasses, to prevent photophobia, had retinal coloboma.

Hearing

Hearing had been assessed in 37 children. Hearing impairment was noted in 92% of these ($n = 34$) with 70% ($n = 26$) of the children having been prescribed hearing aids. Children who needed hearing aids had statistically ($P = 0.027$) more chance of having balance problems. There were 23 (62%) children who underwent grommet operations with a mean of 1.5 operations (one child had five operations for grommet insertion).

Motor development

The children showed marked delays in their motor development and 18 of them bottom or back shuffled and did not crawl. There was a marked delay in both crawling (mean age 25 months) and bottom/back shuffling (mean age 20 months) and this correlates with the late mean age of walking, which is 4 years.

The bottom/back shufflers ($n = 15$) walked at a mean age of 56.7 months (SD 20.3) as compared with the crawlers ($n = 12$) who walked at 35.2 months (SD 10.4) which is a statistical significant association (Mann-Whitney U -test $P < 0.001$) (Figure 1).

TABLE 2. Coloboma and the age at walking in children with CHARGE association

Bilateral retinal Coloboma	n	Age of walking (months)	
		mean	SD
Yes	17	52.6	21.4
No	10	37.9	11.9

Non-parametric test $P = 0.042$.

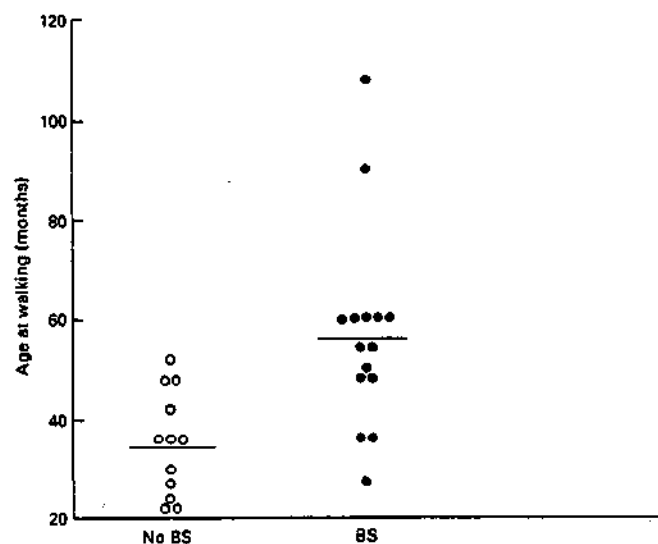


FIGURE 1. Age at walking for CHARGE association children. No BS = No Bottom Shuffling; BS = Bottom Shuffling; — mean age of walking for the two groups.

Education

Of the 30 children in school placements at the time of the survey (Table 3), 26 (87%) were in special schools and four (13%) were in mainstream schools. Only five children were in residential school placements. Of the 20 children not in SLD (severe learning difficulties) schools, 11 had normal intelligence, however, many of the remaining children had not received a relevant assessment by an expert in the 'deaf blind' field. It is also important to note that this group is self-selected, there are at least 8 CHARGE children known to

TABLE 3. School placement at time of questionnaire

School	Number of children	%
Hearing impaired	11	37
Severe learning difficulties	10	33
Mainstream with support	4	14
Hearing impaired*	2	7
Deaf blind unit	1	3
Visually impaired	1	3
Physically impaired	1	3
<i>n</i> = 30		100%

*Hearing impaired and special needs.

the authors, who are of normal intelligence but their families do not wish to be associated with a family support group.

Twenty-four (63%) of the children had received a Statement of Special Educational Needs but there were 10 children over 3 years of age who did not have a statement.

A teacher for the hearing impaired had provided input for 61% of the children. Only 31% of the children had received input from a teacher for the visually impaired. These are surprisingly low figures when 86% of these school age children have hearing aids and 75% have functional visual impairment.

Hospital specialists

The frequency of hospital visits for out-patient (OPD) appointments was recorded. On average, parents and their children attended OPD a mean of eight times a year. This meant substantial rearrangements of the families' daily routines and time away from vital education. Out-patient appointments with different specialists were rarely organized for the same day. This is a consideration that needs addressing so that children can attend the hospital to see different specialists on the same day. The general health of the children improved as they grew older, which is reflected in only one school-aged child needing a physically impaired school placement (Table 3).

Feeding problems

Feeding problems were very common in these children (84%) and many parents (92%) noted a specific difficulty with weaning their children onto lumpy foods.

Therapists

Speech therapy was available for 67% of the children but this was mainly input for school age children. Few infants had input from a speech therapist at the time of weaning. Only 24% of children had input from an occupational therapist and the majority of these children having therapy attended schools for children with severe learning difficulties.

Support from voluntary agencies

Only 46% of families reported as having received support from voluntary agencies other than the CHARGE Family Support Group. The overall picture was very fragmented and agencies named included the National Deaf Children's Society, Contact a Family, Mencap, The Tracheoesophageal Fistula Society and Heart Line.

Given the frequency of dual sensory impairment (68%), it was disappointing that only seven families (18%) reported as having been referred to SENSE (support organization for the deaf blind). The general support that the parents received was quoted as being most helpful in the early stages of the child's life when it was important to meet other parents and families with children with disabilities, even if these children did not have CHARGE association.

Aetiology

A prominent cause of anxiety amongst the parents was the possibility that the condition is caused by an environmental toxin. In this group there were 36% ($n = 14$) of reported contacts with pesticides/insecticides in the early weeks of pregnancy. Seven families had extensive exposure in their own house and were all living and sleeping in the house when the fumigation was taking place. These substances were; Lindane (organophosphate) in house fumigation, wood worm treatment involving all the house, old house renovation involving fumigation with unknown substances (each of the above in two families) and actellic (pirimiphos methyl) house fumigation (in one family). The final seven families had less extensive and more tenuous contact. Five families had close contact with aerial crop spraying. One mother was working in a varnish factory and another mother was working at school when it was fumigated.

The parents were on average older than the general population at the time of delivery of their child. The mean age (\pm SD) of fathers at the birth of their affected child was 32 (\pm 6.1) years and that of mothers 29 (\pm 4.7) years. The population data for the UK shows a mean maternal age of 27.7 (\pm 3.2) years. There are no statistics for paternal age. However, the difference between the mean maternal ages were not statistically significant.

DISCUSSION

Vision

The children with retinal colobomata were diagnosed at a later date than the children with the iris or combined iris and retinal colobomata. This shows that it is very important to look for the hidden defects of the CHARGE association at an early stage; the mnemonic provides a useful reminder for these. The introduction of visual aids at an early

age can help with the child's compliance and development. The parents can also be more aware of the child's visual limitations. Complications like retinal detachment and corneal abrasions are well documented in children with CHARGE association (Russell-Eggitt *et al.* 1990). So it is vital that the eyes are reviewed regularly.

Photophobia was a significant problem that was only addressed at a later date in the children's management. Tinted spectacles were of great benefit to the children and in the summer most wore some kind of hat or visor. Some parents felt that many of their child's behavioural problems were resolved by the use of such simple remedies.

Hearing

The external ear anomalies in CHARGE association can be so distinctive that a presumptive diagnosis of CHARGE may be possible from this alone (Davenport *et al.* 1986). This may then be a marker for the mixed hearing loss in CHARGE as well as all the other features. Assessment of hearing is often difficult in children who have multi-sensory deprivation and this needs to be undertaken by a team of specialists. It is vital to involve the peripatetic teacher of the deaf who can offer invaluable help in counselling as early as possible (Blake *et al.* 1990). The children are often supplied with hearing aids too late and this can result in poor compliance, especially if they have acquired the habit of disregarding sounds (McInnes & Treffry 1982). Regular checks by an experienced audiologist are necessary as hearing loss can develop, progress or be under-diagnosed (Thelin *et al.* 1986).

Thelin also reports that auditory brain stem responses contribute little to the understanding of hearing loss in CHARGE association but that a characteristic 'wedge' shape audiogram may be unique to the condition. Parents will often be the first to know if their child can hear or not and their concern needs to be taken seriously.

Chronic serous otitis media is a common condition in these children and is improved with grommet insertion. However, it is important to note that children with CHARGE association are at greatest risk of dying in the post-operative interval. This is probably due to the laryngopharyngeal inco-ordination which results in aspiration of secretions (Blake *et al.* 1990). It is preferable that procedures like grommet insertion should coincide with other operative indications for a general anaesthetic, producing the opportunity for combined procedures. Anaesthetists and surgeons should be fully aware of potential complications in this population even for minor procedures

which should be carried out at hospitals with adequate senior staff on site.

Education

The assessment and educational placement of children with multi-sensory impairments is very complex (Best 1983, Andrew 1989). A growing number of writers have sought to convey the unique and far-reaching implications of multi-sensory impairment (McInnes & Treffry 1982, Fox 1983, Bond 1986). There are a number of multi-handicapped children in this and other studies (Goldson *et al.* 1986) who presented as severely multi-sensory impaired in the very early months but ultimately functioned well in mainstream settings with only minimal additional support.

In considering the results of this study it is interesting that there is a vast discrepancy between the sensory disabilities of these children and the amount of therapeutic and educational support provided for them. Shortages of skilled and qualified staff, and the lack of local educational provision for the multi-sensory impaired, may explain some of the shortfalls. It is likely that inadequate assessment techniques combined with the discrepancy between the child's chronological age and their functional age, has often lead professionals to a diagnosis of 'mental retardation'. Much of the literature on CHARGE association reinforces this tendency by stating that mental retardation is almost inevitable in CHARGE children (Hall 1979, Curatolo *et al.* 1983, Lin *et al.* 1990). With increasing knowledge amongst the medical profession about the crucial impact of early intervention, this tendency is now beginning to be questioned (Oley *et al.* 1988; Blake *et al.* 1990).

The present writers believe that the letter 'R' in the mnemonic 'CHARGE' should be taken to indicate retarded growth only, and that mental retardation (or retarded development), if present, should be regarded as an outcome of the other disabilities rather than as an integral anomaly in the association.

Motor development

The CHARGE children are showing a similar pattern in their walking age to that shown by able-bodied children who bottom shuffle. It is a well documented fact that children with severe visual and/or multi-sensory impairment are likely to be delayed in their motor development (Van Dijk 1982, Fox 1983, Sonksen *et al.* 1984). The results from

the questionnaire confirm this pattern, yet over one-third of children did not receive any input from a physiotherapist. Physiotherapy at an early stage of the child's development may have helped some of the balance problems that were common in this group. Reassurance from a physiotherapist that the child's movement patterns are primitive rather than abnormal can have an enormous impact on the parents' ability to take a positive view of the future.

Feeding problems

Many of the children had difficulty with swallowing lumps and many parents reported the continuation of liquidized foods as a consequence of this. In some cases there were obvious physiological reasons for these problems (i.e. cleft palate, facial palsy and tracheoesophageal fistula repair). The not so obvious hidden anatomical anomalies of the pharynx and larynx have been reported (Blake *et al.* 1990) and need to be considered. This paper also reports that the children with the most severe feeding problems had 'Bilateral Posterior Choanal Atresia'. They had significant failure to thrive and all this group suffered from chronic serous otitis media and needed grommet operations as compared with the unilateral atresias or stenoses. One needs to consider the other contributory factors like visual impairment and extended hospitalization (Kitzinger 1980, Evans Morris 1987).

Therapists

Involvement of a speech therapist and/or occupational therapist may be beneficial in the early stages of weaning to help with the feeding difficulties which have been outlined above. Our results have confirmed a paucity of input at this early stage. The important role of speech therapy in the area of speech and language development also needs to be remembered in view of the prevalence of hearing and visual impairment in this population.

In fact, involvement of speech therapy seems only to have begun at the stage of delayed language, except in the children with orofacial clefts.

Support from voluntary agencies

The support that the parents received was most welcome at the crisis period following the diagnosis and it was often the initial organization that they contacted that continued to be of help in the future. The important elements in offering support are practical help, advice and

resources (Andrew 1989). Given the frequency of dual sensory impairment reported in this survey it is disappointing that so few families reported having been referred to SENSE. The parents in this study speak very enthusiastically about the benefits of involvement with the CHARGE Association Family Support Group. Contact for most parents has been through correspondence, telephone contact, the group's national newsletter and the annual summer family day.

Aetiology

A number of parents felt that an organophosphate pesticide like Lindane might cause the CHARGE anomalies. Lindane has been linked to an increased risk of miscarriage and other reproductive problems (The Daily Hazard No. 22, June 1989). Since February 1989 Lindane's use in domestic premises (in wood preservatives and pest exterminators) has been banned in the UK. Many of these parents were exposed to a number of toxins including Lindane between the 5th and 11th week of uterine life. This is a crucial stage of embryonic development when failure of the primitive bucconasal membrane to rupture (day 35-38) brings about choanal atresia. Septum primum appears at around the 32nd day to be replaced by septum secundum 10 days later. Conotruncal defects, which are common cardiac anomalies in CHARGE can result from aberrations here. The cochlear duct begins to develop from 36th day which is the same time as facial differentiation.

Other evidence for a teratogen comes from Pagon *et al.* (1981) who noted that except for the absence of phocomelia, the CHARGE association shows a striking similarity to thalidomide embryopathy. There were no exposures to thalidomide in the mothers surveyed, but in the literature one child with CHARGE association was exposed *in utero* to diphenylhydantoin (Bartoshesky *et al.* 1982). As Conley *et al.* (1979) pointed out, it seems likely that multiple genetic and environmental factors play a role in the aetiology of CHARGE association. It is suggested that high resolution chromosome analysis should be performed (Clementi *et al.* 1991) in new and old cases of the CHARGE association as a chromosome deletion may be possible. Studies in the UK and USA are at present looking for the presumed microdeletion of chromosome 21q11 (Fibison *et al.* 1990) that may result in the CHARGE association.

CONCLUSION

Most parents with a child with CHARGE association are likely to find medical and educational services fragmented and they may have to take a major co-ordinating role themselves. At least with a diagnostic label like CHARGE association there is the possibility that all the disabling conditions will be identified early. However, this will not necessarily lead to prompt, or even tardy, referral to vital therapeutic and educational services. It may be that through family support groups the parents of less well known conditions like CHARGE can share their experiences with each other and with professionals and so play an active part in creating, changing or expanding the services that they require.

We believe that the diagnosis of mental retardation needs to be made with caution in these children as their capabilities are often underestimated. It is important that parents are not given too negative a picture initially, as the child's learning and acquisition of skills depends very much on the attitudes of the parents. Many of the parents found that when their children were allocated an appropriate educational placement there was a rapid improvement in the childrens' capabilities and intellectual development.

We further believe that any child with multiple problems, whether they be with the CHARGE association or other complex conditions, needs early evaluation, regular follow-up and a comprehensive intervention programme. An inter-disciplinary approach is necessary but there should be one named co-ordinator of services for each child who has links with the family support group and professionals who have a more in-depth knowledge of the condition. The authors feel that as the CHARGE association is a heterogeneous phenotype both genetic and environmental factors are involved in its aetiology. There is recognition of aetiologic heterogeneity in various clinical syndromes (Kallmans and Di George) and this diversity may be attributable to the CHARGE association. Therefore, teratogens, single gene disorders and subtle chromosome aberrations need to be considered in each family.

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