

Williams and Smith-Magenis syndromes

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Introduction

Williams syndrome and Smith-Magenis syndrome are both rare, genetically determined conditions with an assumed prevalence of 1 in 25 000 live births, an equal sex ratio and an association with learning disabilities, mostly in the mild to severe range. Both syndromes are associated with distinctive patterns of cognitive and behavioural characteristics, although in each case the pattern of characteristics is different and carries very different implications for adjustment in adulthood and for educational and behavioural interventions.

While rare, these syndromes are becoming better known among health professionals, and more and more affected individuals are being identified. These individuals are also quite likely to be referred to health and mental health specialists because the particular behavioural and psychological characteristics associated with the conditions place them at increased risk for difficulties in adjustment and psychopathology in both childhood and adult life. In recent years there has been a growth in research on the psychological characteristics, difficulties and needs of children with Williams syndrome, and to a lesser extent Smith-Magenis syndrome. Research findings are also beginning to accrue on the long-term course of these conditions and adjustment in adulthood. This is vital for parents and professionals in order to facilitate the sharing of information about appropriate educational and behavioural approaches, to inform intervention efforts and to help plan for adulthood. Moreover, as Turk & Sales (1996) point out, the knowledge that particular behaviours are caused by, or at least associated with, underlying genetic abnormalities rather than parental handling or other environmental factors, can assist parents and other carers to generate a sense of control, rather than guilt, anger or helplessness in relation to their children's difficulties.

This chapter will briefly discuss the genetic underpinnings, physical features and natural history of Williams syndrome and Smith-Magenis syndrome, and the cognitive and behavioural characteristics associated with these conditions

in childhood, and then go on to explore their long-term course, their effects on adjustment in adulthood and implications for support and intervention for affected individuals across the life span.

Williams syndrome

Aetiology, epidemiology and physical presentation

Williams syndrome is a developmental disorder involving the vascular, connective tissue and central nervous systems. Recent research indicates that it is a contiguous gene deletion syndrome, involving a microdeletion on chromosome 7 (at locus 7q 11.23) that includes the elastin gene (Ewart et al., 1993). Elastin is an important constituent of connective tissue, especially in arterial walls, and reduced or abnormal elastin could explain the vascular and connective tissue pathology found in the syndrome, as well as the atypical facial appearance. Other phenotypic features might be accounted for through the involvement of contiguous genes. Most cases of Williams syndrome are the result of a new mutation, although the condition can be inherited as an autosomal dominant disorder.

The mean birth weight of affected individuals is reduced, and cardiac murmurs and an unusual facial appearance are often noted at birth (Martin, Snodgrass & Cohen, 1984). Difficulties with feeding are a major problem in infancy, and with vomiting, constipation and irritability, lead to failure to thrive. A proportion of children are found to have raised levels of blood calcium. This subgroup is generally treated with a low-calcium and vitamin D-restricted diet, and serum calcium levels return to normal and the feeding difficulties improve with dietary treatment, or simply with the passage of time. However, other features of the condition persist. Physical features of the children include a distinctive face with full prominent cheeks, a wide mouth, long philtrum, a retroussé nose with a flat nasal bridge, heavy orbital ridges, medial eyebrow flare and stellate iris pattern (Joseph & Parrott, 1958); dental anomalies, including microdontia, missing teeth and enamel hypoplasia; and renal and cardiovascular abnormalities (most commonly supravalvular aortic stenosis and peripheral pulmonary artery stenosis) (Morris et al., 1988; Pober et al., 1993). The cardiovascular symptoms vary in severity and may change over time. Commonly found skeletal abnormalities include radio-ulnar synostosis, joint contractures and laxity. Gait abnormalities are common and include immature gait and abnormal stress gait, with early hypotonia giving way to hypertonia in older individuals (Chapman, du Plessis & Pober, 1996). Growth retardation, short stature and a hoarse voice are further frequent findings,

and an early starting and fast progressing puberty has been reported in many cases.

Many adults with Williams syndrome appear to age prematurely, and greying hair and a coarse facial appearance are common even in the early to mid-twenties. Progressive multi-system medical problems have been identified in at least some adults, and can lead to premature death. These include cardiovascular complications, hypertension, gastrointestinal problems, urinary tract abnormalities and progressive joint limitations (Morris et al., 1988). However, it is not clear how common these problems are.

Cognitive and behavioural characteristics in childhood

Studies have highlighted a distinctive psychological profile, and unusual personality and behavioural characteristics that are associated with Williams syndrome that differentiate affected children from other groups with learning disabilities (Udwin, Yule & Martin, 1987; Udwin & Yule, 1991).

Approximately 95% of the children have mild to severe learning disabilities and the mean Full Scale IQ is around the mid-50s (Bennett, La Veck & Sells, 1978; Kataria, Goldstein & Kushnick, 1984; Udwin et al., 1987). Most of the school-aged sample investigated by Udwin and her colleagues required special schooling, and only about half were able to attain some score in reading and spelling. Language may be slow to develop in the pre-school years but by school-age verbal abilities are in most cases markedly superior to visuo-spatial abilities and to gross and fine motor skills. Most children with Williams syndrome have an unusual command of language: their comprehension is usually far more limited than their expressive language, which tends to be grammatically correct, complex and fluent at a superficial level, but verbose and pseudo-mature. The children tend to be very chatty, and their auditory memory, verbal processing and the social use of language are particularly well developed. They typically have a well-developed and precocious vocabulary, with excessive and frequently inappropriate use of clichés and stereotyped phrases, but accompanied by various syntactic, semantic and pragmatic deficits and problems with turn taking and topic maintenance (Udwin & Yule, 1990; Bellugi, Wang & Jernigan, 1994; Karmiloff-Smith et al., 1996, 1998). They also show significant deficits in the integration of visual-perceptual information, in sequencing, performance speed, and fine motor skills, when compared with their verbal abilities and with groups of children matched for verbal IQ (Crisco, Dobbs & Mulhern, 1988; Udwin & Yule, 1991). However, even in non-verbal areas there is an uneven profile, with consistent relative strengths on tasks of face recognition (Udwin & Yule, 1991; Bellugi et al., 1994).

Most children with Williams syndrome have poor relationships with peers but are outgoing, socially disinhibited and excessively affectionate towards adults, including strangers; they also appear acutely attentive to the feelings of others (Udwin et al., 1987; Diltz, Morris & Leonard, 1990; Gosch & Pankau, 1994; Dykens & Rosner, 1999). Their relatively good verbal abilities, engaging personalities and excessive sociability can be deceptive and result in an overestimation of their general cognitive abilities, as well as being a major worry for parents, particularly as the children approach adolescence.

Affected children show higher rates of emotional and behavioural disturbance when compared with the rates that have been reported for other children with learning disabilities, particularly in terms of overactivity, poor concentration and distractibility, attention seeking behaviours and generalized anxiety (Einfeld, Tonge & Florio, 1997; Udwin et al., 1987). Parents describe the children as worrying excessively about unfamiliar situations, anticipated events and all kinds of imagined disasters. They tend to be over-eager to please and constantly seek reassurance from adults. They show high rates of preoccupations and obsessions with particular activities, objects or topics such as electrical gadgets, cars, disasters and illness, and also particular people, for example a neighbour or a teacher at school. Over 90% of the children are hypersensitive to particular sounds, which may include electrical noises like vacuum cleaners, drills, music and thunder. The basis for this hyperacusis is not clear but it tends to diminish in frequency and severity in adulthood (Udwin et al., 1987; Klein et al., 1990).

It is important to note that although the characteristics described above are typical of Williams syndrome, they show some variability across children, and are not necessarily all present in every case.

Abilities, behaviour and adjustment in adult life

Recent studies of adults with Williams syndrome indicate that the characteristic cognitive and personality profile and typical behavioural difficulties that have been identified in affected children persist into adulthood with the same or even greater frequency. These characteristics can cause major difficulties for the individuals in terms of independent living, employment and in developing social and emotional relationships (Udwin, 1990; Davies, Howlin & Udwin, 1997; Davies, Udwin & Howlin, 1998; Udwin et al., 1998).

On assessment, most adults with Williams syndrome have mild learning disabilities (IQ between 50 and 70); only 4% of the group assessed by Howlin, Davies & Udwin (1998) had moderate to severe learning disabilities (IQ below 50), while 10% had borderline cognitive abilities. On the basis of a longitudinal

study, Udwin, Davies & Howlin (1996) concluded that adults with Williams syndrome, at least within the 20–40 year age group, do not appear to show the decline in cognitive abilities over time that is found in certain other conditions, for example Down syndrome (Carr, 1994) and fragile X syndrome (Hagerman et al., 1989). Instead, as in the general population, there was a slight increase in IQ scores from WISC-R to WAIS-R re-testing. The pattern of cognitive functioning reported in the adults was very similar to that described in affected children; they tended to do relatively well on tests of vocabulary and abstract reasoning but performed poorly on tasks involving general knowledge, memory, numeracy and visual sequencing. Assessment of receptive and expressive language indicated persisting deficits in both areas, while attainments in reading, spelling and mathematical abilities, and functioning in the areas of communication, independence and socialization (as assessed on the Vineland Behaviour Scales) were poorer still. The average levels reached in all these areas were equivalent to the 6–8 year level. Thus, although general cognitive abilities appear to be well maintained in adults with Williams syndrome, they make little progress in literacy and numeracy beyond the early teenage years, and their ability to use these skills within a general social context appears to be extremely limited.

In line with this conclusion, Davies et al. (1997) reported that most of the adults in their study lived at home with their families (69%) or in sheltered accommodation (24%), and most required substantial amounts of supervision and support in the areas of self-care and daily living skills. According to their carers, about half of the sample required at least some assistance with washing and dressing and between 80% and 94% were wholly dependent on others for the preparation of food and domestic chores such as cleaning, shopping and laundry. Only one of the sample of 70 could use money appropriately and controlled her own finances. In all the remaining cases, the caregivers took responsibility for budgeting and shopping. Although 40% of the group were able to use public transport unaccompanied on familiar journeys, only two (3%) of the group were able to use public transport for unfamiliar journeys. Moreover, many carers reported being wary of letting the adults go out alone because their friendly and over-trusting nature made them vulnerable to exploitation, while their visuo-spatial difficulties and poor appreciation of speed and distance made crossing roads dangerous. Three adults (4%) were living independently but were receiving considerable supervision and support from family members and community workers to help them cope with the demands of daily life, particularly domestic chores and dealing with money.

Only one adult in the sample of 70 described by Davies et al. (1997) had an

independent job and four worked in sheltered employment, as shop or kitchen assistants. A further five people had part-time voluntary jobs, while 11 were undertaking part-time work placements organized by their adult training centres or further education colleges, for example as packers, shop assistants or nursery helpers. Supervisors reported 'considerable difficulties' for about half of these adults, and 'at least some difficulties' for a further third. Thus, despite their relatively good cognitive abilities, most of the adults had very limited self-care and independence skills and required considerable supervision and support in their occupational and daily living environments.

Problems reported by carers, supervisors and employers, which necessitated supervision and prompting for most, even when performing routine tasks, included the adults' distractibility and poor persistence, anxiety, inappropriate social behaviours and motor difficulties, all characteristics that are typically associated with Williams syndrome. These characteristics appear to limit the levels of independence, self-care and occupational status attained by adults with Williams syndrome, when compared with other groups of adults with mild or moderate cognitive impairment (e.g. Dykens et al., 1992; Carr, 1994).

The characteristic behavioural and emotional difficulties described in children with Williams syndrome have been found to persist into adulthood with the same or greater frequency (Davies et al., 1998). Almost all of Davies et al.'s sample of 70 adults were reported to have difficulties making or maintaining friendships, and nearly three-quarters were said to be socially isolated. At the same time the majority continued to be socially disinhibited, over-friendly and too trusting of others. Over half were reported to be physically over-demonstrative, often seeking attention and affection in inappropriate ways such as touching, hugging and kissing others. While these characteristics are often regarded as endearing and appealing in children, they become increasingly problematic in adolescence and adulthood and can make individuals vulnerable to sexual exploitation and abuse. At least 20% of the sample had reportedly been victims of sexual abuse and in half of these cases police intervention had been sought. A particular problem, seen in over 50% of the adults, was the tendency to focus their attention and affection on television or film personalities or familiar people such as neighbours. In some cases these attachments developed into all encompassing infatuations, causing significant difficulties for those involved.

Preoccupations and circumscribed interests were highly characteristic of the adult sample and, as with affected children, typically centred on fascinations and obsessive interests in cars, electrical appliances, machinery, disasters and violence in the news, and future events such as birthdays and holidays. In many

cases these preoccupations significantly disrupted daily life and restricted activities; for example some adults were reported to spend hours dismantling electrical appliances. Most adults with Williams syndrome exhibit high levels of anxiety, which tends to be triggered by excessive worries about perceived threat, inappropriate demands, uncertainty or changes in routine. Even relatively minor changes in the environment can prove very upsetting, while major life events, such as the death of a parent or a move to new accommodation, can result in prolonged periods of anxiety or depression (Davies et al., 1998). Ten per cent of the sample investigated by Davies et al., were said to have had a period of low mood or depression in their adult lives and a further 10% were said to have had marked mood swings. Phobias and hypochondria were reported in around half of the group and were often sufficiently intense to restrict activities. Excessive worries about their health often resulted in frequent visits to doctors and necessitated considerable reassurance about health-related matters. Hyperactivity, which is prominent in children with Williams syndrome, is reported to diminish considerably in adulthood, but concentration problems and distractibility continue to cause difficulties in 90% of cases. Stereotyped motor movements such as rocking, hand rubbing and skin picking, are also common, particularly when individuals become angry or anxious.

The characteristic cognitive and behavioural profiles of children and adults with Williams syndrome carry important implications for psychological and educational interventions. These will be examined in the following section.

Implications for interventions and educational and training approaches

As illustrated above, a diagnosis of Williams syndrome can help families and professionals to gain a better understanding of the strengths and difficulties of affected children and adults, and to plan to better meet present and future needs. Moreover, the finding that most psychological difficulties identified in childhood persist into adulthood highlights the need for early interventions to address these difficulties. Although research evidence on the effectiveness of interventions with this population is sparse, clinical experience suggests that the fact that particular behavioural and emotional difficulties are linked with this genetic condition does not mean that they are not amenable to modification. On the contrary, there are many reports that behaviourally-based interventions for characteristic difficulties such as overactivity, anxiety and social disinhibition can be as effective with individuals with Williams syndrome as they are with other groups. Moreover, the similarities identified in the patterns of learning and behaviour of these children and adults have helped to refine

appropriate educational strategies and behavioural management approaches through the sharing of information and experiences between parents and professionals.

Given that feeding difficulties and delayed language development are characteristic in the early years, programmes to encourage pre-linguistic and feeding skills should be introduced early, with an emphasis on sucking, swallowing and chewing. Early speech and language therapy should focus on helping children to attend to and comprehend auditory stimuli, and on building up vocabulary, syntax and turn taking skills (Meyerson & Frank, 1987). The introduction of signing and other communication systems to augment speech expression and comprehension in the early years can also be beneficial. In addition, physiotherapy and occupational therapy input will be needed in areas of particular difficulty, including co-ordination, balance, gross and fine motor activities and visuo-spatial skills. These therapists can also advise on developing an array of self-help skills, including dressing, washing, eating with a knife and fork, and writing.

Udwin & Yule (1998a,b) have produced guidelines for parents and teachers of children with Williams syndrome, in which they describe the main features of the condition and advise on the management of behavioural difficulties using standard behavioural techniques, and on appropriate educational approaches. For example, given their characteristic social disinhibition and overfriendliness, parents and teachers are advised on the need to teach appropriate social skills and to set clear boundaries from the start, teaching appropriate greeting behaviours and discouraging the child from approaching strangers and from excessive and inappropriate verbalizations. Obsessions and preoccupations should, where possible, be nipped in the bud by diverting the child's attention and introducing new activities and interests. Where preoccupations are well established, carers should try to keep them within acceptable bounds, for example by allocating specific amounts of time to activities related to the preoccupations, and then gradually reducing the amount of time spent in this way. Alternatively, time spent engaged in the preoccupation could be used as a reward for desired behaviour in other areas. The obsessional interest could also be channelled into useful activity, for example practising pencil control by drawing or writing about a favourite topic.

Clinical experience suggests that temper outbursts and aggressive behaviours displayed by children with Williams syndrome can be effectively addressed with standard behaviour management approaches, including identifying triggers for such behaviours, anticipating these and diverting the child's attention elsewhere; teaching the child more appropriate ways of communicating needs, wants or frustrations, and removing adult attention when the child

displays unacceptable behaviours. In general, children with Williams syndrome do best with a predictable schedule and a set routine, and they benefit from preparation before changes in activities or routines. Stress and anticipatory anxiety can often be reduced by talking the child through a change or difficult task ahead of time. Where children appear to be more nervous or anxious than usual, the home and school environments should be examined to ensure that excessive demands or pressures are not being placed on them.

Treatments for hyperacusis have not been systematically evaluated. Filtered ear-protectors are sometimes recommended, but since these may well filter out certain speech frequencies as well, their use should be limited. Reassurance and an explanation about the source of the noise often helps the child, and a warning just before predictable noises (e.g. before switching on a food processor) means that children can prepare themselves for the noise and leave the room if necessary. Parents report that the reactions will often diminish if the child is able to exercise some control over the sounds that cause discomfort, for example practising switching a vacuum cleaner on and off. Repeated, gentle exposure to the sounds may also help to desensitize the child, for example by tape recording distressing sounds and then encouraging the child to play these back, quietly at first, then gradually increasing the volume.

Since the children's good spoken language and outgoing personalities can give a false expectation of their functioning in other areas, careful assessment of their cognitive abilities and profile of strengths and weaknesses is essential. Most require special schooling, though some attend mainstream schools with additional support. Because of their unusual pattern of abilities they have special educational needs that are different from those of other children with learning disabilities, and it can be difficult to find a school that is exactly suited to their particular needs. Finding the most appropriate school will depend on the individual child's level of abilities and profile of strengths and weaknesses, and also on the provisions in the particular schools that are available locally. Because poor concentration, distractibility and hypersensitivity to sounds are among the most common problems of children with Williams syndrome, they are likely to concentrate best in one-to-one or small group settings that are as quiet and free from distractions as possible. Activities should be varied, of short duration and with frequent breaks, and regular prompting and reminders will help the child to stay on task. Programmes of positive reinforcement for remaining seated and on task for increasing lengths of time are also recommended, while self instructional training may be particularly effective with older children and adolescents. In a series of placebo-controlled case studies Bawden, MacDonald & Shea (1987) showed that treatment with methylphenidate benefited two children with Williams syndrome in terms of improved attention, and

reduced activity, impulsivity and irritability, with no signs of serious side effects. No effects were discernible in the other two children included in the study. The trial used only a single dosage of medication, was of short duration and included just four children. Further trials are needed but it is likely that methylphenidate is a useful adjunct in the treatment of some children with Williams syndrome.

Advice to teachers might include suggestions for harnessing the children's superior spoken language abilities in training perceptual and motor skills to help them to focus their attention on the tasks, and on ways of providing verbal reinforcement and support for the activities, for example encouraging children to talk themselves through each step of an exercise while they are doing it. The use of topics and objects in which children have a particular interest can help to motivate them to work on activities that are not intrinsically interesting, for example practising eye-hand co-ordination and pencil control skills by copying and tracing over pictures of cars, washing machines, etc. (Udwin & Yule, 1998b). Thought should also be given to the way work is presented to the child with Williams syndrome; books and programmes with many pictures and colours may lead to visual overstimulation, and materials or worksheets with relatively little information on each may be preferable. In teaching reading, strategies that use the child's superior verbal skills (i.e. phonetic approaches) are likely to have the greatest success. Teaching through music and songs, which many children with Williams syndrome enjoy, can further speed up the learning process and make it more enjoyable. Finally, many of the children enjoy working on computers and may become very proficient in computer use. Such skills should be encouraged and can support school-based learning.

The needs of siblings of children with Williams syndrome should not be forgotten. Many siblings are poorly informed about the syndrome and may harbour unnecessary worries about the possibility that they may be at risk of having a child with the condition, or of developing the condition themselves. It is important for parents to give siblings information about the condition, its cause and long-term course since accurate information will serve to allay unnecessary fears and worries, and increase understanding among siblings of the Williams syndrome child's difficulties and needs.

Adults with Williams syndrome are probably easier to live with and to manage than individuals with certain other conditions, for example Prader-Willi syndrome (Greenswag, 1987). Parents frequently point out how helpful their adult Williams syndrome children are with both practical matters and in terms of providing emotional and social support (Udwin, 1990). However, given the significant medical, psychological and psychiatric difficulties identified in many adults, and their continued need for supervision and support,

routine health screening and assessment of their cognitive profile, mood and behaviour are essential to ensure that their living and occupational environments are appropriate to their ability levels and needs, and to facilitate access to health and social services as necessary.

Moreover, given that many adults continue to live with their families into their 30s and 40s (Udwin et al., 1998), attention must be paid to the families' needs for support, advice on management issues and also occasional breaks from caring for their children. In reality, Udwin et al. (1998) found that most families caring for adults with Williams syndrome had minimal if any contact with medical or mental health professionals or with social services.

As already noted, most adults with Williams syndrome experience substantial difficulties in the work place and have severely limited self-care and independence skills, mostly due to the cognitive and personality characteristics known to be associated with the condition, notably anxiety, social disinhibition, poor social functioning, visuo-motor difficulties and distractibility. As a result, they require substantial supervision and support in everyday activities. Yet their comparatively good spoken language and outgoing personalities often give a false expectation of their abilities in other areas. This can lead to their being placed in residential, training and employment settings which place excessive demands on them, with a concomitant deterioration in behaviour and mood. Careful thought needs to be given to finding daytime occupations and living arrangements that are appropriate to their ability levels and take account of their particular personality traits and interests, and their characteristic profile of cognitive strengths and deficits. For example, routine manual tasks such as stacking shelves, packing or assembly-line work, which are typically considered suitable for people with learning disabilities, may not be appropriate for people with Williams syndrome because of their visuo-motor difficulties, lack of stamina and tendency to tire easily. Their distractibility means that they may get bored with repetitive tasks, though at the same time they tend to dislike change and are reported to perform better when given structured routine tasks to carry out. Many people with Williams syndrome get particular pleasure from meeting and helping others, and working in a helping capacity (e.g. as an assistant in a nursery or hospital) with adequate supervision may be appropriate in some cases. Noisy and busy work and living environments tend to be distressing because of the hypersensitivity of individuals to sounds and visuo-perceptual difficulties; quiet environments that are structured and ordered are to be preferred.

Psychiatric and psychological difficulties in adults with learning disabilities often go undiagnosed and untreated. The high levels of anxiety exhibited by many adults with Williams syndrome may be triggered by excessive worries

Table 12.1. Adults with Williams syndrome: implications of the cognitive and behavioural phenotype for carers and supervisors

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- Considerable support and supervision are needed:
 - in self-care and daily living tasks
 - when out of the house, because over-friendliness and disinhibited behaviours place individuals at risk of exploitation and abuse
 - in the workplace, due to distractibility, poor persistence, anxiety, inappropriate social behaviours and motor difficulties
 - Training in social skills and appropriate social behaviours will be required to address social isolation, inappropriate overfriendliness and disinhibition
 - Working and living environments must be tailored to the individual's abilities. Placements that are too demanding may result in a deterioration in behaviour and mood
 - A predictable environment and set routines are preferred. Where possible changes should be prepared for well ahead of time
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Table 12.2. Implications of the Williams syndrome phenotype for health and mental health professionals

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- Regular health checks to monitor cardiac and kidney function and blood pressure
 - Assessment of the cognitive profile will help clarify areas of strengths and weaknesses, since individuals' superior expressive language and outgoing personalities may be misleading, resulting in an overestimation of underlying abilities.
 - Psychological interventions, with or without medication, may be required for:
 - anxiety
 - depression
 - obsessions and preoccupations
 - phobias, hypochondria
 - Carers will require support and advice on management issues
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about perceived threat, inappropriate demands, uncertainty, or when faced with changes in routine. Major life events such as the death of a parent or a move to new residential accommodation can, in some cases, result in prolonged periods of anxiety or depression (Davies et al., 1998). Additional psychological support at such times to prepare individuals for change or to help them cope with unforeseen events may prevent long-term psychological difficulties. In addition, training in social skills, appropriate social behaviours and wariness of others is a priority for individuals with Williams syndrome, given their social disinhibition. Teaching independence in self-care, including dressing, washing, shopping and cooking is also important.

The above recommendations are based on clinical experience and reports from parents and professionals on approaches that have been found to be helpful with this population (Udwin, Howlin & Davies 1996a,b). Studies are urgently needed to examine their effectiveness under controlled conditions and in comparison with other intervention approaches.

For a summary of the implications of the cognitive and behavioural phenotype for carers and supervisors see Table 12.1 and for health and mental health professionals see Table 12.2.

Smith-Magenis syndrome

Aetiology, epidemiology and physical presentation

Like Williams syndrome, Smith-Magenis syndrome is a chromosomal disorder associated with learning difficulties and a specific pattern of physical, behavioural and cognitive characteristics. The syndrome was first described by Smith, McGavran and Waldstein in 1982 and is believed to have an incidence of at least 1 in 25 000 births, with an equal sex ratio (Greenberg et al., 1991). It is caused by an interstitial deletion of chromosome 17p11.2, and most cases are sporadic, suggesting a low recurrence risk for parents, although at least one case of vertical transmission of the deletion from mother to daughter has been reported (Zori et al., 1993). Several candidate genes have been identified in the deletion region (Chevallard et al., 1993; Zhao et al., 1995; Chen, Potocki & Lupski, 1996b; Elsea et al., 1996), but further investigations are required to clarify their significance to the clinical and behavioural phenotype.

Associated dysmorphic features reported in over two-thirds of affected individuals include a flat, broad head (brachycephaly) and prominent forehead, epicanthal folds, a broad nasal bridge, flat mid-face, abnormal ear shape and position, down-turned mouth with cupid's bow, broad hands with inbent fingers, small toes, short stature and a hoarse deep voice (Greenberg et al., 1991, 1996). The latter may be related to features such as polyps, nodules, paralysis of the vocal chords and structural vocal-fold abnormalities which have been reported in individuals with Smith-Magenis syndrome. With age there is a general coarsening of the facial features. Infantile hypotonia, early feeding difficulties, failure to thrive, and frequent ear infections leading to progressive hearing loss are common. Clinical signs of peripheral neuropathy have been found in approximately 75% of cases, which include decreased deep tendon reflexes, decreased sensitivity to pain and temperature, reduced leg muscle mass, gait disturbances and muscle weakness (Greenberg et al., 1996; Webber, 1999). Eye abnormalities are also common, and include iris anomalies,

microcornea, strabismus, cataracts and myopia (Finucane et al., 1993; Chen et al., 1996a). Affected individuals are particularly prone to retinal detachment, possibly as a result of the combination of high myopia, self-injurious head banging, aggression and hyperactivity.

Less consistent features include cardiac defects (in 37% of cases), renal and thyroid abnormalities (in 35% and 29% of cases), scoliosis (in at least 24%), seizures (in 11–30%), and also genital abnormalities, and abnormal palmar creases. Several individuals in their 60s and 70s have been described in the literature (e.g. Greenberg et al., 1991), suggesting that life expectancy may be normal.

Cognitive and behavioural characteristics in childhood

There are relatively few published reports on the cognitive and behavioural characteristics of children with Smith-Magenis syndrome and these are mainly clinical descriptions of small samples. There is an urgent need for systematic investigations of representative samples using standardized instruments and appropriate comparison groups. Nevertheless, on the basis of the information available to date some general conclusions can be drawn regarding the cognitive and behavioural phenotype of Smith-Magenis syndrome.

It is suggested in the literature that all affected individuals have mild to severe learning disabilities, with the majority in the moderate range (IQ 40–50; Moncla et al., 1991; de Rijk-van Andel et al., 1991; Greenberg et al., 1996; Udwin, Webber & Horn, 2001). Of Udwin et al.'s sample of 29 school children, 26 attended special schools or units, mostly for children with mild, moderate or severe learning difficulties; only two of the younger children attended mainstream schools, and one attended a remedial class in a mainstream school. On the other hand, Crumley (1998) recently reported on a child cytogenetically diagnosed with Smith-Magenis syndrome who on assessment did not have associated learning difficulties in non-verbal areas of functioning. Clearly more able individuals with the syndrome are less likely to come to the attention of paediatricians and geneticists, and hence are less likely to be represented in the studies undertaken to date.

In contrast to the Williams syndrome phenotype, in Smith-Magenis syndrome speech delay tends to be more pronounced than motor delay, and expressive language abilities are more impaired than receptive language skills (Chen et al., 1996a; Moncla et al., 1991). Dykens, Finucane & Gayley (1997) examined the cognitive profiles in 10 children and adults, and identified relative weaknesses in sequential processing and in short-term memory, and relative strengths in long-term memory, alertness to the environment, attention to

meaningful visual detail and reading. However, Udwin et al. (2001) failed to confirm a strength in reading ability in her sample of affected children.

Behaviourally, children with Smith-Magenis syndrome tend to pose severe management problems for their carers due to hyperactivity, aggressive outbursts, self-injurious behaviours and sleep disturbance (Smith et al., 1986; Stratton et al., 1986; Greenberg et al., 1991; de Rijk-van Andel et al., 1991; Dykens et al., 1997; Dykens & Smith, 1998; Webber, 1999). Between 50% and 100% of individuals investigated have been described as hyperactive, restless, impulsive and distractible, and 70% to 100% are reported to show attention-seeking behaviours, hostility, temper outbursts and aggression towards people and property. These rates are much higher than the rates reported for other groups of children with learning disabilities. The behaviours are often very severe and, according to parent and teacher reports, may be triggered by tiredness, frustration, changes in routine, inability to get one's own way, attempts to avoid situations, or they may have no identifiable triggers (Webber, 1999). Self-injurious behaviours have been observed in children as young as 18 months and are reported in between 67% and 100% of the samples investigated (Greenberg et al., 1991; de Rijk-van Andel et al., 1991; Dykens & Smith, 1998; Webber, 1999). These rates, too, are higher than the rates reported in children with learning disabilities of unknown aetiology but equivalent to rates of self-injury reported in some genetic syndromes, for example Lesch-Nyhan disease (Anderson & Ernst, 1994). The self-injury is often a response to frustration or anger and can be extreme, possibly due to the decreased sensation in the extremities and relative insensitivity to pain that is characteristic of affected individuals. Boredom or habit may be other reasons for self-injurious behaviours. The self-injurious behaviours typically include hand-biting, self-pinching/scratching and picking at sores, hitting the head or body, picking skin around the fingernails and tearing or pulling at the nails. Greenberg et al. (1991) reported two additional types of self-injurious behaviours as striking features of the syndrome – pulling out fingernails and toenails, and inserting foreign objects into bodily orifices. However, a systematic investigation by Webber (1999) found few examples of the latter two behaviours, and she concludes that these may not be characteristic of the syndrome. There have been anecdotal accounts of affected individuals who have strangled pets, possibly as a result of violent hugging which may be linked to reduced sensation in the hands (Smith, Dykens & Greenberg, 1998a; Webber, 1999).

Single cases have been described of children with Smith-Magenis syndrome who fulfil the diagnostic criteria for autism (Smith et al., 1986; Stratton et al., 1986; Vostanis et al., 1994), and autistic-type behaviours including resistance to

change, repetitive questioning, and preoccupations with particular themes have been described in many cases. In the first systematic investigation of the association between autism and Smith-Magenis syndrome, Webber (1999) found that 93% of a sample of 29 children aged 6 to 16 years qualified for a diagnosis of autism using Wing's (1980) Schedule of Handicaps, Behaviour and Skills. While this instrument is considered by some to over-diagnose autism, Webber's findings highlight the high rates of autistic-type behaviours associated with the syndrome. At the same time children with Smith-Magenis syndrome are less impaired in their communicative abilities and sociability than one might expect from autistic children.

Severe sleep disturbance is a further hallmark of the syndrome and has been reported in up to 100% of children (Greenberg et al., 1996; Smith, Dykens and Greenberg, 1998b; Webber, 1999). The problems described include difficulties falling asleep, shortened sleep cycles, frequent and prolonged night awakenings, early morning waking, excessive daytime sleepiness and daytime napping. Eighty per cent of Webber's sample of 29 children aged 6–16 exhibited two or more of these difficulties. Of the 25 (86%) who exhibited early waking (5.00 a.m. or earlier), 59% did this on a daily basis and about half of the total sample regularly slept during the day. Nocturnal enuresis is a common problem even in older children, possibly due to (or aggravated by) a hypotonic bladder. Abnormalities of REM sleep have been reported in over half of those studied with polysomnography (Greenberg et al., 1991). These abnormalities, abnormal melatonin levels and sleep cycle disturbances are suggestive of an underlying biological clock problem in the syndrome (Potocki et al., 1997).

On the positive side, children with Smith-Magenis syndrome are frequently described as loving and caring, eager to please and with a good sense of humour. They like adult attention and enjoy interacting with adults, though the desire for individual attention from adults may be intense. Many also love music, which can be used as a reinforcer as well as helping to calm children down. They react well to consistency, structure and routine. An unusual spasmodic upper body squeeze has been reported in 90–100% of affected individuals, comprising hand clasping and squeezing at chest or chin level, or crossing both arms tightly across the chest and spasmodically tensing the upper body. Excitement and pleasure can trigger this behaviour, which appears to be quite involuntary and may be an important diagnostic marker for the syndrome (Finucane et al., 1994; Webber, 1999).

The sizes of samples investigated to date, and the fact that the investigations are largely descriptive, limit the conclusions that can be drawn thus far about a cognitive and behavioural phenotype in Smith-Magenis syndrome. Moreover,

it is likely that as case recognition improves an increasing number of less severely affected children will be identified and the figures on the rates of severe behavioural problems may fall. Nevertheless, the above findings are strongly suggestive of a set of behaviours and cognitive features that are characteristic of the syndrome and differentiate it from other disorders associated with learning disabilities.

Abilities, adjustment and behaviour in adult life

Little is known about the natural history of Smith-Magenis syndrome and the persistence of characteristic behavioural features into adulthood. Information currently available comes from a handful of descriptive studies of small, mixed samples of affected children and adults, and from one more systematic study of a sample of 21 adults aged 16–51 years undertaken by Udwin et al. (2001). Udwin et al. completed psychometric assessments on 19 affected adults; one adult scored at the floor of the test, a quarter had Full Scale IQs below 50, while just under three quarters had IQs within the mild learning disability range (IQ 50–69). IQs were on average somewhat higher than those reported for affected children. While this may be a result of the different cognitive tests that were used (WAIS versus WISC), it does suggest that adults with Smith-Magenis syndrome, at least those aged up to 50 years, do not show a decline in cognitive abilities over time. As is the case for children with the syndrome, long-term memory (for past events and routes), computing and perceptual skills were found to be areas of strength, while visuo-motor co-ordination, sequencing and response speed were highlighted as areas of weakness.

Despite their intellectual abilities falling largely in the mild learning disabilities range, the attainments of the adults in Udwin et al.'s sample in reading and spelling were on average only at a six to seven year level. Moreover, they showed little independence in daily living skills and were more dependent on carers than might be expected from their level of intellectual functioning. About 70% were unable to dress independently, while 85–90% could not cook a meal or undertake other household chores without supervision. No adults were able to travel any considerable distance on their own; 86% of the sample could only be left on their own for short periods of time, while 57% could only be left alone for a matter of minutes. No adult lived independently; around half lived with their families, while the remainder lived in residential communities or group homes. Only one adult worked in sheltered employment, as a kitchen assistant. The remainder attended day centres, adult training centres or college courses for people with learning disabilities. A few had work placements on day release programmes; in almost all cases these adults were

reported by carers to require either substantial or continuous supervision.

A study by Horn (1999) confirmed previous reports of the persistence into adulthood of the severe behaviour difficulties associated with the syndrome. Most of the adults continued to show marked impulsivity and distractibility, although the rate of overactivity appears to decline in adolescence and adulthood. Over 80% were reported to exhibit high rates of verbal and physical aggression, and self-injurious behaviours were reported in 100% of cases. The behaviours had very similar triggers and were similar in type to those described in children. The pattern of persistence from childhood to adulthood was variable, with some showing improvement in adulthood, but others showing a worsening of the aggression and self-injury or no change. These findings are consistent with previous reports based on smaller samples of children and adults (Greenberg et al., 1991; Dykens et al., 1997), although the finding of 100% prevalence of self-injury is higher than rates previously reported. The rates of aggression and self-injury are unquestionably higher than those reported in general learning disability populations as well as in samples comorbid for psychiatric disorders (Eyman & Call, 1977; Jacobson, 1982). They are, however, similar to those observed in certain other genetic syndromes, notably Lesch-Nyhan syndrome and Prader-Willi syndrome (Greenswag, 1987; Anderson & Ernst, 1994).

Horn (1999) highlighted the violent and alarming nature of the aggressive outbursts exhibited by some affected adults. In some cases, the outbursts were of such severity that the police had to be called; three adults had been admitted to hospital under a section of the Mental Health Act, and two were placed in regional secure units for people with learning disabilities. Five carers reported that adults had attempted to 'strangle' them on occasions when they were angry. Strangulation of pets was reported in two cases. As noted earlier, strangulation may be related to the self-hug that is characteristic of the syndrome, which in turn may be related to the peripheral neuropathy reported by Greenberg et al. (1996). If so, it is possible that this behaviour is not intentional, but rather that individuals with Smith-Magenis syndrome have difficulties gauging their own strength due to reduced sensation in their hands and arms.

Horn's (1999) study is the first to use a standardized instrument – the Diagnostic Interview for Social and Communication Disorders (Wing & Gould, 1994) – to examine autistic features in adults with Smith-Magenis syndrome. She found that 70% of her sample fulfilled diagnostic criteria for autism according to ICD-10 and DSM-IV criteria. This rate, and the rate reported by Webber (1999) for children with Smith-Magenis syndrome, are

considerably higher than the rates reported in the general population (Fombonne, 1999), in populations of adults with moderate learning disabilities (Callacott et al., 1992) and in other genetic syndromes, including fragile X syndrome (Bailey et al., 1993). However, as Horn points out, while the behavioural characteristics associated with the syndrome might qualify for a diagnosis of autism on a standard diagnostic measure, they are quite distinct in a number of ways. Over 50% of adults with Smith-Magenis syndrome show marked stereotypic and repetitive behaviours, including a limited pattern of self-chosen activities, an insistence on sameness, repetitive questioning, a tendency to communicate around repetitive themes, and routine and stereotypical hand movements. Few show appropriate emotional responses, non-verbal communication or body postures, and social approaches are described as one-sided and on their own terms. Yet most affected individuals show some social awareness, are able to maintain eye-contact, greet people appropriately and seek social and physical comfort from others. Their communicative abilities, too, appear less impaired than might be expected for autistic individuals.

Sleep disturbance into adulthood continues to be a prominent feature of Smith-Magenis syndrome (Greenberg et al., 1996; Smith et al., 1998b; Horn, 1999). Seventy-five per cent to 100% of samples of adults are reported to have significant sleep problems which tend to be of a long-standing nature and are characterized primarily by night-time waking, early morning waking and difficulties falling asleep. These rates are significantly higher than rates for adults with general learning disabilities (Espie & Tweedie, 1991). The adults investigated by Horn (1999) woke an average of once or twice a night and took a mean time of 46 minutes to return to sleep. Their mean morning wake-up time was 6.00 a.m., though the majority woke at 5.00 a.m., and they slept for an average of 6 hours 40 minutes. Smith et al. (1998b) reported very similar findings, and also found that increased age was related to earlier wake-up times, shorter duration of sleep and an increased number of wakings in the night. Interestingly, carers reported that in most cases adults' sleep problems had shown some improvement over time (Horn, 1999). Horn concluded that this was not because adults slept for longer or woke less in the night, but because with age individuals became less disruptive during periods of wakefulness and were able to occupy themselves. Behaviours reported to have occurred during these periods in childhood, such as climbing out of windows, cooking breakfast and rearranging bedroom furniture, were replaced by more adaptive behaviours such as listening to tapes and watching television.

Horn (1999) and Webber (1999) found significant associations between

severity of aggressive behaviours, severity of sleep disturbance and the presence of autistic features in their studies of children and adults. This combination of difficulties means that many affected individuals are extremely hard to manage. Given that many continue to live at home with their parents, the stress on families is likely to be considerable, and their need for support and input from health and social services is evident.

Implications for interventions

Given the physical and medical problems associated with Smith-Magenis syndrome, there is a need for regular medical checks, including eye examinations, hearing checks, ear, nose and throat examinations, heart and kidney investigations, and evaluations for thyroid function and scoliosis. Behaviourally, affected children and adults pose severe management problems for their carers, indicating a need for considerable support for families, as well as information about effective intervention approaches. Controlled treatment trials are lacking and urgently needed; however, anecdotal information gathered from parents, teachers and other carers has been useful in indicating that many of the behavioural difficulties described above may be modifiable, and in identifying helpful interventions and educational strategies for this population (Haas-Givler & Finucane, 1996; Smith et al., 1998a,b; Horn, 1999; Webber, 1999).

In childhood, oral motor and feeding training are important. Speech and language therapy using a total communication approach (including the use of sign and symbol systems) is likely to be helpful in promoting speech development and comprehension, and in alleviating frustration associated with poor expressive language skills (Smith et al., 1998a). Occupational therapy for difficulties with visuo-spatial skills, sequencing and co-ordination is also recommended. Since children with Smith-Magenis syndrome are typically distractible and overactive, they are likely to work best in classroom settings that are small, free from distractions and highly structured (Haas-Givler & Finucane, 1996). They are described as preferring consistency, structure and routine. Dykens et al. (1997) stress the need for teaching strategies that recognize their weaknesses in sequential processing and take advantage of their strengths in visual reasoning and other non-verbal areas. The use of visual cues in the form of pictures and symbols can aid recall of more complex sequential tasks and generally help with comprehension. Their particular interest in computers can also be used in teaching pre-reading and reading skills and promoting visuo-spatial skills. Individuals with Smith-Magenis syndrome tend to be eager to please and very responsive to adult attention; hence praise and attention from

teachers and other adults, if used judiciously, can serve as useful reinforcers.

Parents and teachers describe a range of situations and characteristics that are likely to trigger aggressive outbursts and self-injurious behaviours (Haas-Givler & Finucane, 1996; Horn, 1999; Webber, 1999). These include an insatiable need for attention from adults and competition for their attention, transitioning from one activity or setting to another, unexpected changes in routine, tiredness, frustration, being reprimanded and not getting their own way. Attempts to anticipate and avoid such situations, for example by preparing the child for any change of routine well ahead of time, using clear instructions, rewards and distraction techniques (music, for example) are often effective in diffusing the situation. If not, ignoring aggressive behaviours or removing the child to another room and letting outbursts run their course may be the only remaining course of action. The range of triggers for aggressive behaviours and self-injury highlights the importance of carrying out a thorough functional analysis in each case so that appropriate interventions can be introduced. Moreover, in view of the prevalence of autistic-type behaviours in individuals with Smith-Magenis syndrome, it is recommended that multidisciplinary assessment for autistic spectrum disorders is undertaken. This would allow for a greater understanding of their communication difficulties and needs by parents and professionals, and could facilitate access to appropriate educational and mental health services.

A range of medications has been tried in an attempt to reduce the characteristic aggressive outbursts (Horn, 1999; Webber, 1999), but there have been no controlled trials of their effectiveness. Anecdotally, some medications have proven to be ineffective; others have been beneficial in some cases, but resulted in a worsening of behaviour for others. Clearly, if medication is going to be introduced for any one individual, it will need to be carefully monitored.

As regards the sleep difficulties of individuals with Smith-Magenis syndrome, parents' interventions have focused on keeping their children safe at night and attempting to minimize the disruption caused by night-waking. Implementing a firm and consistent approach, removing all small objects and breakables from the bedroom, locking the bedroom door or other doors in the house, use of blackout curtains to minimize light, firm and consistent instructions to return to bed, and providing soft toys, magazines, a tape recorder or television (in the case of older individuals), have all been reported to be helpful in minimizing night-time disruption in at least some cases, although not necessarily in increasing the amount of sleep (Smith et al., 1998b; Horn, 1999; Webber, 1999). Reducing daytime sleep is also effective for some individuals, though it can result in a worsening in behaviour in other cases. There have been anecdotal

Table 12.3. Smith-Magenis syndrome: implications of the phenotype for carers and professionals

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- Regular medical checks should include:
 - eye examinations
 - hearing checks
 - ear, nose and throat checks
 - heart and kidney investigations
 - thyroid function
 - scoliosis
 - Despite intellectual abilities mostly in the mild learning disabilities range, most individuals require substantial assistance with daily living skills and show little independence
 - Severe behavioural difficulties requiring psychological interventions, and possibly also medication, include:
 - aggressive outbursts
 - self-injurious behaviours
 - sleep disturbance
 - hyperactivity and impulsivity
 - Support and advice for carers is critical in view of severely challenging behaviours
 - Assessment for autistic spectrum disorders is advisable in view of the high prevalence of autistic type behaviours in the syndrome
-

reports from the United States of improvements in sleep patterns with the administration of melatonin, but formal treatment trials are required before any recommendations can be made in this regard. Other medications for sleep have anecdotally shown mixed responses, with many individuals finding them ineffective (Horn, 1999; Webber, 1999).

The high prevalence rates of aggressive and self-injurious behaviours and the severe sleep disturbance found in both children and adults with Smith-Magenis syndrome underline the urgent need for research into effective management techniques and medications, and for appropriate and accessible mental health and social services provision for this population. There have been a number of cases in the UK and United States where concerns were raised about possible physical abuse by adults towards their children with Smith-Magenis syndrome, before the correct attribution of self-inflicted injuries by the children was made. In other cases parents have been blamed by teachers, social workers and others for the aggressive outbursts and excessive daytime sleepiness of their children. It is imperative that professionals have a good understanding of the implications of syndrome diagnosis for cognitive and behavioural characteristics, and that they are able to consider the often severe and disturbing behaviours

exhibited by individuals with Smith-Magenis syndrome in the context of the underlying genetic syndrome.

For a summary of the implications of the phenotype for carers and professionals see Table 12.3.

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