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# Oral features and dental health in Hurler Syndrome following hematopoietic stem cell transplantation

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**Background.** Hurler Syndrome is associated with a deficiency of a specific lysosomal enzyme involved in the degradation of glycosaminoglycans. Hematopoietic stem cell transplantation (HSCT) in early infancy is undertaken to help prevent the accumulation of glycosaminoglycans and improve organ function.

**Aim.** To investigate the oral features and dental health of patients with Hurler Syndrome who have undergone successful HSCT.

**Materials and methods.** Twenty-five patients (median age 8.6 years) post-HSCT (mean age 9.4 months) underwent oral assessment (mean of 7.5 years post-HSCT).

**Results.** Dental development was delayed. Numerous occlusal anomalies were noted including: open-bite, class III skeletal base, dental spacing, primary molar infra-occlusion and ectopic tooth eruption. Dental anomalies included hypodontia, microdontia, enamel defects, thin tapering canine crowns, pointed molar cusps, bulbous molar crowns and molar taurodontism. Tooth roots were usually short/blunted/spindle-like in permanent molars. The prevalence of dental caries was low in the permanent dentition (mean DMFT 0.7) but high in the primary dentition (mean dmft 2.4). Oral hygiene instruction with plaque and or calculus removal was indicated in 71% of those that were dentate.

**Conclusion.** Patients with Hurler Syndrome post-HSCT are likely to have delayed dental development, a malocclusion, and dental anomalies, particularly hypodontia and microdontia.

## Introduction

The mucopolysaccharidoses are a group of inherited disorders resulting from a lack of specific lysosomal enzymes involved in the degradation of glycosaminoglycans (GAGs). The accumulation of these partially degraded GAGs causes interference with cell, tissue and organ function, leading to a variety of systemic manifestations[1]. Mucopolysaccharidosis type 1 (MPS1) is an autosomal recessive condition with severe (Hurler), moderate (Hurler-Scheie) and mild (Scheie) clinical phenotypes. The reported incidence of MPS1 in Ireland is 0.08 per 10,000 births. However, the highest recorded incidence of MPS1 worldwide is amongst Irish Travellers (an endogamous nomadic group in Ireland who are ethnically distinct from Roma gypsies) at 1 in 371 births.[2]

Hurler Syndrome is associated with a deficiency of the enzyme α-L-iduronidase and is characterised by growth failure after infancy, learning impairment, craniofacial dysmorphism, dysostosis multiplex, corneal clouding, hernias and hepatosplenomegaly. Cardiovascular, respiratory, dermatological and other musculoskeletal anomalies are usually present to varying degrees. Children may appear normal at birth and develop the characteristic appearance over the first years of life.[1] Without intervention, Hurler Syndrome is associated with severe morbidity and early mortality. Life expectancy is limited to 5–8 years as patients succumb to cardiorespiratory failure.

Craniofacial features include a slight coarsening of the face, large head and snub nose

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with a depressed nasal bridge, broad nasal tip, and anteverted nostrils. Hypertelorism, prominent lower eyelids and enlarged lips with open mouth posture are other features that are associated with this syndrome.[3] Numerous oral features have been described in association with Hurler Syndrome including a short and broad mandible, macroglossia, gingival hyperplasia and flattened alveolar ridges. Palatal anatomy has been reported as high and arched and often with pronounced rugae. Delayed eruption of teeth, a spaced dentition and an anterior open bite may be present. Teeth have been described as misshapen, peg shaped, small, short, poorly formed and hypoplastic. Radiographic features that have been reported include small, flattened or absent condyles and dentigerous cysts in association with mandibular molars.[4–7]

Allogeneic hematopoietic stem cell transplantation (HSCT) has undoubtedly improved the quality of life in those affected with Hurler Syndrome, particularly if undertaken in the first few years of life. Donor stem cells provide sustained levels of α-L-iduronidase resulting in resolution of excess GAGs in body tissues that in turn reverses many of the features associated with this condition. Current practice is to administer weekly infusions of recombinant enzyme replacement therapy from the time of diagnosis of Hurler Syndrome until there is evidence of engraftment post-transplant.[8] Infants born to affected families are screened in the first few weeks of life and usually transplanted in infancy, often before they have developed the characteristic phenotypic appearance.

There has been little reported in the literature on the effects of HSCT on the oral features of patients with Hurler Syndrome. Fleming *et al.*[9] reported a reduction in gingival hypertrophy and macroglossia in patients with Hurler Syndrome post HSCT. Hingston *et al.*[10] and more recently Wadenya *et al.*[11] have carried out a detailed dental examination of a child with Hurler Syndrome post-HSCT and noted that many of the features that had previously been described in patients with Hurler Syndrome were present in their case together with a newly reported feature of hypodontia. The aim of our study was to assess the oral features and dental health of a large cohort of patients with Hurler Syndrome who had successful engraftment following HSCT.

## Patients and methods

All patients attending the annual, multidisciplinary Hurler clinic at the National Paediatric Hematopoietic Stem Cell Transplant Unit at Our Lady's Children's Hospital, Dublin were included in the study. Demographic data were recorded for all those who were examined. Written informed consent was obtained from all parents.

Patients underwent a clinical examination by trained and calibrated examiners (EMG, JN) seated in a dental chair with a conventional dental light for illumination. A clinical examination of all oral soft tissues was followed by an assessment of the occlusion and of any dental anomalies of tooth size, shape and structure. Microdontia was recorded when the size of a tooth crown was judged on clinical examination to be less than 50% the size considered 'normal' for that tooth. Abnormality of tooth shape was descriptive and the modified Developmental Defects of Enamel (DDE) index, was used to assess enamel defects (FDI, 1992).

Radiographic examination was undertaken if indicated for clinical treatment planning on an individual patient basis. Radiographs taken by the patient's local dental practitioner were also included for assessment, if available. Assessment of radiographs was undertaken by a dental radiologist (AB).

The prevalence of dental caries was determined using the World Health Organisation criteria (1987),[12] with the addition of visual non-cavitated dental caries as used in the All-Ireland Child Dental Health Survey in 2002.[13] DMFT/S, dmft/s were reported in the mixed dentition until 8 years of age, after which age dft and dfs were reported in conjunction with DMFT and DMFS. The teeth were examined wet and a periodontal probe used only to remove food debris. The periodontal tissues were examined without probing and an assessment was made of the need for oral hygiene

instruction, plaque and calculus removal or the need for urgent periodontal treatment.

Erosion was measured using the criteria developed for the oral health examination as part of the UK National Diet and Nutrition Survey (NDNS) of 4–18 year olds.[14] The buccal and palatal surfaces of the mandibular and maxillary central and lateral incisors, and the occlusal surfaces of the first permanent molars and second primary molars were included in the assessment of erosion.

An oral health questionnaire for each patient was completed by a family member at the time of the dental examination. Questions in relation to dental attendance, history of dental pain, oral hygiene practises and consumption of sugary foods and drinks were included in the questionnaire.

## Results

### *Sample*

A total of 25 patients were examined, ranging in age from 6 months to 20 years (mean age 8.7 years, median age 8.6 years). There were 13 males and 12 females. All patients had undergone allogeneic, related or unrelated transplant following full myeloablative conditioning with busulphan and cyclophosphamide. The mean age of patients at HSCT was 9.4 months (range 5–20 months). The median age of years post-transplant was 7.5 years. All patients were receiving longterm pneumococcal prophylaxis with either amoxicillin and clavulinic acid or penicillin.

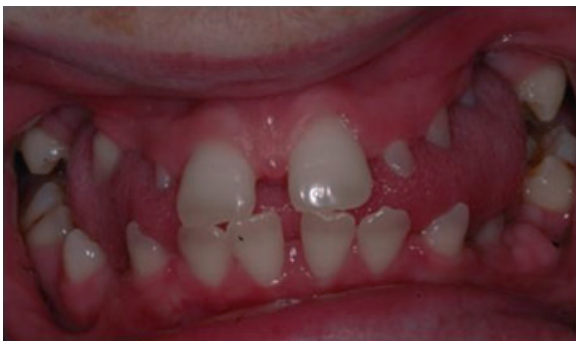

**Fig. 1.** Oral features of patients with Hurler Syndrome post HSCT. Note the Class III occlusion, bilateral posterior openbite and macroglossia.

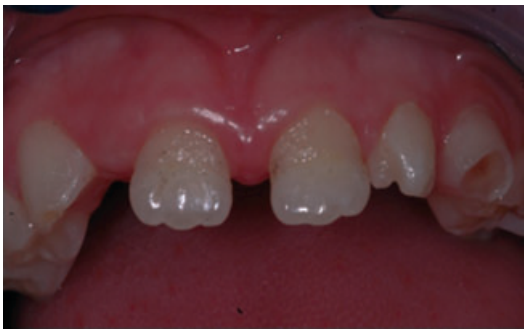

**Fig. 2.** Oral features of patients with Hurler Syndrome post HSCT. Note the missing 12 and the notched 22.

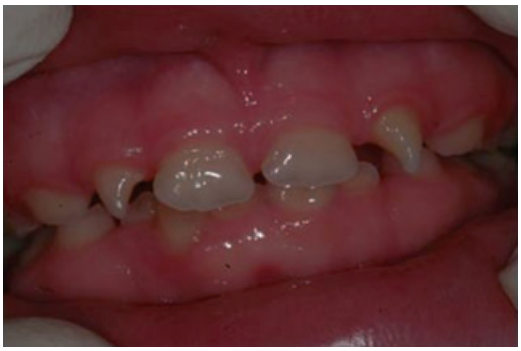

**Fig. 3.** Oral features of patients with Hurler Syndrome post HSCT. Note the missing 12 and 22 and the thin incisal edges of 11 and 21.

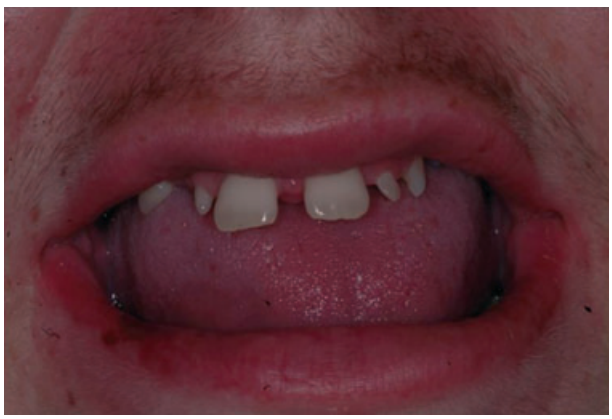

**Fig. 4.** Oral features of patients with Hurler Syndrome post HSCT. Note the macroglossia, microdonts (12 and 22) and splayed incisors.

### *Oral features*

There were no signs of graft versus host disease (GVHD) in any of the 25 patients in this group. A number of the oral features identified are presented in Figs 1–6. Enlarged lips

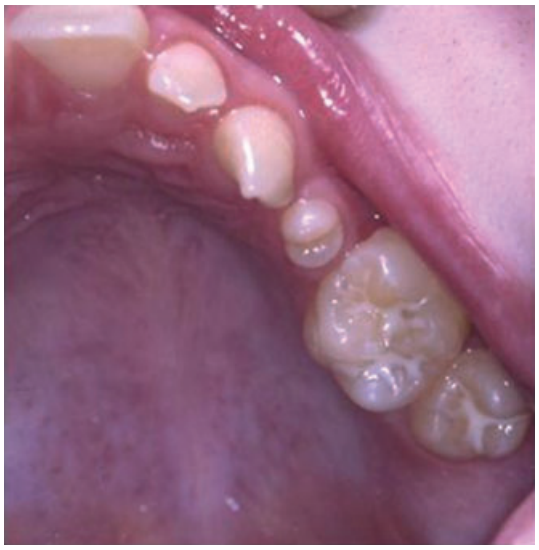

**Fig. 5.** Oral features of patients with Hurler Syndrome post HSCT. Note the pointed cusp of 23, microdonts (24 and 27), and the missing 25.

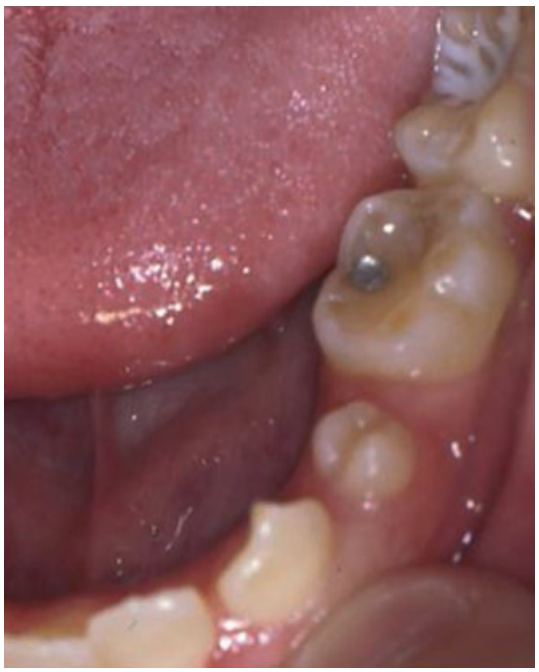

**Fig. 6.** Oral features of patients with Hurler Syndrome post HSCT. Note the pointed cusp of 33, microdont 34 and missing 35.

were noted in three patients and macroglossia in eight. Anomalies in palatal anatomy varied among the group and included grooves, both horizontal and vertical, and U, V, flat or broad shaped palatal vaults. The alveolar ridges appeared to be normal apart from two cases where the ridge was either flattened or

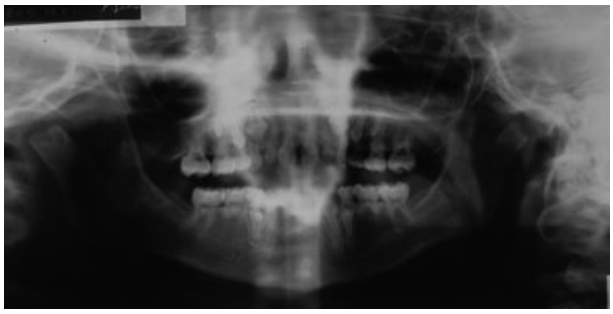

**Fig. 7.** A dental panoramic tomograph demonstrating concave deformity of the condylar heads, short rami and an obtuse gonional angle. There is marked hypodontia with all second permanent molars and the lower second premolars absent. Erupted teeth demonstrate bulbosity of the crowns with shortened root patterns. Developing upper premolars and canines also demonstrate abnormalities of the crown and root structure.

enlarged. An eruption cyst was observed in one infant.

Skeletal classification was assessed clinically in 21 cases: eight presented with an Angles Class I, seven with a Class II, and six with a Class III relationship. Molar and incisor relationships followed an identical pattern. An anterior open bite was noted in nine patients and a posterior open bite was observed in two cases. Sixteen patients had generalised spacing. A delayed and abnormal eruption sequence was noted in nine patients. Ectopic eruption of the first permanent molars was observed in three patients and primary molar infraocclusion was observed in four patients.

Microdontia of permanent teeth was noted clinically in thirteen of the seventeen patients with a mean of five teeth affected. Other anomalies of the permanent teeth included: thin tapering canine crowns in nine patients, pointed molar cusps in five patients, thin incisal edge enamel in three patients, notching of the incisal edge in two patients and mild incisor crown dilacerations in one patient. Enamel hypoplasia, hypomineralisation or opacities were noted in seven patients. All 25 patients had at least one dento-skeletal/soft tissue abnormality.

### *Radiographic findings*

Dental panoramic tomographs (DPTs) were available for sixteen of the 25 patients

**Table 1. Dental panoramic tomographic findings of 16 patients with Hurler Syndrome post-HSCT.**

| | Patient number | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Feature** | **1** | **4** | **6** | **7** | **8** | **9** | **10** | **15** | **16** | **17** | **19** | **20** | **21** | **22** | **23** | **25** |
| Obtuse gonional angle | * | | | * | | | | | | * | | | | * | | |
| Enlarged styloid process | | | | * | * | | * | | | | | | | | | * |
| Condylar features | * | * | * | * | * | * | * | * | | | * | * | | | | * |
| Missing articular eminence | | | | | | | | | | | | | | | | * |
| Short ramus | * | | * | | | | | | | | * | | | | * | |
| Cyst formation | | | | | | | Possible | | | | | * | | | | |
| Bulbous crowns | * | * | * | * | | * | * | * | | * | * | * | | | * | * |
| Short and blunted roots | * | | * | | * | * | * | | * | | * | | | | * | * |
| Taurodontism | * | | | * | Possible | | * | | * | | | * | | | | |
| Hypodontia | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * |
| *Teeth missing* | 15 | 15 | 12 | 15 | 14 | 17 | 12 | 13 | 15 | 15 | 17 | 25 | 15 | 12 | 14 | 15 |
| | 44 | 25 | 15 | 25 | 15 | 27 | 15 | 15 | 25 | 35 | 25 | 35 | 25 | 22 | 15 | 17 |
| | | 35 | 22 | 37 | 24 | 35 | 25 | 17 | 35 | 37 | 27 | 37 | 35 | | 24 | 24 |
| | | 45 | 25 | 47 | 25 | 37 | 35 | 25 | 37 | 45 | 35 | 44 | 45 | | 25 | 25 |
| | | | 35 | | 34 | 45 | 45 | 27 | 45 | 47 | 37 | 45 | | | 35 | 27 |
| | | | 45 | | 35 | 47 | | 35 | | | 44 | | | | 45 | 34 |
| | | | | | 44 | | | 45 | | | 45 | | | | 47 | 35 |
| | | | | | 45 | | | | | | 47 | | | | | 37 |
| | | | | | | | | | | | | | | | | 45 |
| | | | | | | | | | | | | | | | | 47 |
| *Total number of missing teeth* | 2 | 4 | 6 | 4 | 8 | 6 | 5 | 7 | 5 | 5 | 8 | 5 | 4 | 2 | 7 | 10 |
| Microdontia | * | * | * | * | * | | * | * | * | * | * | * | * | | * | * |

*****Identifies the presence of the feature. [Correction added after online publication 2 June 2010: Values in Row 6 of 'Teeth Missing' and asterisks in last row were realigned].

(Fig. 7) and bitewing radiographs for two of the group. A summary of findings from the DPTs is presented in Table 1. Eleven of the sixteen DPTs demonstrated flattened or concave shaped condylar heads. In one DPT there was evidence of a decrease in the size of the articular eminence. Pronounced and thickened stylohyoid ligaments were noted in DPTs exposed for four patients.

Hypodontia, excluding absent third permanent molars, was noted in all sixteen patients for whom DPTs were available (range of 2–10 missing teeth per patient, mean 5.5). The second premolars and second permanent molars were the most commonly missing teeth. Microdontia was noted radiographically in fourteen of the sixteen patients. Short and blunted tooth roots, particularly affecting the permanent first molars, were noted in nine cases. Spindle like roots of permanent molar teeth were also observed. Permanent incisors were noted radiographically to have short roots, although this may have been due to the inclination of the teeth and difficulties in positioning the patients for the DPT. Teeth with bulbous crowns and cervical constriction were observed in both primary and permanent molars. Taurodontism was noted in five patients, affecting either the second permanent molars or the first and second primary molars.

### *Dental health indices*

Fourteen (14/24) of the dentate group were caries-free with no evidence of past caries experience. The mean caries prevalence of the dentate patients was: DMFT 0.7 (range 0–3), DMFS 1.1 (range 0–5), dmft 2.4 (range 0–11), dmfs 7.1 (range 0–49), dft 0.9 (range 0–3), and dfs 1.2 (range 0–5). The periodontal treatment needs were high with seventeen patients requiring oral hygiene and plaque or calculus removal. Erosion was evident in the teeth of eight of 24 dentate individuals with a mean of two teeth affected per individual. Erosion of both enamel and dentine was evident, with one third to two thirds of the index surfaces involved in over half of the teeth affected and greater than two thirds of the surfaces involved in the remaining teeth.

### *Dental health questionnaire*

Twenty-two questionnaires were completed by parents. Nineteen of the group reported that their child attended the dentist every 6–12 months and two reported a history of dental pain that resulted in missing days from school. Thirteen parents reported that their children were frightened or a little worried about attending the dentist and nineteen parents wished to be in the dental surgery during their child's dental visit. Seven parents noted that their child had had their first dental visit and had started tooth brushing by their first birthday. Eleven parents brushed their children's teeth twice daily. Sixteen (72%) of the group reported the consumption of sugary/fruit drinks at least once a day and six reported the consumption of such drinks at least three to four times per day.

## Discussion

Many of the previously reported oral features of Hurler Syndrome such as macroglossia and abnormalities in palatal shape, were observed in this study. However, features such as lip enlargement presented in just two patients and gingival hyperplasia not at all. The absence of such features may be attributed to early HSCT eliminating or greatly decreasing the deposition of excess GAGs into body tissues. More than one third of our group of patients demonstrated delayed dental development and eruption despite the absence of gingival hypertrophy. It would seem, therefore, that gingival hypertrophy is unlikely to be the primary cause of the delayed dental development in Hurler Syndrome as previously thought.[15] While a small minority of patients had minimal GVHD of the skin, no patients experienced GVHD of the gut or oral cavity. This is not surprising as all patients had fully matched grafts.

In keeping with other reports on Hurler Syndrome,[5] a spaced dentition was frequently noted in the study population along with other occlusal anomalies such as an anterior open bite and a tendency towards a class three occlusion. Not all cases of anterior open bite were associated with macroglossia. Ectopic tooth eruption and primary molar infraocclusion added to the occlusal abnormalities in a number of patients.

Abnormalities of tooth number, size, shape and structure were widespread among the study group. Hypodontia of the permanent dentition, excluding third molars, was observed in all sixteen patients who underwent radiographic examination with a DPT (mean of 5.5 missing permanent teeth per person). The prevalence of hypodontia in the general population has been reported to be between 3.5 and 6.5% in the UK,[16] and as high as 17% in patients treated for neuroblastoma in early childhood.[17] Holtta *et al.* reported a 31% prevalence of hypodontia among young patients who had undergone HSCT for malignant disease, with a 77% prevalence of hypodontia in those who had undergone HSCT under 3 years of age.[18] The most frequently missing teeth were second premolars followed by second molars, first premolars and maxillary lateral incisors.[18] These were also the most frequently missing teeth in our patients who had undergone HSCT for management of Hurler Syndrome. Hypodontia with similar missing teeth has previously been reported in two cases of children with Hurler Syndrome post-HSCT.[10,11]

Microdontia (permanent dentition) was present in 76% of the dentate patients examined clinically and in 88% of patients with DPTs. Previous reports of patients with Hurler Syndrome have made reference to the occurrence of 'short stubby teeth' and 'small peg shaped incisors'.[7] Microdontia has also been observed in patients who have undergone HSCT for malignant disease with a prevalence of 75% in patients who had received transplant before 3 years of age.[18] It is not known if the high prevalence of hypodontia and microdontia noted in our patients is associated with their distinctive genotype, their early HSCT and conditioning regime or a combination of both of these factors. Irrespective of the aetiology, it can be anticipated that patients with Hurler Syndrome who have undergone HSCT will have a number of missing (most likely the second premolars and second permanent molars) and small teeth.

Abnormalities of tooth shape ('peg shaped teeth and malformed teeth') are well described in Hurler Syndrome. In our study of patients with Hurler Syndrome post HSCT numerous anomalies were noted. They included thin incisal tips, thin tapering (pointed) canine and molar cusps, mild crown dilacerations (particularly affecting incisors) and accessory molar cusps. It is interesting to note that pointed canines were also observed in a previous case report of a child with Hurler Syndrome, post-HSCT.[10] Enamel defects (hypoplasia or hypomineralisation) were noted in 28% of our patients.

The crowns of primary and permanent molars were noted to be bulbous with marked cervical constriction. Roots tended to be short and blunted or in some cases spindle-like on radiographs. Dilaceration of the distal root of first and second permanent molars and delayed root formation was noted by Worth in his report on patients with Hurler Syndrome in 1966. Disturbed dental root development has also been observed in patients who have received HSCT as part of their management of malignant disease.[21] Such disturbances were more extensive in the patients who were between 3.1 and 5.0 years at time of transplant.[21] The mean age of transplant in our group was 9.4 months. Taurodontism of the primary and permanent molars was evident in our patients and had also been described in a recent case report of a 13-year-old boy with Hurler Syndrome who had not been transplanted.[19]

In keeping with previous reports[5,10,20] on Hurler Syndrome, many characteristic radiographic features were observed in our group such as flattened or concave shaped condylar heads, a decreased size in the articular eminence and thickened stylohyoid ligaments. The presence of dentigerous, cyst-like lesions in the jaws has been previously described as a prominent radiographic feature.[5,19] It is likely that the absence of dentigerous cyst like lesions in our patients reflects the metabolic improvement following HSCT, as the cystic lesions in untreated patients with Hurler Syndrome were believed to represent collections of GAGs.

The prevalence of dental caries was low, with 58% of the dentate individuals being caries-free. The mean DMFT of 0.7 was lower than the national average for 12-year-olds of 1.1 in fluoridated areas and 1.5 in non fluoridated areas of Ireland.[13] However caries prevalence was higher in the primary dentition with the mean dmft (2.4, $n = 10$) being greater than the national average for 5-year-olds (mean dmft of 1 and 1.8 in fluoridated and non fluoridated areas respectively). Only 60% of children less than 5 years of age were caries-free compared to 70% of the national population at 5 years of age in fluoridated areas of Ireland.[13] The generalised spacing and microdontia in the permanent dentition may help explain the lower prevalence of dental caries in that dentition, as may the regular and appropriate use of fluoridated toothpaste in half of the group. The daily use of antibiotic prophylaxis following HSCT may have also been a contributory factor. However, antibiotic compliance was not recorded. As many of the patients in our study were Irish Travellers determination of past fluoride exposure was impossible. There were however no signs of fluorosis in any of the group examined.

The health of the periodontal tissues was based on treatment need. Oral hygiene and plaque with or without calculus removal was indicated in 71% of the group. This compares to 17% of 5–15 year olds in a recent national oral health survey in Ireland.[12] None of the patients with Hurler Syndrome in our study group required urgent treatment for periodontal disease.

Erosion was prevalent in eight of the group and may be attributed to the high frequency of fruit and/or sugary drinks consumed in this group, with 72% of the group reporting consumption of fruit/sugary drinks at least once a day.

In conclusion this group of patients with Hurler Syndrome who were on average 7.5 years post-HSCT at the time of assessment displayed many soft tissue and dento-skeletal anomalies that were in keeping with previous reports on Hurler Syndrome. The absence of a number of expected abnormalities such as gingival hyperplasia and dentigerous cyst type lesions may be attributed to the early HSCT eliminating or reducing the excess deposition of GAGs in body tissues. There was a very

high prevalence of hypodontia and microdontia. These and other dental anomalies may occur due to the patients' distinctive genotype, the HSCT and conditioning regime at a very young age, or due to a combination of both of these factors.

**What this paper adds**

- This paper identifies the oral features and dental health of a unique cohort of 25 patients with Hurler Syndrome following successful HSCT in infancy.
- It reports that all patients have dento-skeletal anomalies including delayed dental development, malocclusion and a spaced dentition.
- It identifies a very high prevalence of hypodontia affecting the second premolars and second permanent molar teeth.
- It identifies a high prevalence of microdontia, anomalies of tooth shape, enamel defects and root anomalies in this group.
- It reports a low prevalence of dental caries in the permanent dentition and poor gingival health.

**Why this paper is important for paediatric dentists**

- Paediatric dentists should be aware of the high rate of dento-skeletal and dental anomalies and the tendency towards poor gingival health in this population of patients.
- Patients with Hurler Syndrome should be enrolled in specialist paediatric dental services from an early age in order to optimise dental development and oral health.

## Acknowledgements

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## References

1 OMIM #607014. http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=607014. Accessed September, 2009.
2 Murphy AM, Lambert DM, Treacy EP, O'Meara A, Lynch SA. Incidence and prevalence of mucopolysaccharidosis Type 1 in the Irish Republic. *Arch Dis Child* 2009; **94**: 52–54.
3 Gorlin RJ, Chaudhary AP, Kelln EE. Oral manifestations of the Fitzgerald-Gardner, Pringle-Bourneville, Robin. Adrenogenital, and Hurler-Pfaundler syndromes. *Oral Surg Oral Med Oral Pathol* 1960; **13**: 1233–1244.
4 Thomas S, Tandon S. Hurler syndrome: a case report. *J Clin Pediatr Dent* 2000; **24**: 335–338.
5 Gardner DG. The oral manifestations of Hurler's syndrome. *Oral Surg Oral Med Oral Pathol* 1971; **32**: 46–57.
6 Worth HM. Hurler's syndrome. A study of radiologic appearances in the jaws. *Oral Surg Oral Med Oral Pathol* 1966; **22**: 21–35.
7 Leroy JG, Crocker AC. Clinical definition of the Hurler-Hunter phenotypes. A review of 50 patients. *Am J Dis Child* 1966; **112**: 518–530.
8 Cox-Brinkman J, Boelens JJ, Wraith JE *et al.* Haematopoietic cell transplantation (HCT) in combination with enzyme replacement therapy (ERT) in patients with Hurler syndrome. *Bone Marrow Transplant* 2006; **38**: 17–21.
9 Fleming DR, Henslee-Downey PJ, Ciocci G *et al.* The use of partially HLA-mismatched donors for allogeneic transplantation in patients with mucopolysaccharidosis-I. *Pediatr Transplant* 1998; **2**: 299–304.
10 Hingston EJ, Hunter ML, Hunter B, Drage N. Hurler's syndrome: dental findings in a case treated with bone marrow transplantation in infancy. *Int J Paediatr Dent* 2006; **16**: 207–212.
11 Wadenya RO, Stout AM, Gupta A, Monge J. Hurler syndrome: a case report of a 5-year follow-up of dental findings after bone marrow transplantation. *Spec Care Dentist* 2010; **30**: 14–17.
12 World Health Organisation. *Oral Health Surveys: Basic Methods*. Geneva: WHO, 1987.
13 National Children's Oral Health Survey in Ireland in 2002. http://www.dohc.ie/publications/pdf/oral_health_report.pdf?direct=1&bcsi_scan_D6F1EE213C459C76 = 0&bcsi_scan_filename=oral_health_report.pdf. Accessed 7th January 2008.
14 Walker A, Gregory J, Bradnock J, Nunn J, White D *National Diet and Nutrition Survey: Young People Aged 4 to 18 Years. Report of the Oral Health Survey*, Vol. 2. London: The Stationery Office, 2000.
15 Cawson RA. The oral changes in gargoylism. *Proc R Soc Med* 1962; **55**: 1066–1070.
16 Brook AH. Dental anomalies of number, form and size: their prevalence in British schoolchildren. *J Int Assoc Dent Child* 1974; **5**: 37–53.
17 Kaste SC, Hopkins KP, Bowman LC, Santana VM. Dental abnormalities in children treated for neuroblastoma. *Med Pediatr Oncol* 1998; **30**: 22–27.
18 Hölttä P, Alaluusua S, Saarinen-Pihkala UM, Peltola J, Hovi L. Agenesis and microdontia of permanent teeth as late adverse effects after stem cell transplantation in young children. *Cancer* 2005; **103**: 181–190.
19 Guven G, Cehreli ZC, Altun C *et al.* Mucopolysaccharidosis type I (Hurler syndrome): oral and radiographic findings and ultrastructural/chemical features of enamel and dentin. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008; **105**: 72–78. Epub 2007 Jun 29.
20 Oestreich AE. The stylohyoid ligament in Hurler syndrome and related conditions: comparison with normal children. *Radiology* 1985; **154**: 665–666.
21 Hölttä P, Hovi L, Saarinen-Pihkala UM, Peltola J, Alaluusua S. Disturbed root development of permanent teeth after pediatric stem cell transplantation. Dental root development after SCT. *Cancer* 2005; **103**: 1484–1493.