

The oral health needs of children after treatment for a solid tumour or lymphoma

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Background. With increasing survival rates for childhood cancer, late effects are of growing importance. Oral health is central to general health, level of nutrition, quality of life, and is significant in the holistic care of children during cancer therapy.

Hypothesis. The oral health needs of children treated for solid tumours/lymphoma will be greater than the general population, groups will differ according to tumour and treatment.

Design. One hundred and twenty patients, 0–17 years, under follow-up from 01/07/06 to 07/02/07 were investigated for caries, opacities, microdontia, and gingivitis. Analysis was per-

formed with stratification according to tumour and treatment. Comparisons made with the UK 2003 Child Dental Health Survey.

Results. The neuroblastoma group and high-dose chemotherapy with stem-cell rescue (HDCSCR) therapy group had increased caries of the primary teeth. Chi-squared analysis revealed a statistically significant relationship ($P < 0.03$) between the age at receipt of chemotherapy (<3.5 years) and the presence of microdont teeth.

Conclusion. Oral health care is important for all patients particularly those with a neuroblastoma, or who received HDCSCR. Patients should be advised about the possibility of microdontia in the permanent dentition following chemotherapy under 3.5 years.

Introduction

Childhood cancer is fortunately rare in the UK with incidence rates being in the range of 110–150 per million children per year¹. There has been a large reduction in mortality as a result of early diagnosis and improved treatment regimes. By the year 2000, one in 900 adults aged 16–34 years were survivors of childhood cancer². One-third (32%) of childhood cancers are leukaemia's, 10% lymphomas, 24% brain and spinal tumours, and 15% embryonal tumours, such as neuroblastoma, retinoblastoma, Wilm's tumour, and hepatoblastoma. The remaining 19% comprise other types of cancer¹. The late effects of childhood cancer are becoming increasingly important to diagnose and manage, as the number of survivors rises.

Maintaining good oral health is important for all children. The UK Child Dental Health

Survey 2003 (CDHS) found that 43% of 5-year olds and 57% of 8-year olds had experienced obvious caries in their primary teeth³. In the permanent dentition 14% of 8-year olds, 34% of 12-year olds, and 49% of 15-year olds had experienced obvious caries⁴. This knowledge of the state of children's general dental health highlights the importance of dental input prior to, during and after cancer therapy. The effects of cancer treatment are well reported to be associated with oral complications⁵ as well as systemic medical complications, such as neutropenia and thrombocytopenia⁶. The management of oral problems becomes more challenging with the addition of risk factors such as these.

The literature covering the effects of cancer therapy on the oral cavity in children is limited. Studies employ small sample sizes because of the nature of the disease and significant numbers of confounding factors within the groups makes comparison between studies difficult. Table 1 details previous studies investigating the effects of cancer therapy on the developing dentition. This study focused on the solid tumour group

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Table 1. Previous studies investigating the effects of cancer therapy on the developing dentition.

Authors (year), country	Study group + disease type	Control group	Main findings
Alpaslan <i>et al.</i> (1999) ¹³ , Turkey	30 children 4- to 15-year old with Hodgkins or non-Hodgkins disease	20 healthy children 4–15 years	Significant differences ($P < 0.05$) in the prevalence of enamel hypoplasias, discolourations and agenesis in the study group. Increased level of plaque in the study group. No differences for gingival index, dental caries and craniofacial growth
Kaste <i>et al.</i> (1998) ¹² , America (Memphis)	52 children 1.9- to 19.3-year old with a neurolastoma	Normal population but no details of methods	Increase in dental abnormalities (71% with an abnormality). Including microdontia, caries of the primary dentition, hypodontia, root stunting and enamel hypoplasia
Maguire <i>et al.</i> (1987) ¹⁴ , UK (Newcastle)	52 children 3- to 22-year old. 27 leukaemia, 25 solid tumours	49 siblings ages 2–23 years	Increased opacities and hypoplasia in the study group. Large number of radiographic abnormalities in the study group including failed root development, microdontia, hypoplasia and missing teeth. No significant differences in dental caries, gingivitis and oral hygiene and mouth opening
Nunn <i>et al.</i> (1991) ¹⁵ , UK (Newcastle)	52 children 4.75–24.25 years. Childhood cancer (breakdown not specified)	41 siblings ages 3.4–20.8 years	Study group showed significantly more radiographic evidence of enamel hypoplasia, taurodontism, microdontia, thin roots and root constrictions. Increased level of enamel opacities, enamel hypoplasia but not statistically significant. No significant differences in dental caries and gingival health
Purdell-Lewis <i>et al.</i> (1988) ¹⁷ , The Netherlands	45 children 7–13 years. Leukaemia and solid tumours	National data	Higher prevalence of dental caries and enamel opacities. Radiographic evidence of delayed tooth malformation, shortened malformed roots and smaller crown size. No difference in oral hygiene

which in this investigation also included children with Hodgkin's lymphoma and non-Hodgkin's lymphoma.

Materials and methods

The study took place over 8 months from July 2006 to February 2007. Ethical approval was obtained from Dudley Primary Care Trust Research Ethics Committee (reference 05/Q2701/93). The research and development departments of both South Birmingham Primary Care Trust and Birmingham Children's Hospital NHS Foundation Trust approved the research protocol. A small grant was awarded by the Birmingham Children's Hospital Research Foundation BCHRF149f.

Any child who had finished cancer treatment and had received a course of

chemotherapy as part of their cancer therapy was invited to take part in the study. The only exclusions were those children who had received radiotherapy to the head and neck area specifically. The study group consisted of 120 patients (69 males and 51 females) attending the oncology follow-up clinic. Overall 147 children were invited by letter, 10 refused, and the remainder had not attended the expected medical review appointment.

As a result of difficulties gaining access to schools and the request at the time of the study to obtain positive consent, accessing a healthy age- and sex-matched population was not possible. Therefore, the national published data available in the public domain was used as a control database for this study. This included the CDHS 2003 and the British

Association for the Study of Community Dentistry (BASCD) epidemiological studies.

The primary investigator was a specialist registrar in paediatric dentistry and was trained in the examination of caries using the criteria of diagnosis as described by the BASCD⁷. The primary investigator also worked through the 2003 DHS of children and young people computer training program as required by the national examiners in the 2003 CDHS. Because of practical constraints, the enamel opacities in this study were recorded in the dental chair at the same time as the dental examination.

A dental charting was performed, which included, decayed missing, and filled teeth (DMFT for adult dentition; dmft for primary dentition), enamel opacities, fissure sealed, microdont (the tooth was visually less than 50% of its expected size) or traumatized teeth were recorded on specific data collection sheets. A basic periodontal examination and gingival bleeding score were recorded in patients with fully erupted permanent incisors and first molars.

The dental examination was carried out in accordance with the BASCD specifications written for dental screenings in epidemiological studies⁸. The CDHS 2003 followed similar criteria except a flat table was used for the patient to lie on for the dental examination⁹.

Medical diagnosis, date of diagnosis, date of birth, gender, address, treatment regime, length of chemotherapy, and date follow-up commenced was recorded by the medical doctor before the dental examination on a specific data sheet.

The results were tabulated in Microsoft XP Excel spreadsheets. The data were entered twice on separate occasions, then compared, and corrected for any discrepancies before data analysis began. Any inconsistencies were highlighted and checked with the original data sheets. Once all the data had been collected, the details of which type of chemotherapeutic agents had been used for each subject were added to the identification code by the research supervisor. This was done blindly with regard to any results. The details were then added to the main data sheet according to their subject number. The data

analysis was largely descriptive, given the small sample size and large number of variables. Where appropriate, a chi-squared test and the Fisher's exact test were used to investigate the relationship between two specific variables. The Microsoft Excel programme (Microsoft Office XP) was used for the calculations.

Results

The medical diagnoses of the study group include: Wilm's tumour – 29 patients (24.2%), rhabdomyosarcoma – 10 patients (8.3%), Hodgkin's lymphoma – 14 patients (11.7%), non-Hodgkin's lymphoma – 10 patients (8.3%), neuroblastoma – 21 patients (17.5%), and other solid tumour types – 36 patients (30.0%).

The age range at examination was 1–17 years and the age range at diagnosis was 0–15 years. The number of patients receiving chemotherapy aged 0–4 years was 79 patients, aged 5–9 years was 20, and 10–15 was 21 patients. The range in the length of time patients received chemotherapy for was from 1 month to 4.5 years, the mean was 8.19 months (SD = 7.39) the median was 6 months.

There were four principal groups of chemotherapeutic agent used for the patients in the reported study. These were high-dose chemotherapy with stem-cell rescue (HDCSCR), anthracycline drugs, alkylating agents, and platinum drugs. There were however, overlapping regimes. The amount of time elapsed since completion of chemotherapy ranged from <1 year to 14 years. The mean period of time was 51.97 (SD = 40.3) months; the proportions are shown in Fig. 1. Sixty-six per cent of the study patients were from the West Midlands, and the remaining 34% from the surrounding areas. Seventy-three per cent were receiving a fluorinated water supply at the time of the study.

Experience of dental caries

Overall 67 (55.8%) patients in the study population were caries free with the remaining 53 (44.2%) having experienced obvious caries

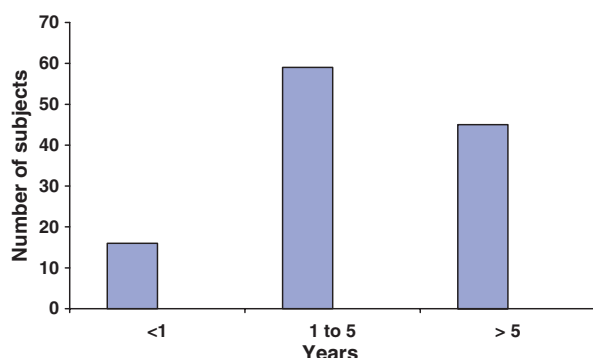


Fig. 1. Amount of time elapsed since completion of the chemotherapy to dental examination.

at the time of the dental examination. The mean DMFT of the study group was 0.56 (range: 0–7), the mean dmft of the study group was 0.84 (range: 0–9) indicating higher caries levels in the primary dentition. Figure 2 demonstrates that the 8-year-old study population had a higher dmft value by comparison with the CDHS 2003⁴. Table 2 compares the DMFT study data for 8, 12, and 15-year olds with the 2003 CDHS⁴. Despite there being low numbers in each group, the figures show the 8-year-old primary dentition data showing a higher dmft, and the 12- and 15-year-old study groups showing a lower DMFT. The percentage without obvious caries experience in the 12- and 15-year-old group is higher than the 2003 CDHS figures for the UK, England, and the West Midlands.

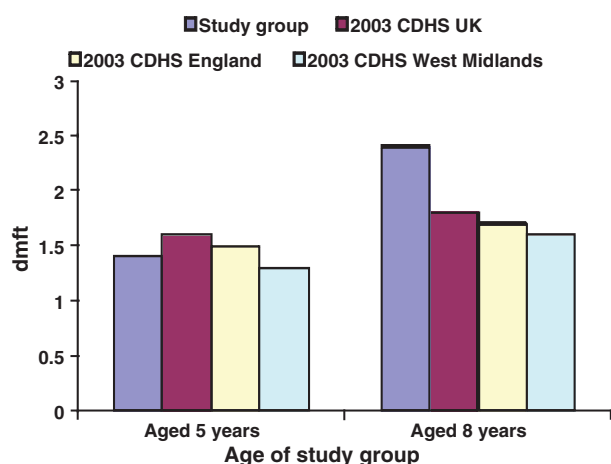


Fig. 2. Decayed missing filled primary teeth (dmft) values for patients who were 5 ($n = 9$) and 8-year old ($n = 5$) at the time of examination, within the study group by comparison with the 2003 Child Health Survey (2003 CDHS) data.

Table 2. Comparison of DMFT values and percentage without any obvious caries experience for 8-, 12- and 15-year olds within the study and compared with national data (2003 CDHS)⁴.

	Obvious caries experience (mean no. teeth)	Percentage without obvious caries experience (%)
8 year study group ($n = 5$)	0.2	80.0
8 year UK 2003	0.3	86.0
8 year England 2003	0.3	83.0
8 year West Midlands 2003	0.3	83.0
12 year study group ($n = 7$)	0.3	85.7
12 year UK 2003	1.1	66.0
12 year England 2003	1.0	59.0
12 year West Midlands 2003	0.9	61.0
15 year study group ($n = 11$)	2.0	72.7
15 year UK 2003	2.0	51.0
15 year England 2003	1.8	45.0
15 year West Midlands 2003	1.9	47.0

Dental caries experience of different treatment regime groups

Dental caries experience following stratification into medical chemotherapy treatment groups are represented in figure III. The HDCSCR group demonstrated considerably higher dmft values by comparison with the other groups. This group comprised patients suffering mainly from neuroblastoma who were young at diagnosis. The DMFT values are similar between the different treatment groups.

Dental caries experience by tumour diagnostic group

The neuroblastoma group had the highest decay experience in the primary dentition, as shown by the number of teeth affected. The neuroblastoma group had received more significant treatment with many being included in the HDCSCR treatment group (Fig. 3). The rhabdomyosarcoma group also showed an increased level of decay experience in the primary dentition. Figure 4 illustrates differences in DMFT and dmft values within the different groups, stratified by diagnosis.

Enamel opacities

Eighty patients had their dental enamel opacities recorded in the eight upper anterior teeth (upper right 4,3,2,1 and upper left

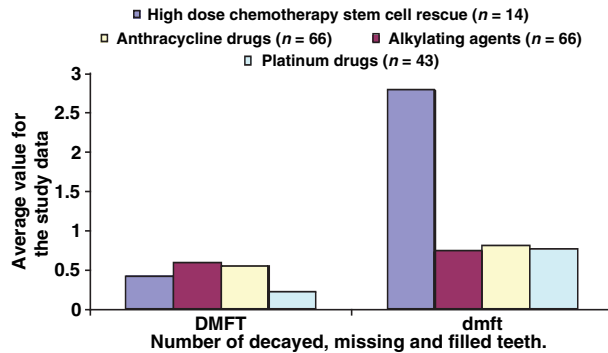


Fig. 3. Average decayed missing filled adult teeth (DMFT) & decayed missing filled primary teeth (dmft) values for each treatment group within the study.

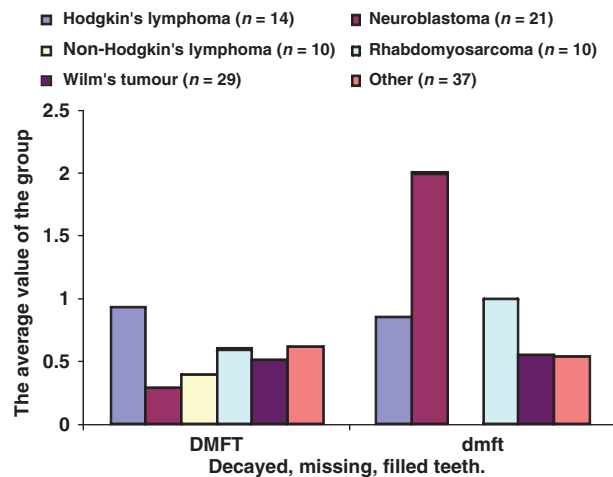


Fig. 4. Decayed missing filled adult teeth (DMFT) & decayed missing filled primary teeth (dmft) values of the different diagnostic groups within the study.

4,3,2,1). Opacities were found in 50 (62.5%) patients from the study group. In the CDHS, only 12-year-olds were examined for enamel opacities. Thirty-five per cent in England had one or more opacity¹⁰. As opacities are stable and do not change over time this figure can also be compared with all age groups within this study. The proportion of patients with opacities and the type of opacity within the study group are shown in Tables 3 and 4. There were symmetrical defects in 27 teeth on 13 (16.3%) patients. The data demonstrated more diffuse defects (52.5%) than demarcated defects (15%). Compared with the CDHS data where both categories show, 18% the study data showed more diffuse defects but slightly fewer demarcated defects. It is worth noting some patients demonstrated

Table 3. Proportion of patients with opacities and the type of opacity within the study group.

Opacity code	Opacity type	No. teeth with that opacity code	No. patients with that code (%) n = 80	CDHS 2003 England (%)
1	Demarcated	16	12 (15.0)	18
2	Diffuse	120	42 (52.5)	18
3	Hypoplasia	0	0 (0.0)	2
4	Demarcated and diffuse	4	3 (3.8)	3
5	Demarcated and hypoplasia	3	3 (3.8)	1
8	Other defects	2	1 (1.3)	1
9	No assessment made	4	1 (1.3)	0

Table 4. Extent of opacities within the study group.

Opacity extent code	Extent	No. teeth	No. patients n = 80 (%)
1	Less than 1/3	115	50 (62.5)
2	At least 1/3–2/3	23	15 (18.8)
3	At least 2/3	7	4 (5.0)
9	No assessment made	4	1 (1.3)

more than one type of opacity on their front teeth. No significant trends were identified within the data for both the tumour group and/or treatment groups.

Gingival health

The gingival health of the study population was similar to that of the general population. There were no obvious differences in gingival health within tumour diagnostic or treatment groups.

Microdontia

There were 26 microdont teeth present in nine patients from the study population. All these patients had received chemotherapy under the age of 3.5 years. Chi-squared analysis showed a significant ($P = 0.025$) relationship between the age at which chemotherapy was received and the presence of microdont teeth. Using Fisher's exact test to account for the small numbers the relationship was still found to be significant ($P = 0.027$).

The neuroblastoma and rhabdomyosarcoma groups demonstrated the largest number of patients affected with microdont teeth. The rhabdomyosarcoma group had 20% ($n = 10$) of patients affected and the neuroblastoma group 14.2% ($n = 21$) affected. Twenty per cent ($n = 14$) of the HDCSCR group were affected with microdont teeth. The most frequently affected teeth were upper (19.2%, $n = 26$) and lower (19.2%, $n = 26$) first premolars, followed by the upper second premolar (15.4%, $n = 26$).

Fissure sealants

The study population included 32 sealed permanent teeth in 11 patients (9%, $n = 120$). When the study data by age group is compared to the 2003 CDHS data for England and the UK, the study population was found to have a lower level of fissure sealants (Table 5). The study group did have a below average prevalence of fissure sealants.

Discussion

This series of 120 patients who had been treated for solid tumours and lymphoma in childhood represents one of the largest cohorts to undergo detailed investigation of oral health during follow-up. Patients were grouped into those who had received HDCSCR, alkylating agents, anthracyclines, and platinum drugs, as it was thought that these treatments would be more likely to affect the developing dentition. This investigation was performed as part of a research programme leading to an MPhil, and was a cross-sectional, observational study. The following points should be considered when interpreting the data: (i) sample size, although a large sample size was

employed there were too many variables to perform valid statistical analysis for most of the comparisons. Ideally, each diagnostic group would have been larger and the treatments standardized therefore limiting variables. A multi-centre approach would facilitate more robust conclusions and also allow comparisons between centres; (ii) Age- and gender-matched control groups with the same demographics would have been preferable to a national data set control group. By utilizing the CDHS data, the study groups became small, thus precluding definitive conclusions; (iii) where possible the conditions of examination matched those of the 2003 CDHS. Ideally the enamel opacities should have been observed under natural light. The pragmatic study design involved utilizing the only room available to the investigator. This room only had one small window and it was not therefore possible to match CDHS conditions for this particular aspect; (iv) formal calibration of the primary investigator and CDHS examiners. If this had been possible it would have improved the validity of the results. During the data collection period unfortunately, because of staff shortages no other dental examiners could be present at the time of the dental examination of the patients, and it was not practicable to bring the patients to a further appointment for a second examination by the primary investigator; and (v) the data of this study included the family's current address only. To draw conclusions regarding the enamel opacity data and the potential effect for the water supply, we would require the patients address from 0 to 3 years, as this would correspond to the time when the tooth was at its most vulnerable developmentally.

Overall 44.2% of the study group had experienced decay in one or more teeth, 18.3% had untreated primary decay, and 18.3% had untreated secondary decay. The figures for the level of untreated decay are similar for both the primary, and the permanent dentitions despite the recent debate in the literature over whether or not restoration of the primary dentition is necessary¹¹. The 2003 CDHS from 1983 to 2003 reports that the number of restorations being placed in

Table 5. Number of fissure sealants placed per age group.

Age	2003 CDHS England fissure sealed permanent teeth %	2003 CDHS UK fissure sealed permanent teeth %	Study data fissure sealed permanent teeth, n (%)
8	11	13	0 (0.0)
12	22	25	1 (14.3)
15	28	30	3 (27.3)

the primary dentition had declined in both 5- and 8-year olds, but the proportion of filled permanent teeth had increased from 1983 to 2003 in 8, 12, and 15-year olds⁴.

The groups showing a high-dental caries rate in the primary dentition included the HDCSCR group and the neuroblastoma group. These results are largely based on the same patients because all patients who received HDCSCR had a neuroblastoma except for one patient. Kaste *et al.*¹² reported an increased level of decay in the primary dentition in patients being treated for a neuroblastoma. The caries experience of the permanent teeth was the same as the general population; a finding consistent within this study. The increased decay rate in the primary dentition could be attributed to the high level of systemic upset resulting from the cancer therapy as neuroblastomas are usually experienced at a young age when the patient is in the primary dentition. The chemotherapy frequently results in the development of mucosal ulcerations and a sore mouth. During medical treatment, the calorific intake for these children is important and it is often difficult to achieve an adequate level, hence these patients are fed on high-calorie diets which, by their nature, are likely to be cariogenic. Also they are likely to be receiving more medical interventions with sweets often given as rewards thus contributing to a cariogenic diet. The chemotherapy during this period may also induce a xerostomia, altered salivary consistency, and disturbances in taste, and therefore perhaps contribute to an increase in susceptibility to dental caries during this time. Often in cancers of younger children, the treatment affects an age group where the primary teeth are present, and whom parental assistance is required to effectively brush their teeth. In this group, dental hygiene may be sub-optimal, especially in the presence of mucositis.

Apart from the neuroblastoma and HDCSCR groups, the study population actually showed a decreased caries experience compared with the general UK population. This finding is consistent with other groups of cancer patients and is supported by Alpaslan *et al.*¹³, Maguire *et al.*¹⁴, Nunn *et al.*¹⁵, and

Oguz *et al.*¹⁶ but unsupported by Purdell-Lewis *et al.*¹⁷ and Pajari *et al.*¹⁸.

The criteria used to assess opacities in the study population were as close as possible to the 2003 CDHS to allow direct comparisons but it is important to note the examination was not in natural light⁹. This index is based on the modified Defects of Dental Enamel (DDE) index¹⁹ but included symmetry of diffuse lesions.

Of the study group tested 62.5% (50, $n = 80$) had enamel opacities present, compared with 35% of the 2003 CDHS 12-year olds in England²⁰. Within this study, there were a large number of patients with diffuse defects [42 (52.5% $n = 80$)], when compared with the 16% in the 2003 CDHS national data. Looking between the different sub-groups, there were no significant differences between them. The study showed a large number of diffuse opacities to have been present in those patients currently living in a fluorinated area (38 patients in a fluorinated area compared with 12 patients with opacities not living in a fluorinated area); a known cause of opacities that could be related to the effects of fluorination as opposed to chemotherapy. Moreover, it is difficult to draw any firm conclusions from these data, because analysis was carried out using the present address, and does not take into account the fact that the people may have moved in and out of the area.

Many studies in the literature report that cancer patients to have a higher incidence of enamel opacities and hypoplasias. Nunn *et al.*¹⁵, another study carried out in a known fluorinated area showed an increase in hypoplasias in the study group but all other enamel defects, were not found to be significantly different to the sibling group. Pajari *et al.*¹⁸ and Alpaslan *et al.*¹³ both showed a statistically significant difference in the level of opacities experienced in the cancer groups. Given the number of different indices described it is difficult to draw conclusions about enamel opacities. But, many of the studies mention enamel opacities as a significant finding within study populations. The cause of enamel opacities and hypoplasias has been attributed to many different factors, one of which could be chemotherapy. Other

factors include fluoride, spikes of temperature during fever, and infections, nutritional deficiencies, and trauma²¹.

The gingival health of the study group when compared to the 2003 national data was similar. Many other studies in the literature report to have found no difference in gingivitis, and the oral hygiene levels of test and control groups^{13,14}.

Microdontia was found in nine of the study group patients. The most significant factor noted regarding microdont teeth, was that all patients who had a microdont tooth within the study population had received chemotherapy before the age of 3.5 years, $P = 0.03$. Maguire *et al.*¹⁴ assessed the level of microdontia, and found that within the solid tumour group 16.2% ($n = 37$) had microdontia in the upper arch, and 2.7% ($n = 37$) in the lower arch. It is interesting to note that as with this study population, all children presenting with microdont teeth in the Maguire study also received their chemotherapy treatment under the age of 3.5 years¹⁴.

The highest percentage of microdont teeth in the study data were found in the HDCSCR group (20%). This finding would be consistent with the type of medical treatment, as it is more likely to affect the developing germ cells in the developing dentition. Because there is no current validated index classifying what a microdont tooth is, it is difficult to draw definitive conclusions and comparisons between studies. There are no epidemiological studies assessing microdontia in the UK population, but the research by Hölttä *et al.*²² describes the Japanese population as having a prevalence of 1.9% microdontia, and Hawaiian population prevalence to be higher at 3.1%.

The most recent study investigating microdont teeth in this field is by Hölttä *et al.*²². They found microdontia in 44% of the study population against 2% in the control group. They found the most commonly affected teeth to be first premolars (46%) followed by second premolars (26%) and second molars (23%)²². These results are consistent with the findings of this study population in that the first premolar (38.5%) was the most commonly affected tooth.

From this data, only limited observations can be drawn because of the small sample size. Microdontia and the presumed association with chemotherapy is well supported by several studies^{12,14,16}.

Fissure sealants have been shown to protect the occlusal surfaces of teeth against caries²³. A recent Cochrane review investigating the use of fissure sealants concluded fissure sealants are a recommended method of preventing occlusal caries in molar teeth. Moreover, the application of sealants should be based on the prevalence of caries in the individual and the local population²⁴. The level of fissure sealants in the study population is low by comparison with national data. Nine per cent of the study population had fissure sealants compared with 13–15% of 8-, 12-, and 15-year olds in the 2003 CDHS. This is possibly due to the fact that the caries rate is lower in the West Midlands, and some dentists feel the need for fissure sealants in the Midlands area is reduced by comparison with elsewhere in the UK. But, what was concerning was that none of the patients in the neuroblastoma group, and only one subject in the HDCSCR group had received fissure sealants, when these are the two groups that would benefit most from such a preventative technique.

What this paper adds

- The oral health needs of individual groups of solid tumour oncology patients differ according to the type of tumour and treatment regime.
- The neuroblastoma, rhabdomyosarcoma patient groups, and those patients receiving high-dose chemotherapy with stem-cell rescue require a greater dental input with more emphasis on prevention techniques, such as fissure sealants, oral healthcare regimes, and long-term dental follow-up to address the likely dental anomalies arising.
- Children receiving chemotherapy under the ages of 3.5 years appear more likely to have one or more microdont teeth in the adult dentition by comparison with those who are older when they receive their chemotherapy.

Why this paper is important to paediatric dentists

- Paediatric dentists are often involved, upon diagnosis during and after the care of patients who have solid tumours and lymphomas.
- It is important to understand their specific oral healthcare needs and know the long-term outcomes of their medical treatment.

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